# PSYKIATRIENS Forskningsdag

# Program og abstracts



## 2. november 2022 kl. 12.00 – 16.00

Auditorium G206-145 Aarhus Universitetshospital Palle Juul-Jensens Boulevard 99 8200 Aarhus N





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- kl. 12.00-12.30 Posterudstilling med sandwich
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- Kl. 12.35-12.40 Tale v. hospitalsdirektør Tina Ebler
- kl. 12.40-13.40 Oplæg: Moderator, professor Søren Dinesen Østergaard
- kl. 12.40-12.55 Kazi Ishtiak-Ahmed, Afdeling for Depression og Angst (ADA), AUHP
  "Patterns and associated user characteristics of antidepressant prescriptions in older adults: A nationwide descriptive cohort study in Denmark"
- **KI. 12.55-13.10** Malene Overby, Clinical Medicine, Translational neuropsychiatry unit (TNU), AUHP "Regulation of Sortilin cleavage through a novel switch with relevance to depressive symptoms in dementia"
- Kl. 13.10-13.25 Katherine Musliner, Afdeling for Depression og Angst (ADA), AUHP
  "Do polygenic risk scores improve our ability to predict recurrence in patients with bipolar disorder?"
- Kl. 13.25-13.40 Sabine Jansson, Børne- og Ungdomspsykiatrisk Afdeling (BUA), AUHP
  "Psychiatric disorders in pediatric-onset immune-mediated inflammatory diseases- a nationwide Danish study"
- Kl. 13.40-14.30 Pause, Posterudstilling med kaffe/te og kage
- Kl. 14.30-15.30 Oplæg: Moderator: professor Gregers Wegner
- Kl. 14.30-14.45 Anna Lee Waszkiewicz, Translational Neuropsychiatry Unit (TNU), AUHP
  "S-Ketamine acutely increases hippocampal synaptic vesicle glycoprotein 2A density in Flinders Sensitive Line rats"
- Kl. 14.45-15.00 Nicolai Ladegaard, Afdeling for Depression og Angst (ADA), AUHP "Development and validity of the Aarhus Structured Clinical Interview for ICD-11 and DSM-5-TR Prolonged Grief Disorder (PGD-SCI)"
- Kl. 15.00-15.15 Christopher Rohde, Afdeling for Depression og Angst (ADA), AUHP
  "Risk factors associated with mortality among individuals with type 2 diabetes and depression across two cohorts"
- KI. 15.15-15.30 Arndis Simonsen, Afdeling for Psykoser (P), AUHP
  "Investigating the relationship between parent and child cognition in parents with schizophrenia or bipolar disorder and their 7-year-old offspring"
- Kl. 15.30-16.00 Afslutning med prisoverrækkelse for bedste foredrag og bedste poster v. professor Per Hove Thomsen



#### Abstracts – foredrag

Patterns and associated user characteristics of antidepressant prescriptions in older adults: A nationwide descriptive cohort study in Denmark

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Regulation of Sortilin cleavage through a novel switch with relevance to depressive symptoms in dementia

#### Malene Overby<sup>1</sup>, Postdoc Clinical Medicine, Translational neuropsychiatry unit

Co-authors Ann Kathrine Christiansen<sup>1</sup>, Jason P. Weick<sup>2</sup> and Heidi K. Müller<sup>1</sup>

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Alzheimer's disease (AD) and other forms of dementia are among the most common causes of disability in the elderly. Dementia is often accompanied by depression, especially during the early and middle stages. In the early stages of dementia and during diagnosis, depressive symptoms are often treated before dementia itself.

We hypothesize that the depressive symptoms might be the early stages of an imbalanced sortilinmediated mechanism that later causes dementia. Sortilin is a multitasking protein that mediates endocytosis of immature and mature forms of neurotrophins, in particular, Brain-Derived Neurotrophic Factor (BDNF) which is involved in depression and AD. Reduced levels of BDNF have been found in AD patients and depressed patients. In some AD cases, it correlates with the severity of the disease.

We have established two novel binding partners to sortilin neuronal-specific gene 1 (NSG1) and neuronal-specific gene 2 (NSG2) that play a role in the regulation of sortilin. Sortilin is a transmembrane protein that acts as a receptor in its full-length form but is also cleaved by Metalloproteases, generating a soluble form that can act as a decoy molecule. An increase in soluble sortilin has been found in depressed patients and increased fragments of sortilin have been found and correlated with different stages of AD. An imbalance in this cleavage process can therefore potentially affect the BDNF levels.

We found that NSG1 associates with sortilin making sortilin more susceptible to cleavage and thereby generating more soluble sortilin. In contrast, the related protein NSG2 which also associates with sortilin protects sortilin from cleavage. Our data clearly illustrates divergent functions of NSG1 and NGS2 in the regulation of sortilin cleavage. These data suggest that balancing NSG1 and NSG2 expression levels or activity could be important for normal sortilin function.

Future research will investigate NSG1 and NSG2 effects on BDNF levels through sortilin-mediated processes. The expression levels of NSG1 and NSG2 in the brains of dementia patients as well as serum levels of soluble sortilin in early stages of AD patients with depressive symptoms will be investigated.

Consequently, this finding holds the potential to develop an innovative strategy for neuron-specific sortilin regulation, which can affect AD and the early stages of depressive symptoms.



Do polygenic risk scores improve our ability to predict recurrent hospital admission in patients with bipolar disorder?

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#### Background

Polygenic risk scores (PRS) are of great interest to the scientific community, however their utility as diagnostic or decision aids in clinical settings has yet to be proven. Our goal was to test if PRS can improve prediction of recurrence in patients with bipolar disorder beyond what is achievable through non-genetic risk factors alone.

#### Methods

Data were obtained from the iPSYCH2015 cohort, which includes all individuals diagnosed with bipolar disorder (ICD-10 codes F30-31, F38.00) in Danish psychiatric hospitals from 1995-2015. Our sample included 2,989 patients (64% female). We defined recurrence as a subsequent contact for bipolar disorder starting at least 8 weeks after the first contact. Potential predictors included demographic (e.g. gender), clinical (e.g. polarity), and socio-economic characteristics as well as family history of psychiatric disorders. PRS for bipolar disorder, major depression, schizophrenia, and ADHD were created using a metaPRS method. Prediction models were developed using flexible parametric survival analysis. Patients were followed from the end date of their first bipolar contact to the start of their second contact, death, emigration, or December 31, 2016, whichever came first.

#### Results

947 (32%) of patients experienced ≥1 recurrent contact(s). The following predictors were selected in the multivariable model: gender (Hazard Ratio=1.20, 95% Confidence Intervals=1.04-1.38); polarity (depressive [1.58, 1.28-1.95], mixed [1.35, 1.04-1.75], other [1.36, 1.02-1.82], unspecified [1.37, 1.11-1.69]); psychotic symptoms (1.53, 1.19-1.98), substance abuse disorders (1.26, 1.05-1.51), inpatient (1.53, 1.30-1.79) and emergency (0.74, 0.57-0.96) treatment settings, prior antipsychotic prescription (1.29, 1.11-1.49), family history of depression (1.20, 1.04-1.37), and 1st month treatment duration (1.05, 1.01-1.09). PRS for bipolar disorder was significant in the univariable model (1.07, 1.01-1.05) but not the multivariable model (HR=1.04, 0.96-1.13). Comparison of model performance measures show that the model including PRS did not differ significantly from the model without PRS.

#### Conclusion

Our results suggest that including PRS does not improve our ability to predict recurrence in patients with bipolar disorder. Future studies should investigate whether PRS can help predict other outcomes in patients with psychiatric disorders.



