Volume xx Supplement x

Acta Neuropsychiatrica

An International Journal of Translational Neuropsychiatry

EDITOR-IN-CHIEF **Gregers Wegener**

ABSTRACTS

Educational Symposium in Psychiatry 20 June 2024

CAMBRIDGE UNIVERSITY PRESS journals.cambridge.org/neu



Poster 1

Molecular Interaction of Antidepressants with Estrogen Receptor Alpha

<u>Arjmand, Shokouh</u>^{1,2}; Rossi, Rachele³; Vægter, Christian B.³; Sinning, Steffen⁴; Müller, Heidi K.¹; Schiøtt, Birgit ⁵; Cecchi, Claudia¹; Sahana, Jayashree²; Landau, Anne M.¹; Wegener, Gregers¹; Joca, Sâmia²; Biojone, Caroline^{1,2}

¹Translational Neuropsychiatry Unit, Aarhus University, Denmark ²Department of Biomedicine, Aarhus University, Aarhus, Denmark ³Department of Biomedicine, Danish Research Institute of Translational Neuroscience, Aarhus University, Aarhus, Denmark ⁴Department of Forensic Medicine, Aarhus University, Aarhus, Denmark

⁵Department of Chemistry, Aarhus University, Aarhus, Denmark <u>shokouh@clin.au.dk</u>

Abstract: Not available

Poster 2

Efficacy, acceptability, and safety of pharmacological interventions for insomnia in severe mental disorders: A systematic review and metaanalysis

<u>Nina B. Fuglsang</u>^{1,2}, Nanna Marker Madsen^{1,2}, Søren Lundorff Jacobsen^{1,2}, Julie Eg Frøkjær^{1,2}, Nicolai Ladegaard⁵, Marc Alberg Sørensen^{1,2}, Christoph U. Correll⁷⁻¹¹, Christian Otte^{6,7}, Mikkel Højlund^{3,4}, Ole Köhler-Forsberg^{1,2}

¹Psychosis Research Unit, Aarhus University Hospital - Psychiatry, Aarhus, Denmark

²Department of Clinical Medicine, Aarhus University, Aarhus, Denmark

³Clinical Pharmacology, Pharmacy, and Environmental Medicine, University of Southern Denmark, Odense, Denmark

⁴Department of Psychiatry Aabenraa, Mental Health Services Region of Southern Denmark, Aabenraa, Denmark

⁵Department of Affective Disorders, Aarhus University Hospital – Psychiatry, Aarhus, Denmark

⁶Charité – Universitätsmedizin Berlin, Department of Psychiatry and Neuroscience, Campus Benjamin Franklin, Berlin, Germany

⁷DZPG, German Center for Mental Health, partner site Berlin

⁸Department of Psychiatry and Molecular Medicine, Zucker School of Medicine at Hofstra/Northwell, Hempstead, NY, USA.

⁹Center for Psychiatric Neuroscience, Feinstein Institute for Medical Research, Manhasset, NY, USA.

¹⁰Department of Child and Adolescent Psychiatry, Charité Universitätsmedizin, Berlin, Germany

¹¹Department of Psychiatry, Zucker Hillside Hospital, Northwell Health, Glen Oaks, NY, USA.

ninbak@clin.au.dk

Abstract: Background: Pharmacological interventions for insomnia are frequently used in severe mental illness, such as schizophrenia, bipolar disorder (BD) and major depressive disorder (MDD) and contribute to the risk of polypharmacy. There is a need for an overview of the efficacy and acceptability of both off-label and licensed drugs.

Objectives: To perform a systematic review and metaanalysis of randomised controlled trials (RCT's) investigating the efficacy, acceptability and safety of pharmacological interventions for insomnia in severe mental disorders.

Methods: We performed a systematic literature search in March 2023 to identify all RCTs comparing any oral pharmacological intervention for insomnia against placebo or an active, pharmacological control in adults (age ≥ 18 years) with a diagnosis of schizophrenia, MDD or BD using a validated, self-rated or clinician-rated sleep questionnaire. Screening of studies, data extraction, and risk of bias assessment with the RoB-2 tool was performed by two independent reviewers. The co-primary outcomes were efficacy (total sleep time and sleep quality) and acceptability (all-cause dropout) of the pharmacological intervention. We computed mean differences (MD's) and standardized mean differences (SMD's) including 95% confidence intervals (95%CIs) for continuous outcome measures. For binary outcomes, we calculated risk ratios (RR) including 95%CI.

Results: The systematic review identified 24 studies in total, with the majority being in patients with MDD (17 trials, n = 2171). Very few trials were found in BD (4 trials, n = 162) and schizophrenia (3 trials, n = 115). Studies were generally of low quality, with 21 out of 24 studies having a high risk of bias. The most frequently studied pharmacological interventions for insomnia were melatonin (3 RCT's), agomelatine (3 RCT's) and z-drugs (4 RCT's).

Compared to placebo, pharmacological interventions improved total sleep time by 33 minutes and improved sleep quality by a moderate effect size. Compared to placebo, pharmacological interventions for insomnia had similar discontinuation rates, but increased risk of side effects. The opposite was seen when compared to active controls, where discontinuation rates and risk of side effects was lower in pharmacological interventions.

Conclusion: Pharmacological interventions for insomnia in severe mental illness showed better efficacy, similar acceptability, but increased risk of side effects compared to placebo. Yet, surprisingly few RCTs have studied this clinically important aspect, especially in schizophrenia and BD. Furthermore, studies were generally of poor quality. Large, highquality clinical trials evaluating the efficacy and safety of pharmacological interventions for insomnia in representative patients with severe mental illnesses are required to better address this frequent clinical issue.

Poster 3

Functional consequences of genetic variants in the sortilin 1 gene associated with increased risk of frontotemporal dementia

<u>Ann Kathrine Christiansen</u>¹, Malene Overby¹, Heidi Kaastrup Müller¹

¹Translational Neuropsychiatry Unit, Department of Clinical Medicine, Aarhus University

a.k.c@clin.au.dk

Abstract: Not available.

Poster 4

Resolution of Inflammation to Enhance Depression Treatment and Diagnostics

<u>Yane Chaves</u>¹, Fernanda Crunfli², Lívea Godoy³, Sâmia Joca⁴, Gregers Wegener¹

¹Translational Neuropsychiatry Unit, Department of Clinical Medicine, Aarhus University, Aarhus, Denmark

²Laboratory of Neuroproteomics, Institute of Biology, University of Campinas (UNICAMP), Campinas 13000-000, Brazil

³Department of Biomolecular Sciences, School of Pharmaceutical Sciences of Ribeirão Preto, University of São Paulo, Ribeirão Preto, SP, Brazil

⁴Department of Biomedicine, Aarhus University, Aarhus, Denmark yach@clin.au.dk

Abstract: 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 nonresponders 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-pituitaryadrenal (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.

Poster 5

Can health anxiety be distinguished from other anxiety phenomena in youth?

<u>Charlotte Steen Duholm</u>^{1,2}, Davíð R.M.A Højgaard¹, Eva Ørnbøl^{2,3}, Kaare Bro Wellnitz^{2,3}, Per Hove Thomsen^{1,2}, Martin Køster Rimvall^{4,5}, Charlotte Ulrikka Rask^{1,2}

¹Department of Child and Adolescent Psychiatry, Aarhus University Hospital Psychiatry, Denmark

²Department of Clinical Medicine, Aarhus University, Denmark

³Department for Functional Disorders, Aarhus University Hospital, Denmark

⁴Child and Adolescent Mental Health Center, Mental Health Services, Capital Region of Denmark

⁵Department of Clinical Medicine, Faculty of Health and Medical Sciences, University of Copenhagen, Denmark

chaduh@rm.dk

Abstract: Health anxiety (HA) is characterized by excessive worry about being or becoming seriously ill. There is a considerable phenomenological overlap between HA and other anxiety disorders. This study explored if HA could be distinguished from other anxiety phenomena in adolescents regarding depression, physical symptoms, bodily dissatisfaction, health-related quality of life (HRQoL) and healthcare use.