Psychiatric disorders in pediatric-onset immune-mediated inflammatory diseases - a nationwide Danish study

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#### Co-authors

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#### Background

Anxiety and depression are well known among patients with pediatric-onset immune-mediated inflammatory diseases (pIMID). However, data on a wider spectrum of psychiatric disorders are scarce.

#### Methods

In this nation-wide study from 1996-2018, we investigated psychiatric disorders in patients with pediatric-onset inflammatory bowel diseases, autoimmune liver diseases, and rheumatic diseases, using Danish national health care and population registers. Each case was matched with up to 10 controls from the background population. A cumulative incidence for psychiatric disorders prior to pIMID onset was calculated and compared with that for controls. We used cox proportional regression to estimate adjusted hazard ratios (aHR) with a 95% confidence interval (CI) between cases and controls without psychiatric disorders prior to the index date (ID).

#### Results

We included 11,208 cases (57% female) and 98,387 controls. The median age at disease onset was 12.5 years (interquartile range: 8-15) and follow-up time 9.8 years (interquartile range: 5-15). We found an association between psychiatric disorders before ID and a diagnosis of subsequent pIMID (odds ratio: 1.3, 95%CI: 1.2-1.4). After ID, cases had an increased risk (aHR: 1.6, 95%CI:1.5-1.7) of psychiatric disorders compared to controls. The risk was increased for neurodevelopmental-, psychotic-, emotional-, and other disorders. Female patients had an increased risk of suicide attempt (aHR:1.4, 95%CI: 1.1-1.8).

#### Conclusion

Both before and after receiving a pIMID diagnosis, patients with pIMID had an increased risk of psychiatric disorders. Our results strongly underscore the importance of being attentive to not only somatic but also psychiatric problems in this patient group.



# S-Ketamine acutely increases hippocampal synaptic vesicle glycoprotein 2A density in Flinders Sensitive Line rats

#### Anna Lee Waszkiewicz<sup>1,2</sup>, Research Year student Translational Neuropsychiatry Unit

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Up to 30% of patients with depression face inadequate treatment. Classically available pharmaceuticals can take 3-6 weeks to reach full effect. Aiming to bridge this gap, S-ketamine is used in patients with treatment-resistant depression, as a fast-acting agent. Ketamine is a synaptic modulator, inducing synaptic plasticity in certain regions of the brain, which is hypothesized to be part of its mechanism of antidepressant action. To investigate this, we treated 8 Flinders Sensitive Line (FSL) rats, considered a genetic model of depression, with an intraperitoneal injection of 15 mg/kg of S-Ketamine and compared them to 6 saline-injected FSL rats. We then performed autoradiography on selected regions of brains removed 1-hour post-injection. Fresh frozen brain sections were processed using [3H]-UCB-J, a radioligand of synaptic vesicle glycoprotein 2A, considered a biomarker of pre-synaptic density. We found significantly higher [3H]-UCB-J binding in ventral (22% increase, p=0,01) and dorsal hippocampus (13% increase, p=0,05) of ketamine-injected FSL rats compared to the saline group. No significant increases were found in the remaining areas. These findings suggest ketamine's effect to be based in synaptic modulation of the hippocampus. We suggest further investigation at different time points and with left-right discrimination. We are currently investigating the effects of ketamine on post-synaptic density using a ligand of metabotropic glutamate receptor 5.



#### Development and validity of the Aarhus Structured Clinical Interview for ICD-11 and DSM-5-TR Prolonged Grief Disorder (PGD-SCI)

#### Nicolai Ladegaard Department of Affective Disorders

#### **Background and rationale**

Prolonged Grief Disorder (PGD) is a newly established diagnosis in ICD-11 and DSM-5-TR that captures disordered grief and is currently being implemented worldwide [1, 2]. A reliable, valid, and easy-to-use diagnostic interview for PGD is therefore needed [3]. The aim of this study is to develop, test, and validate the Aarhus Structured Clinical Interview for Prolonged Grief Disorder (PGD-SCI).

#### Design

PGD-SCI was developed from ICD-11 and DSM-5-TR PGD criteria through a rigorous process involving clinicians, focus groups of bereaved adults, pilot testing, and thorough clinical supervision. The interview was then tested in a sample of approximately 124 bereaved adults who completed diagnostic interviews and self-report scales for PGD, depression, PTSD, and generalized anxiety (GAD). A total of 51 bereaved adults were retested after 1 to 2 weeks.

#### **Results:**

- The test-retest stability is moderate for ICD 11 and substantial for DSM 5
- The inter-diagnostic stability between ICD 11 and DSM 5 Tr is moderately stable at T1 and substantial at T2
- DSM 5 Tr PGD criteria may be more stable and thus more reliable than ICD 11 PGD
- The Aarhus PGD interview is a valid and reliable structured clinical interview that captures PGD DSM 5 Tr and in part ICD 11 PGD

#### **References:**

- Lenferink, L.I.M., et al., Valid measurement of DSM-5 persistent complex bereavement disorder and DSM-5-TR and ICD-11 prolonged grief disorder: The Traumatic Grief Inventory-Self Report Plus (TGI-SR+). Comprehensive Psychiatry, 2022. 112: p. 152281.
- WHO, ICD-11: Prolonged Grief Disorder2021, World Health Organisation: https://icd.who.int/dev11/lm/en#/http%3a%2f%2fid.who.int%2ficd%2fentity%2f1183832314.
- O'Connor, M., et al., Valid ICD-11 PGD Scales and Structured Clinical Interviews Needed. Frontiers in Psychology, 2020. 11(1120).



# Risk factors associated with mortality among individuals with type 2 diabetes and depression across two cohorts

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#### Introduction

Depression has been linked to excess mortality in individuals with type 2 diabetes, but it remains unclear what drives this association. We examined if the association depends on unhealthy lifestyle and medical comorbidity.

#### Methods

We followed a clinically recruited cohort of Danish people with type 2 diabetes (n=8,175) with finegrained clinical information and a population-wide register-based cohort of Danish individuals with HbA1c-defined type 2 diabetes (n=87,500) representing everyday clinical practice. Antidepressant drug use prior to the onset of type 2 diabetes was used as a proxy for preexisting depression. In both cohorts, we first estimated the association between depression and five-year mortality following type 2 diabetes, using a Cox proportional-hazards model, yielding sex- and age-adjusted mortality rate ratios (MRRs). We subsequently examined how further adjustment for markers of unhealthy lifestyle (smoking, physical inactivity, obesity, alcohol abuse, marital status), and medical comorbidity affected the association.

#### Results

Preexisting depression was associated with an approximately 50% increased age- and sex-adjusted all-cause mortality rate in both the clinically recruited- (5-year MRR: 1.46; 95%CI: 1.12-1.90) and the register-based type 2 diabetes cohort (5-year MRR: 1.51; 95%CI: 1.45-1.57). The excess mortality associated with depression almost disappeared when the analyses were adjusted for unhealthy lifestyle and medical comorbidity in both the clinically recruited- (MRR: 1.05; 95%CI: 0.72-1.52) and the register-based type 2 diabetes cohort (MRR: 1.14, 95%CI: 1.09-1.19).

#### Conclusion

A large fraction of the excess mortality associated with preexisting depression in type 2 diabetes is attributable to the unhealthy lifestyle and medical comorbidity accompanying depression.