Data from the 16/17-year follow-up (N = 2521, 16-17) years old) from the general population-based Copenhagen Child Cohort 2000 was used. Self-report questionnaires assessed HA, anxiety, depression, physical symptoms, bodily dissatisfaction, and HROoL, and register data on healthcare use was retrieved. Latent profile and latent class analyses were used to detect specific anxiety profiles/classes, however unsuccessfully. Four groups based on HA and anxiety symptoms were created: 1) no anxieties, 2) only anxiety, 3) only HA, and 4) both HA and anxiety. Differences between the four groups regarding the various healthrelated areas of interest were examined using general linear models.

Of the 10.4% participants who were defined as having high HA, almost half (4.6%) reported having only high HA without other anxiety symptoms. The HA group (group 3) reported significantly more physical symptoms, fewer depressive symptoms and higher healthcare utilization compared to group 2. Group 3 reported less favourably on all measures compared to group 1. Adolescents who reported high levels of both HA and other anxiety symptoms (group 4) had the most adverse clinical profile.

Our results suggest that HA can be recognized as a separate construct in youth. High HA was associated with several negative health-related outcomes illustrating the clinical importance of recognizing HA also in young persons. More research is required to ensure adequate recognition and treatment of HA in adolescence.

Poster 6

A Macrobiotic Approach to Ameliorate "Chemobrain" and Chemotherapy-induced sickness

Eleonora Genovese¹, Bradley Whitehead², Gregers Wegener¹, Peter Nejsum², Cecilie Bay-Richter¹ ¹Translational Neuropsychiatry Unit ²AUH Department of Infectious disease elgen@clin.au.dk

Abstract: Background: Chemotherapy cause 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 parasite X are a novel source of biologic therapies, which directly modulate the immune response and microbiota.

Objectives: The objective of this project is to examine the protective effects of parasite X on chemotherapyinduced sickness and chemo-brain. Further, we will explore which underlying biological mechanisms that are altered by the parasite. The ultimate goal is to alleviate chemotherapy-induced sickness and chemobrain.

Methods: Once weekly for 4 weeks, Sprague-Dawley rats are treated with the chemotherapy drug doxorubicin (DOX) and parasite X or vehicle. During the DOX+WORM treatment the animals are housed in Noldus Phenotyper cages which allow us to record home-cage behaviour. Subsequently, the animals undergo a battery of behavioural tests and tissue is collected. Microbiome, inflammatory markers, and monoamine levels will be examined.

Results: We have shown that parasite X ameliorates chemotherapy induced weight loss – a proxy for sickness. We expect parasite X to improve cognitive deficits caused by DOX and potentially depressive- and anxiety-like behaviour as well, likely through direct effects on the microbiota and restoration of gut integrity via replenishment of intestinal stem cells

Conclusion: Helminth X improve chemotherapyinduced sickness and we expect that cognitive disturbances (chemo-brain) are also improved.

Poster 7

Mind the Heart - Lived experiences of parents to children with congenital heart disease and mental health issues

<u>Julie L Hejl</u>^{1,2}, Ditte R Hulgaard^{1,3}, Anne Sofie D Rasmussen¹, Lærke Emilie N Larsen¹ and Charlotte U Rask^{1,2}

¹Department of Child and Adolescent Psychiatry, Aarhus University Hospital Psychiatry, Aarhus, Denmark

²Department of Clinical Medicine, Aarhus University, Aarhus, Denmark

³Department of Clinical Research, University of Southern Denmark, Odense, Denmark

julhej@rm.dk

Abstract: Not available.

Poster 8

Clinical validation of the six-item Positive and Negative Syndrome Scale (PANSS-6) obtained via the Simplified Negative and Positive Symptoms Interview (SNAPSI) among adolescents: A study protocol.

<u>Tirill Fjellhaugen Hjuler</u>^{1,2}, Per Hove Thomsen¹, Mark Opler^{3,4}, Christoph U. Correll^{5,6,7}, Søren Dinesen Østergaard^{2,8}, Pernille Kølbæk^{1,2}

¹Department of Child and Adolescent Psychiatry, Aarhus University Hospital - Psychiatry, Denmark,

²Department of Clinical Medicine, Aarhus University, Denmark, ³The PANSS Institute, NY, USA.