Investigating the relationship between parent and child cognition in parents with schizophrenia or bipolar disorder and their 7-year-old offspring

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#### Posteroversigt

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2	Ellen	Bjerre-Nielsen	Novel experimental approach to explore cognitive biases in young people with functional gastrointestinal disorders: A first test on healthy children and young adolescents
3	Matti	Bock Guldager	The role of the dorsal raphe nuclei in the antidepressant-like effects of cannabidiol
4	Ana Lisa	Carmo	The relationship between sexual dysfunction and symptoms and psychotropic side effects among individuals with schizophrenia
5	Caroline	Cristiano Real Gregório	Title: Acute auricular vagus nerve stimulation decreases glucose metabolism measured by 18F-FDG PET uptake in subcortical rat brain
6	Charlotte Steen	Duholm	Specific contamination symptoms are associated with experiencing a limited response of cognitive behavioral therapy in pediatric patients with OCD
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11	David R.m.a.	Højgaard	Exploring Latent Clusters in Pediatric OCD based on Symptoms, Severity, Age, Gender, and Comorbidity
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13	Sabine	Jansson	Psychiatric disorders in pediatric-onset immune-mediated infammatory diseases- a nationwide Danish study
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			glycoprotein 2A density in Flinders Sensitive Line rats



#### Abstracts – posters

#### Poster nr. 1

Stability of diagnostic coding of psychiatric outpatient visits across the transition from the second to the third version of the Danish National Patient Registry

#### Martin Bernstorff<sup>1,2</sup>, MD, PhD-student Department for Affective Disorders, Aarhus University Hospital–Psychiatry,Aarhus, Denmark

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#### Background

In Denmark, data on hospital contacts are reported to the Danish National Patient Registry (DNPR). The ICD-10 main diagnoses from the DNPR are often used as proxies for mental disorders in psychiatric research. With the transition from the second version of the DNPR (DNPR2) to the third (DNPR3) in February–March 2019, the way main diagnoses are coded in relation to outpatient treatment changed substantially. Specifically, in the DNPR2, each outpatient treatment course was labelled with only one main diagnosis. In the DNPR3, however, each visit during an outpatient treatment course is labelled with a main diagnosis. We assessed whether this change led to a break in the diagnostic time-series represented by the DNPR, which would pose a threat to the research relying on this source.

#### Methods

All main diagnoses from outpatients attending the Psychiatric Services of the Central Denmark Region from 2013 to 2021 (n = 100,501 unique patients) were included in the analyses. The stability of the DNPR diagnostic time-series at the ICD-10 subchapter level was examined by comparing means across the transition from the DNPR2 to the DNPR3.

#### Results

While the proportion of psychiatric outpatients with diagnoses from some ICD-10 subchapters changed statistically significantly from the DNPR2 to the DNPR3, the changes were small in absolute terms (e.g., +0.6% for F2—psychotic disorders and +0.6% for F3—mood disorders).

#### Conclusion

The change from the DNPR2 to the DNPR3 is unlikely to pose a substantial threat to the validity of most psychiatric research at the diagnostic subchapter level.



Novel experimental approach to explore cognitive biases in young people with functional gastrointestinal disorders: A first test on healthy children and young adolescents

#### Ellen Bjerre-Nielsen<sup>1</sup>, Research year student Research Unit, Department of Child and Adolescent Psychiatry

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Cognitive biases are distorted perceptions in attention, interpretation and memory of specific stimuli. The interplay of such biases regarding bodily symptoms are suggested to be crucial in the development and maintenance of functional disorders in adults and thereby important targets for psychological interventions. In contrast, similar research on children and adolescents with functional disorders are still limited. We recently developed a novel experimental approach to assess possible cognitive biases in children and adolescents with a functional gastrointestinal disorder (FGID). In the current project we apply this method in healthy children and adolescents to explore their cognitive reactions to FGID-related stimuli. This will both provide us with unique data on potential sex and age-related differences regarding reactions to such stimuli but also serve as comparison material in a larger research project exploring and potentially targeting cognitive biases during treatment in children and adolescents with FGID.



#### The role of the dorsal raphe nuclei in the antidepressant-like effects of cannabidiol

#### Matti Bock Guldager<sup>1</sup>, Research Year Student Department of Biomedicine, Aarhus University, Translational Neuropsychiatry Unit

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Currently available antidepressants have a substantial time lag to induce a therapeutic response and a relatively low efficacy. The development of drugs that address these limitations is critical to improving public health. Cannabidiol (CBD), a non-psychotomimetic component of Cannabis sativa, is a promising compound, since it shows large-spectrum therapeutic potential in preclinical models and in humans. We recently showed that CBD induces rapid antidepressant-like effects in rodents, similarly to ketamine. Although the effects of both drugs seem to involve the modulation of the serotonergic neurotransmission, it is not clear how they differ from conventional drugs (i.e., selective serotonin reuptake inhibitors, SSRIs). Therefore, this study aims at investigating: i) how CBD and ketamine (in comparison to an SSRI, citalopram) regulate the activation of the dorsal raphe nuclei (DRN), the main source of serotonergic neurons to the forebrain in the Flinders Sensitive/Resistant Line animals (FSL/FRL), a genetic model of depression; and ii) whether manipulation of the serotonergic pathways arising from the DRN can interfere with the behavioural and neuroplastic effects induced by CBD and ketamine. First, an immunofluorescence assay will be used to investigate the neurocircuitry activated in the DRN of FSL/FRL rats in response to stress and treatment. Next, a pharmacological and a genetic approach (DREADD) will be used to manipulate serotonergic pathways to depict their involvement in CBD/ketamine effects. Briefly, the DREADD method consists of introducing the gene of a specially designed inhibitory receptor to the subgroup of serotonergic neurons of the DRN projecting to the mPFC using a viral vector. The special receptor is then expressed by these neurons and exclusively activated by the exogenous ligand CNO. By injecting CNO, it is then possible to selectively inhibit this subpopulation of serotonergic neurons, which will help to determine whether these neurons are a necessary part of the neurocircuitry through which CBD exerts its antidepressant-like effects. This investigation can potentially contribute to the advancement of our understanding of the molecular and behavioural effects induced by CBD, especially as a promising new fast-acting antidepressant drug.



The relationship between sexual dysfunction and symptoms and psychotropic side effects among individuals with schizophrenia

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#### Background

Adverse sexual effects such as decreased libido, orgasmic dysfunction, and sexual arousal difficulties often accompany schizophrenia and are associated with reduced quality of life, which may contribute to reduced treatment adherence. Sexual dysfunction can be due to both the mental disorder itself (e.g. delusions with sexual content) and the use of psychotropic medications (e.g. prolactin-raising antipsychotics). Unfortunately, sexual dysfunction is under-recognized by clinicians and scarcely investigated in clinical trials.

The aim of the study is to examine the relationships between sexual dysfunction and i) positive and negative symptoms and ii) side effects to psychotropic medications among individuals with schizophrenia.

#### Methods

A total of 100 participants will be recruited from the psychiatric outpatient clinics and bed units in the Central Denmark Region. Participants will be at least 18 years old, meet the ICD-10 diagnostic criteria for schizophrenia (F20.x), understand written and spoken Danish, and provide written informed consent. Patients will be ineligible to participate if they are subjected to coercive treatment measures, have an organic mental disorder or mental retardation or are under the influence of any substances of abuse. Participants will complete the Patient-Reported Outcomes Measurement Information System Sexual Function and Satisfaction Measure, the 5-item World Health Organization Well-being Index, the Aarhus Side effect Assessment Questionnaire, and the Trauma History Questionnaire. Subsequently, a trained clinician will interview and rate participants on the 6-item Positive And Negative Syndrome Scale and the Udvalg for Kliniske Undersøgelser psychotropic side effect scale. Finally, the temporal relationships between reported adverse sexual effects and symptoms and psychotropic side effects will be evaluated by means of a semi-structured interview.

#### **Results and conclusion**

The study is ongoing.



Acute auricular vagus nerve stimulation decreases glucose metabolism measured by 18F-FDG PET uptake in subcortical rat brain

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Specific contamination symptoms are associated with experiencing a limited response of cognitive behavioral therapy in pediatric patients with OCD

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First-line treatment for pediatric OCD is cognitive-behavioral therapy (CBT). A recent study identified three distinct OCD treatment-response trajectories during and after treatment in a large group of children and found that higher levels of contamination symptoms predicted being a limited responder to CBT. This study is an extension of this, examining what characterizes a group of limited responders to CBT regarding contamination symptoms from baseline to 3-year follow-up. The study sample comprised 269 patients with OCD, aged 7-17 years, from Sweden, Norway and Denmark. Children's Yale-Brown Obsessive-Compulsive Scale was used to assess OCD symptoms and severity. All participants received stepped-care treatment with 14 weekly sessions of manualized CBT. Nonresponders to CBT were randomized to further treatment with CBT or selective serotonin reuptake inhibitors. Differences in the sum of contamination symptoms and differences in single itemreporting between the three groups was examined using linear mixed-effect modeling. Limited responders were characterized by a higher symptom load across all OCD symptom categories at 3year follow-up, dominated by contamination symptoms. A significantly smaller reduction of the sum of contamination items from baseline to 3-year follow-up between the limited responders and the other groups was found. In the limited responders group, five out of 16 contamination items showed persistence from baseline to 3-year follow-up: 1) Obsessions about dirt and germs, 2) Obsessions about bodily waste or secretions, 3) No concern about contamination other than how it might feel, 4) Handwashing compulsions and 5) Ritualized showering, toothbrushing, grooming. The results indicate that specific contamination symptoms may play an important role for a certain group of young patients with OCD and their response to CBT.



Family involvement and patient-experienced improvement and satisfaction with care: a nationwide cross-sectional study in Danish psychiatric hospitals

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#### Introduction

Randomized controlled trials suggest that family therapy has a positive effect on the course of depression, schizophrenia and anorexia nervosa.(1-3) Furthermore, emerging evidence suggests that higher levels of positive patient experiences are associated with more favorable health outcomes but research is scarce regarding the value of using patient reported experience measures (PREM) in psychiatric care.(4, 5) To the best of our knowledge, no prior studies have assessed whether caregivers' perception of involvement is associated with patient-experienced improvement and satisfaction with care.(5)

#### Aim

The study's objective is to examine whether caregiver-reported involvement is associated with PREM regarding patient improvement and overall satisfaction with care in everyday psychiatric hospital care.

#### Method

Using 2018 data from the annual National Survey of Psychiatric Patient Experiences, we conducted a nationwide cross-sectional study in Danish psychiatric hospitals including patients and their caregivers who had been in contact with the hospital. Patients were included in the National Survey of Psychiatric Patient Experiences if they had at least two outpatient contacts preceding an outpatient contact during week 36 – 38 (outpatient care), and if hospital discharge was planned during week 36 – 45 (inpatient care). Furthermore, based on a clinical judgement by the mental health professionals caring for the patients, patients were excluded if they were unable to participate in the survey because of (1) severe psychosis, (2) severe dementia, (3) moderate to severe mental retardation, (4) being moribund, or (5) being acutely transferred to a somatic hospital. A unique patient identifier on two distinct questionnaires for the patient and his/her caregiver enabled unambiguous linkage of data. Five aspects of caregiver involvement were analysed in relation to the two aspects of PREM using logistic regression with adjustment for patient age, gender and diagnosis.

#### Results

The study includes 940 patients and 1,008 caregivers because 55 outpatients and 13 inpatients had two responding caregivers. A high proportion of caregivers reports low or none involvement in patient care ranging from 20.4% (outpatients) for the item 'Is it your impression that the staff supports the patient in having contact with their caregivers?' to 72.2% (inpatients) for the item 'Do you talk to the staff about your expectations for the hospital contact?'. We consistently find that high caregiver-reported involvement is associated with high patient-reported improvement and



overall satisfaction with care with odds ratios (OR) ranging from 1.69 (95 % confidence interval (CI) 0.95-2.99) to 4.09 (95 % CI 2.48-6.76). This applies to the following aspects of caregiver involvement: support for the patient-caregiver relationship, caregiver information, considering caregiver experiences and involving caregivers in decision making. No statistically significant association is observed regarding whether caregivers' talk to the staff about their expectations for the hospital contact.

#### Conclusion

This nationwide study implies that caregiver involvement focusing on the patient-caregiver relationship is positively associated with patient improvement and overall satisfaction with care in everyday psychiatric hospital care.

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Lexical Stability of Psychiatric Clinical Notes from Electronic Health Records over a Decade

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#### Background

Natural Language Processing methods hold promise for improving clinical prediction by utilising information otherwise hidden in the clinical notes of electronic health records. However, clinical practice—as well as the systems and databases in which clinical notes are recorded and stored— change over time. As a consequence, the content of clinical notes may also change over time, which could degrade the performance of prediction models. Despite its importance, the stability of clinical notes over time has rarely been tested.

#### Methods

The lexical stability of clinical notes from the Psychiatric Services of the Central Denmark Region in the period from January 1, 2011, to November 22, 2021 (a total of 14,811,551 clinical notes describing 129,570 patients) was assessed by quantifying sentence length, readability, syntactic complexity and clinical content. Changepoint detection models were used to estimate potential changes in these metrics.

#### Results

We find lexical stability of the clinical notes over time, with minor deviations during the COVID-19 pandemic. Out of 2988 datapoints, 17 possible changepoints were detected. The majority of these were related to the discontinuation of a specific note type.

#### Conclusions

We find lexical and syntactic stability over time, which bodes well for the use of Natural Language Processing for predictive modelling in clinical practice.



#### Bells mania at an age of 76

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#### Background

76-year-old male, living alone as a disability pensioner was committed to hospital, with suspicion of a potentially lethal somatic disease. A history of sudden aggressive behaviour with both verbal and physical threats as well as confusion, started approx. 2 months prior to hospitalisation. Normally he was known as a kind person, with no previous contact to the mental institution and no abuse. The patient underwent a thorough somatic examination including, various blood samples, examination of the urine, lumbar puncture regarding infections and potential bleeding and CT scanning of the head. Nothing was found. The patient was committed to the mental institution. In the first days of observation, the patient condition was described as delirium. Further somatic examination was conducted such as MR-cerebrum, blood samples of syphilis and HIV, ex-ray of the chest and an exhaustive neurological examination. All without pathological findings. Consequently 15 mg of olanzapine was prescribed. Within 1-2 weeks, the patient showed classical signs of mania. Further 3 weeks of treatment was needed before the patient obtained a neutral mood and was discharged.

#### Results

Delirium mania often known as "Bells mania" is a well described syndrome[1]. It's dated back as long as 1849[2]. However, nor ICD or DSM consider this syndrome as a solitary disease and diagnosis. However, the awareness of this syndrome is extremely relevant. Although the syndrome is extremely rare, it may not be forgotten. As the population of old people grow, the incidence of bells mania will increase. Furthermore, bells mania is often coexisting with other highly deadly syndromes and deceases as malignant neuroleptic[1] syndrome, delirium over at prolonged period and late diagnosed mania in old people[3].

#### Conclusion

Despite delirium preceding debut of mania is well described in the literature neither ICD or DSM describes it as a isolated diagnosis. Early diagnosing of this decease may both reduce morbidity and mortality. Although the patient in this case was well examined for at somatic decease, the literature describes sudden emerging of fx neuroleptic syndrome[1]. Furthermore, prolonged condition of mania and delirium is letha[4]I. Therefor detection of the disease in an early stage is essential.

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Treatment of postpartum psychotic- and mood disorder requiring admission: A nationwide study from Denmark

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Exploring Latent Clusters in Pediatric OCD based on Symptoms, Severity, Age, Gender, and Comorbidity

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#### Background

Obsessive compulsive disorder (OCD) has a diverse symptom expression as well as a high comorbidity rate, with around 70% of patients having one or more comorbid disorders. This study aims to explore the underlying commonalities among OCD-affected children and adolescents in order to better conceptualize disorder presentation.

#### Methods

The data used in this study was aggregated from seven international pediatric OCD programs and includes a total of 830 child and adolescent cases. The sample was 54% female and 5-19 years of age. The Children's Yale-Brown Obsessive-Compulsive Scale (CY-BOCS) was used to assess OCD severity and symptom type, and comorbid diagnoses were assessed via diagnostic interviews. Dependent mixture modeling was used to examine latent clusters based on their age- and gender adjusted symptom severity, symptom type and comorbid diagnoses.

#### Results

The mixture modeling resulted in a four-cluster model where groups were distinguished primarily by symptom expression and type of comorbidity. Although fit indices for the 3-7 cluster solutions were



only marginally different, the characteristics of clusters remained mostly stable between solutions with small clusters of distinct presentations added in more complex models.

#### Conclusions

Results supported the use of integrating dimensional, developmental, and transdiagnostic information in the conceptualization of OCD in this sample of children and adolescents. The clusters identified support the centrality of contamination symptoms in OCD, relationships between broader symptom expression and higher levels of comorbidity, as well as the potential for complex/neurodevelopmental presentations. The clusters provide an indication of potentially relevant modifications to treatment.



Patterns and associated user characteristics of antidepressant prescriptions in older adults: A nationwide descriptive cohort study in Denmark

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Psychiatric disorders in pediatric-onset immune-mediated inflammatory diseases - a nationwide Danish study

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#### Background

Anxiety and depression are well known among patients with pediatric-onset immune-mediated inflammatory diseases (pIMID). However, data on a wider spectrum of psychiatric disorders are scarce.

#### Methods

In this nation-wide study from 1996-2018, we investigated psychiatric disorders in patients with pediatric-onset inflammatory bowel diseases, autoimmune liver diseases, and rheumatic diseases, using Danish national health care and population registers. Each case was matched with up to 10 controls from the background population. A cumulative incidence for psychiatric disorders prior to pIMID onset was calculated and compared with that for controls. We used cox proportional regression to estimate adjusted hazard ratios (aHR) with a 95% confidence interval (CI) between cases and controls without psychiatric disorders prior to the index date (ID).

#### Results

We included 11,208 cases (57% female) and 98,387 controls. The median age at disease onset was 12.5 years (interquartile range: 8-15) and follow-up time 9.8 years (interquartile range: 5-15). We found an association between psychiatric disorders before ID and a diagnosis of subsequent pIMID (odds ratio: 1.3, 95%CI: 1.2-1.4). After ID, cases had an increased risk (aHR: 1.6, 95%CI:1.5-1.7) of psychiatric disorders compared to controls. The risk was increased for neurodevelopmental-, psychotic-, emotional-, and other disorders. Female patients had an increased risk of suicide attempt (aHR:1.4, 95%CI: 1.1-1.8).

#### Conclusion

Both before and after receiving a pIMID diagnosis, patients with pIMID had an increased risk of psychiatric disorders. Our results strongly underscore the importance of being attentive to not only somatic but also psychiatric problems in this patient group.



Identifying prodromal biomarkers of schizophrenia and bipolar disorder using magnetoencephalography

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Schizophrenia (SZ) and bipolar disorder (BD) are associated with abnormal neurophysiological responses, including deficits in the auditory mismatch negativity (MMN) and 40-Hz steady-state responses. These abnormalities appear to reflect underlying cortical abnormalities and may serve as early markers of illness susceptibility, however longitudinal studies of at-risk individuals are lacking. As part of the Danish High-Risk and Resilience Study – VIA, we will investigate MMN and 40 Hz ASSR in 15 year old adolescents (n  $\approx$  175) born to parents diagnosed with either SZ (FHR-SZ), BD (FHR-BD), or neither SZ or BD (population-based controls, PBC) using magnetoencephalography (MEG). We will apply dynamic causal modeling (DCM) to investigate whether familial high risk of SZ or BD is associated with changes in synaptic gain or effective connectivity. Furthermore we will test competing hypotheses about the receptors and neuronal types involved, and investigate links with psychopathology, cognition, and genetics. Data collection is ongoing and expected to be completed in 2024. Altogether, the present study will represent one of the world's largest MEG datasets and will allow unprecedented insight into the the links between genetics, brain circuits, and psychopathology of SZ and BD.



# Obsessive-Compulsive Disorder: Long-term Outcome and Investigation of Helpful and Hindering Factors - A Multimethod Study

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#### Baggrund

Formålet er at forbedre behandlingen og monitoreringen af børn, unge og voksne med behandlingskrævende obsessiv-kompulsiv lidelse (OCD). Dette er påkrævet, da det anslås, at ca. 30-50% af patientgruppen ikke responderer tilfredsstillende på standardbehandlingen. Vi mangler viden om patientgruppens grad af belastning på længere sigt, herunder deres behov for sundhedsydelser. Faktorer associeret med langtidsudfald er et ekstremt underbelyst område, så der er brug for at benytte flere metoder for at afsøge bredt. Derfor vil vi både undersøge de store linjer som kan identificeres i de danske registre, herefter bevæge os tættere på individet ved at give tidligere OCDpatienter en række standardiserede spørgeskemaer for til sidst at gennemføre en række åbne kvalitative interviews med tidligere patienter.

#### Metode

Del 1 benytter data fra de danske registre for at undersøge langtidsudfaldet for alle danske OCDpatienter fra 1995 til d.d. Derudover kobles registerdata til klinisk data på ca. 400 patienter, som har modtaget behandling for OCD i Børne- og Ungdomspsykiatrien på AUH i perioden 2008-2016. for at undersøge, om præ- og postbehandlingsfaktorer er associeret med langtidsudfald. Ca. 80 patienter heraf har deltaget i the Nordic Long-term OCD Treatment Study (NordLOTS) i perioden 2008-2012, hvorfor der foreligger en stor datamængde på denne gruppe. De vil bibringe detaljeret information omkring prædiktorer for langtidsudfald.

I del 2 vil vi kontakte de ca. 80 danske tidligere deltagere i NordLOTS for at bede dem svare på en række korte spørgeskemaer om deres oplevede aktuelle status i forhold til 1) OCD-symptomer og sværhedsgrad, 2) funktionsniveau, og 3) livskvalitet 11-15 år efter behandling.



I forlængelse af del 2 inviteres patienterne til at deltage i et kvalitativt interview i del 3. Her vil patienterne bl.a. blive spurgt ind til, hvordan de selv har oplevet længerevarende effekter af behandlingen, og hvad der har været hjælpsomt versus hæmmende for deres langtidsudbytte.

#### Resultater

Projektet er i startfasen. Første resultater forventes ultimo 2023.

#### Konklusion

Det forventes, at resultaterne vil bringe ny viden, som kan forbedre behandlingen og monitoreringen af børn, unge og voksne med OCD. Studiet er særligt unikt i forhold til den yderst velbeskrevne population fra NordLOTS-studiet, som følges op via multiple metoder.



Mobile app-assisted behavioural treatment (MA-BT) in Children and Adolescents with an impairing tic disorder. Randomized clinical trial evaluating treatment response and satisfaction.

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# The efficacy of a transdiagnostic sleep intervention for outpatients with sleep problems and depression, bipolar or attention deficit disorder: a randomized controlled trial

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#### Background

Patients with mental disorders are more likely to suffer from sleep problems than the general population. Sleep problems can include insomnia, circadian rhythm disorders or hypersomnia. A transdiagnostic approach combining Cognitive Behavioral Therapy for Insomnia (CBT-I) with chronotherapy, such as light therapy to address a broad range of sleep problems, has proven efficient in a few American studies. The aim of the study is to investigate the efficacy of this transdiagnostic sleep intervention, delivered as 6 individual sessions provided by Danish healthcare professionals. The hypothesis is, that the intervention will reduce the severity of insomnia and increase sleep quality, compared to a control group receiving short sleep hygiene education.

#### Methods

The study is a randomized controlled trial enrolling 88 outpatient with bipolar disorder, major depression, and attention deficit disorder suffering from sleep problems. Participants are allocated to either an intervention group receiving six sessions of transdiagnostic sleep treatment, or a control group receiving sleep hygiene education at a single session. Assessments are carried out at baseline, at week 2 and after 6 weeks. Actigraphy is performed continuously throughout the 6-week study period. Primary outcomes are changes in the subjective appraisal of sleep quality and the severity of the insomnia problem. Secondary outcomes are changes in sleep efficiency, sleep latency, wake after sleep onset, quality of life, personal recovery, work ability and consumption of sleep medication.

#### **Results and conclusion**

The study was initiated in June 2022, and the inclusion period will continue until the end of 2023. The results could contribute to the development and implementation of treatment options for patients with mental disorders and sleep problems.



Clinical and legal differences in the use of involuntary electroconvulsive therapy across European countries

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#### Background

Electroconvulsive therapy (ECT) can be life-saving in situations where patients are at risk of dying due to severe manifestations of mental illness. In some of these cases, patients are, however, unwilling to consent to ECT. Here, involuntary ECT may be an option. The use of involuntary ECT varies substantially across European countries. The reasons for this variation are unclear, but likely includes differences in national legislations. The aim of this study was to examine clinical and legal differences in the use of involuntary ECT across European countries.

#### Methods

A questionnaire based on a case vignette (a 55-year-old inpatient with psychotic depression at imminent risk of dying from metabolic derangement due to refusal to eat and drink) was sent to one ECT specialist in each of 31 European countries. We made a qualitative synthesis of the responses to this survey.

#### Results

We received response from 18 countries. In 7 of these countries, a psychiatrist can independently prescribe involuntary ECT to be carried out immediately if a patient is at risk of dying. In these clinical situations, involuntary ECT can be carried out within 1-2 days in only 10 of the 18 countries. Notably, the rules regarding involuntary ECT differed for adults and minors (more restrictive for the latter) in 6 countries.

#### Conclusions

There are large differences in clinical practice and legislation regarding involuntary ECT across European countries. In many countries, the legislation likely delays potentially life-saving use of ECT. This is highly unfortunate and should be addressed by clinicians and legislators.



Clinical validation of the self-reported six-item Hamilton Depression Rating Scale (HAM-D6-SR) among inpatients

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Standardized video-based training in the rating of the 17-item Hamilton Depression Scale

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Development and validity of the Aarhus Structured Clinical Interview for ICD-11 and DSM-5-TR Prolonged Grief Disorder (PGD-SCI)

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## Background and rationale

Prolonged Grief Disorder (PGD) is a newly established diagnosis in ICD-11 and DSM-5-TR that captures disordered grief and is currently being implemented worldwide [1, 2]. A reliable, valid, and easy-to-use diagnostic interview for PGD is therefore needed [3]. The aim of this study is to develop, test, and validate the Aarhus Structured Clinical Interview for Prolonged Grief Disorder (PGD-SCI).

## Design

PGD-SCI was developed from ICD-11 and DSM-5-TR PGD criteria through a rigorous process involving clinicians, focus groups of bereaved adults, pilot testing, and thorough clinical supervision. The interview was then tested in a sample of approximately 124 bereaved adults who completed diagnostic interviews and self-report scales for PGD, depression, PTSD, and generalized anxiety (GAD). A total of 51 bereaved adults were retested after 1 to 2 weeks.

## **Results:**

- The test-retest stability is moderate for ICD 11 and substantial for DSM 5
- The inter-diagnostic stability between ICD 11 and DSM 5 Tr is moderately stable at T1 and substantial at T2
- DSM 5 Tr PGD criteria may be more stable and thus more reliable than ICD 11 PGD
- The Aarhus PGD interview is a valid and reliable structured clinical interview that captures PGD DSM 5 Tr and in part ICD 11 PGD

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What makes the difference? Reduction of restrictive interventions in an adolescent psychiatric ward.

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Abstract not available.



## Effects of menstrual cycle and hormonal contraception on alcohol consumption

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Research has shown that alcohol may be more detrimental to the health of women than to men. Risk factors for alcohol dependence in women remain poorly understood, although a link between stress and alcohol use is generally accepted. In addition, the menstrual cycle and use of hormonal birth control alter the stress response, possibly affecting alcohol consumption. In the present study, we aim to investigate the correlation between the menstrual cycle, use of birth control and levels of alcohol consumption in women.

The study was conducted online. One hundred and two women answered questions regarding the use of hormonal contraceptives, alcohol consumption and alcohol cravings. This data will undergo statistical analysis using Jamovi and be compared to existing literature.

It is our hope that by illuminating the side effects of hormonal birth control, women can make a more informed decision when considering contraceptive methods.



Do polygenic risk scores improve our ability to predict recurrent hospital admission in patients with bipolar disorder?

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#### Background

Polygenic risk scores (PRS) are of great interest to the scientific community, however their utility as diagnostic or decision aids in clinical settings has yet to be proven. Our goal was to test if PRS can improve prediction of recurrence in patients with bipolar disorder beyond what is achievable through non-genetic risk factors alone.

#### Methods

Data were obtained from the iPSYCH2015 cohort, which includes all individuals diagnosed with bipolar disorder (ICD-10 codes F30-31, F38.00) in Danish psychiatric hospitals from 1995-2015. Our sample included 2,989 patients (64% female). We defined recurrence as a subsequent contact for bipolar disorder starting at least 8 weeks after the first contact. Potential predictors included demographic (e.g. gender), clinical (e.g. polarity), and socio-economic characteristics as well as family history of psychiatric disorders. PRS for bipolar disorder, major depression, schizophrenia, and ADHD were created using a metaPRS method. Prediction models were developed using flexible parametric survival analysis. Patients were followed from the end date of their first bipolar contact to the start of their second contact, death, emigration, or December 31, 2016, whichever came first.

#### Results

947 (32%) of patients experienced ≥1 recurrent contact(s). The following predictors were selected in the multivariable model: gender (Hazard Ratio=1.20, 95% Confidence Intervals=1.04-1.38); polarity (depressive [1.58, 1.28-1.95], mixed [1.35, 1.04-1.75], other [1.36, 1.02-1.82], unspecified [1.37, 1.11-1.69]); psychotic smptoms (1.53, 1.19-1.98), substance abuse disorders (1.26, 1.05-1.51), inpatient (1.53, 1.30-1.79) and emergency (0.74, 0.57-0.96) treatment settings, prior antipsychotic prescription (1.29, 1.11-1.49), family history of depression (1.20, 1.04-1.37), and 1st month treatment duration (1.05, 1.01-1.09). PRS for bipolar disorder was significant in the univariable model (1.07, 1.01-1.05) but not the multivariable model (HR=1.04, 0.96-1.13). Comparison of model performance measures show that the model including PRS did not differ significantly from the model without PRS.

## Conclusion

Our results suggest that including PRS does not improve our ability to predict recurrence in patients with bipolar disorder. Future studies should investigate whether PRS can help predict other outcomes in patients with psychiatric disorders.



# Effectiveness of Basic Body Awareness Therapy as add-on to Cognitive Behavioural Therapy in Patients with Anxiety Disorders

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#### Background

Severe anxiety disorders, are among the most frequent psychiatric disorders and present major human costs for the individual patient as well as extensive societal expenses, e.g. in frequent sickness leave and increased costs for sickness benefits, and general loss of earnings. Therefore, providing effective treatment for this group of patients is a continuous and highly relevant goal. Cognitive Behavioural Therapy (CBT) is a commonly applied psychiatric treatment focusing primarily on the psychological and behavioural symptoms of anxiety. Although this intervention is effective for a number of patients there is still a need for developing new and more efficient treatment modalities. Interventions focusing also on the bodily symptoms of anxiety might have the potential to improve outcome of treatment further.

It is hypothesized that adding a bodily intervention such as Basic Body Awareness Therapy(BBAT) can reduce the physical symptoms of anxiety and efficient in reducing anxiety, including improved self-efficacy and quality of life.

## Objectives

The primary objective of this study is to compare the effectiveness of BBAT in combination with CBT to CBT alone in patients with Panic Disorder (PD) or Social Anxiety Disorder (SAD).

A secondary objective is to investigate the patients' adherence and experiences with BBAT as add-on to CBT.

#### **Methods and Material**

In this RCT study, 60 patients with an ICD-10 diagnosis of PD (F41.0, F41.1) or SAD (F40.1) are the study population of interest; recruited from the Clinic of PTSD and Anxiety, Dep. of Affective Disorders, Aarhus University Hospital, Psychiatry, Central Region Denmark.

After written, confirmed consent patients are randomized to either 14 sessions of CBT or 14sessions of CBT + 10 sessions of BBAT.

Assessments of anxiety symptoms, bodily symptoms, and quality of life are performed before and after treatment and after 3 months of follow-up. Further, data will be provided in 10-15 in-depth interviews.

The study is approved by the ethical committee; so far 18 patients have been enrolled in the stud. Data will be analysed and all results presented in peer-reviewed scientific journals.



Regulation of Sortilin cleavage through a novel switch with relevance to depressive symptoms in dementia

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Alzheimer's disease (AD) and other forms of dementia are among the most common causes of disability in the elderly. Dementia is often accompanied by depression, especially during the early and middle stages. In the early stages of dementia and during diagnosis, depressive symptoms are often treated before dementia itself.

We hypothesize that the depressive symptoms might be the early stages of an imbalanced sortilinmediated mechanism that later causes dementia. Sortilin is a multitasking protein that mediates endocytosis of immature and mature forms of neurotrophins, in particular, Brain-Derived Neurotrophic Factor (BDNF) which is involved in depression and AD. Reduced levels of BDNF have been found in AD patients and depressed patients. In some AD cases, it correlates with the severity of the disease.

We have established two novel binding partners to sortilin neuronal-specific gene 1 (NSG1) and neuronal-specific gene 2 (NSG2) that play a role in the regulation of sortilin. Sortilin is a transmembrane protein that acts as a receptor in its full-length form but is also cleaved by Metalloproteases, generating a soluble form that can act as a decoy molecule. An increase in soluble sortilin has been found in depressed patients and increased fragments of sortilin have been found and correlated with different stages of AD. An imbalance in this cleavage process can therefore potentially affect the BDNF levels.

We found that NSG1 associates with sortilin making sortilin more susceptible to cleavage and thereby generating more soluble sortilin. In contrast, the related protein NSG2 which also associates with sortilin protects sortilin from cleavage. Our data clearly illustrates divergent functions of NSG1 and NGS2 in the regulation of sortilin cleavage. These data suggest that balancing NSG1 and NSG2 expression levels or activity could be important for normal sortilin function.

Future research will investigate NSG1 and NSG2 effects on BDNF levels through sortilin-mediated processes. The expression levels of NSG1 and NSG2 in the brains of dementia patients as well as serum levels of soluble sortilin in early stages of AD patients with depressive symptoms will be investigated.

Consequently, this finding holds the potential to develop an innovative strategy for neuron-specific sortilin regulation, which can affect AD and the early stages of depressive symptoms.



Electroconvulsive therapy following incident bipolar disorder: When, how and for whom?

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#### Background

Electroconvulsive therapy (ECT) is one of the most effective treatments available in psychiatry. It is most commonly used for depression which has proven resistant to pharmacological treatment, and most clinical guidelines also recommend ECT as first-line treatment for acutely severe conditions, such as catatonia, aggressive behavior or imminent suicidality. As for bipolar disorder (BD), there is solid evidence for the effectiveness of ECT in the treatment of manic, depressive and mixed episodes. However, a comprehensive examination on the patterns of use of ECT in BD in real-world settings is lacking from the literature. Based on data from Danish registries with complete nationwide coverage, this study of patients with incident BD aimed to describe when, how and for whom ECT is used in the context of BD.

#### Methods

We conducted a register-based cohort study involving all patients in Denmark receiving their first diagnosis of BD in the period from 2008 to 2018, and who subsequently received ECT. Descriptive statistics were used to to clarify when, how and for whom ECT is used.

#### Results

We identified 1,338 patients with incident BD who subsequently received ECT. The median age at the first ECT session was 50.6 years (IQR: 26.4) and 62% of those treated with ECT were female. The median time from the diagnosis of BD to the first ECT treatment was 0.6 years (IQR: 2.6) and 58% of the patients receiving ECT had the first treatment within the first year after being diagnosed with BD. The most common indication for the first ECT treatment was depression (mainly non-psychotic depression), followed by mania (mainly psychotic mania). The first ECT session was typically provided under admission (97%), upon patient consent (98%) and with bilateral electrode placement (60%).

## Conclusion

A substantial proportion of the patients with incident BD who receive ECT, require this treatment within the first year after the diagnosis. The most common indication for ECT is depression followed by (psychotic) mania. Inpatient voluntary ECT using bilateral electrode placement is the most common form of administration.



# Metacognition in children and adolescents with obsessive-compulsive disorder treated with cognitive behavioral therapy

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# Background

Metacognitive biases have been proposed to be associated with the development of emotional disorders. This study explores metacognitive biases in children and adolescents with obsessive compulsive disorder (OCD) treated with cognitive behavioral therapy (CBT).

## Methods

56 children and adolescents (7-17 years) with OCD were included in the study. Metacognitive biases and OCD severity was assessed with the Metacognitions Questionnaire – Child Version and the Children's Yale-Brown Obsessive Compulsive Scale before and after treatment with 14 sessions of CBT.

## Results

Results showed that 1) there were significant reductions in all the metacognitive biases from pre- to post-treatment; 2) higher reductions in negative beliefs about worry, beliefs about the need to control thoughts, and cognitive self-consciousness were associated with a lower post-treatment symptom severity; and 3) a higher level of pre-treatment positive beliefs about worry was associated with a lower symptom severity post-treatment.

## Conclusion

Metacognitive biases seem amenable to CBT. As a decrease in metacognitive biases was associated with a better treatment outcome it might be important to target metacognitive biases during treatment. Furthermore, it seems that CBT is equally effective for patients with different levels of metacognitive biases with the exception of positive beliefs about worry. Higher levels of positive beliefs about worry might affect the CBT effect in a positive direction.



# Detailed trajectory of efficacy of internet-CBT for youths with functional abdominal pain disorders

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## Background

Functional abdominal pain disorders (FAPD) are common in young people. They are characterised by recurrent abdominal pain, nausea, bloating, flatulence and change in defecation patterns and can lead to reduced quality of life with high school absence as well as high health care use, and comobid anxiety and depresison. Exposure based Internetdelivered cognitive behavioural therapy (i-CBT) has shown promising treatment results and has the potential to widen treatment access for this large patient group. The effect has been shown to be mediated by changes in gastrointestinal fear and avoidance. However, little is known about the detailed efficacy of i-CBT, including the exact onset of the desired effects on various outcomes. With this study we aim to explore the detailed trajectory of efficacy of i-CBT in children and adolescents with FAPD.

## Methods

We will include Six children (aged 8–12 years) and 6 adolescents (aged 13–17 years) in a single-case experimental design study. A single case design study allows for multiple measurements per participant, at different levels. Patients will undergo 10-weeks i-CBT, and perform digital daily assessment from baseline to end of treatment and at 3-months follow-up. Patients will be randomized to a baseline varying from 5 to 15 days, before starting i-CBT.

The digital daily assessment consist of 8 items covering abdominal symptoms, catastrophizing, avoidance- and control behaviour and symptom acceptance.

Each participant will be its own control where scores during baseline will be compared to scores during treatment and at follow-up. Analyses will include visual inspection and calculation of effect sizes.

## Results

Results are expected to give a detailed description of the efficacy, including exact onset of effect on different outcomes during treatment.

## Conclusion

This study can increase our understanding of i-CBT for children and adolescents with FAPD. It can add knowledge on the influence on suggested treatment targets and outcomes over time and thereby how to enhance the promising effects seen from this treatment even more.



Risk factors for suicide following treatment with electroconvulsive therapy: A nationwide study of 11,780 patients

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Abstract not available.



#### Old brains - new ideas : A non-coding RNA perspective

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We have conducted a technical evaluation of long term stored archival FFPE material from the Danish Human Brain Bank. This material has been collected from patients with mental disorders during the period from 1945 to 1982. We have used commercial state-of-the-art in situ probes from ACD Bioscience targeted against microRNAs, to evaluate the quality of the material. Our technical analysis shows that microRNAs are preserved in sufficient quantities and quality to be useful for in situ hybridization against microRNAs. We therefore optimized an automated protocol for the Leica Bond Autostainer, this can then conduct chromogenic ISH stains on 30 slides a day. In the next phase we will evaluate differentially expressed microRNAs from the Human Brain Bank, which have been identified with Nanostring NCounter technology. Three diseases have been selected and carefully curated, Schizophrenia (SZ), Bipolar Disorder (BD), and Depression (DE) with equal representation of male and females. Spatial investigation of the expression patterns of candidate microRNAs will aid the design of functional experiments. This will improve the understanding of the role of microRNAs in these neurological diseases.



Social responsiveness in families with parental schizophrenia or bipolar disorder – The Danish High Risk and Resilience Study

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## Background

Individuals with schizophrenia or bipolar disorder exhibit social impairments, and their partners display poorer functioning and more psychopathology. Nonrandom mating and transmission of social abilities from parents to their children remain under-investigated. Therefore, we aimed to examine social responsiveness in families with parental schizophrenia or bipolar disorder.

## Methods

The Danish High Risk and Resilience Study – VIA 11 consists of 11-year-old children with at least one parent diagnosed with schizophrenia (n = 179) or bipolar disorder (n = 105) and population-based controls (PBC, n = 181). Children and both parents were assessed with The Social Responsiveness Scale, Second Edition. Duration of time each parent and child have lived together until age 11 was ascertained through interviews.

## Results

Index schizophrenia parents and index bipolar parents (the parent diagnosed with schizophrenia or bipolar disorder) exhibited poorer social responsiveness compared with PBC parents. Index schizophrenia parents displayed poorer social responsiveness compared with index bipolar parents. Non-index (the co-parent without a diagnosis of schizophrenia or bipolar disorder) schizophrenia parents exhibited poorer social responsiveness compared with non-index bipolar parents and PBC parents. We found significant positive associations between parents' and children's social responsiveness, with a significant interaction effect of duration of time living together.



# Conclusion

Parents with schizophrenia or bipolar disorder and co-parents to parents with schizophrenia exhibit poorer social responsiveness. Furthermore, social responsiveness was positively associated between parents and children, irrespectively of familial high-risk status. Considering that social impairments are suggested as a vulnerability marker, this knowledge calls for increased attention towards vulnerable families, particularly those where both parents have social impairments.



## Clinical validation of the Aarhus Side effect Assessment Questionnaire (ASAQ)

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## Background

Psychotropic medications are essential in the treatment of mental illness. Unfortunately, these medications are associated with side effects that may reduce adherence to treatment and quality of life. Therefore, systematic screening for side effects is fundamental to optimize treatment with psychotropic medications. Self-report of side effects is a practical alternative to time-consuming clinical assessments. We developed the Aarhus Side effect Assessment Questionnaire (ASAQ) in an attempt to strike the balance between extensive coverage of side effects and reasonable application time. Aim: The aim of the study was to validate the ASAQ using the clinician-rated Udvalg for Kliniske Undersøgelser (UKU) Side Effect Scale as gold standard reference. Methods: A total of 122 inpatients and outpatients—mainly with psychotic (39%) and affective disorders (43%)—receiving treatment with psychotropic medication completed the ASAQ and the World Health Organization-Five Well-Being Index (WHO-5) and were subsequently rated on the UKU by trained raters. Results: Using the UKU as the gold standard reference, the ASAQ demonstrated sensitivity values >75% for 77% of its 30 items (ranging from 37% for cutaneous disturbances to 98% for increased sweating) and specificity values >75% for 47% of its 30 items (ranging from 28% for reduced sleep to 98% for micturition disturbances). A negative correlation was found between the ASAQ and the WHO-5 and total scores (Pearson's correlation coefficient=-0.44). Conclusions: The self-reported ASAQ seems to be a sensitive tool for detecting side effects of psychotropic medications.



# S-Ketamine acutely increases hippocampal synaptic vesicle glycoprotein 2A density in Flinders Sensitive Line rats

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Up to 30% of patients with depression face inadequate treatment. Classically available pharmaceuticals can take 3-6 weeks to reach full effect. Aiming to bridge this gap, S-ketamine is used in patients with treatment-resistant depression, as a fast-acting agent. Ketamine is a synaptic modulator, inducing synaptic plasticity in certain regions of the brain, which is hypothesized to be part of its mechanism of antidepressant action. To investigate this, we treated 8 Flinders Sensitive Line (FSL) rats, considered a genetic model of depression, with an intraperitoneal injection of 15 mg/kg of S-Ketamine and compared them to 6 saline-injected FSL rats. We then performed autoradiography on selected regions of brains removed 1-hour post-injection. Fresh frozen brain sections were processed using [3H]-UCB-J, a radioligand of synaptic vesicle glycoprotein 2A, considered a biomarker of pre-synaptic density. We found significantly higher [3H]-UCB-J binding in ventral (22% increase, p=0,01) and dorsal hippocampus (13% increase, p=0,05) of ketamine-injected FSL rats compared to the saline group. No significant increases were found in the remaining areas. These findings suggest ketamine's effect to be based in synaptic modulation of the hippocampus. We suggest further investigation at different time points and with left-right discrimination. We are currently investigating the effects of ketamine on post-synaptic density using a ligand of metabotropic glutamate receptor 5.