⁴WCG Clinical. Inc. New York, USA,

⁵Division of Psychiatry Research, The Zucker Hillside Hospital, New York, NY, USA,

⁶Department of Psychiatry and Molecular Medicine, Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Hempstead, New York, NY, USA,

⁷Department of Child and Adolescent Psychiatry and Psychotherapy, Charite Universitätsmedizin, Berlin, Germany,

⁸Department of Affective Disorders, Aarhus University Hospital - Psychiatry, Denmark

TIRHJU@rm.dk

Abstract: Background: Schizophrenia is a severe mental disorder that typically presents in late adolescence or early adulthood. Quantitative monitoring of the severity of illness using rating scales is likely to improve patients' outcomes via more informed clinical decision-making. The brief, six-item Positive and Negative Syndrome Scale (PANSS-6) is a measure of the severity of core symptoms of schizophrenia, which can be obtained via the brief Simplified Negative and Positive Symptoms Interview (SNAPSI). Recent studies have confirmed the validity of PANSS-6 ratings obtained via SNAPSI among adult patients with schizophrenia. However, the psychometric properties of the PANSS-6 obtained via SNAPSI among adolescents remain to be assessed.

Objectives: The primary aim of the present project is to evaluate the following psychometric properties: i) interrater reliability (i.e., rating agreement among trained clinicians) of the PANSS-6 obtained via the SNAPSI; ii) criterion validity (i.e., agreement with a gold-standard instrument) and responsiveness (i.e., sensitivity to change) of the PANSS-6 obtained via the SNAPSI, using the full 30-item PANSS (PANSS-30) obtained via the Structured Clinical Interview for PANSS (SCI-PANSS) as the reference; and iii) relationship between PANSS-6 ratings, side effects of psychotropic medication, and quality of life (i.e., levels of daily functioning and psychological well-being).

Methods: The assessment of the inter-rater reliability of the PANSS-6 via SNAPSI (aim I) has been successfully completed. Thirteen raters (psychiatrists, medical doctors, psychologists, and nurses) attended six brief training sessions prior to the inter-rater reliability test. Ten patients, aged between 12 and 18 years, diagnosed with psychosis-spectrum disorders were recruited from the Department of Child and Adolescent Psychiatry in the Central Denmark Region. Each participant was interviewed by one of the raters using SNAPSI, and the video-recorded. interviews were All raters independently conducted PANSS-6 ratings based on the recorded SNAPSI interviews.

To address the remaining aims (II and III), we are in the process of recruiting 80 patients, aged between 10 and 19 years, diagnosed with psychosis-spectrum disorders, who will be interviewed independently with the SNAPSI by a PANSS-6 rater and with SCI-PANSS by a PANSS-30 rater. Moreover, the participants will complete the following short questionnaires: the fiveitem World Health Organization Well-being Index; Aarhus Side Effect Assessment Questionnaire; Strengths and Difficulties Questionnaire; Symptom Self-rating Scale for Schizophrenia; and the Selfevaluation of Negative Symptoms scale. Approximately three months after the first interview, the participants will be interviewed and complete the questionnaires again.

Preliminary results: The intra-class correlation coefficient for the PANSS-6 total score was 0.87, with individual item scores ranging from 0.60 (blunted affect) to 0.86 (hallucinatory behavior). These results

indicate a high level of inter-rater reliability among the thirteen raters.

As of May 2024, we have assessed a total of fourteen participants to address aims II and III.

Perspectives/Conclusion: The preliminary results indicate promising psychometric properties of the PANSS-6 obtained via the SNAPSI among adolescents with psychosis-spectrum disorders. Given that the raters were clinicians with minimal, feasible training, we anticipate a similar level of inter-rater reliability when implementing our approach in clinical practice, affirming the generalizability of our findings. If our ongoing study confirms the validity and responsiveness of the PANSS-6 obtained via SNAPSI, it will allow for consistent measurement of symptoms across both research and clinical settings, thereby facilitating measurement-based care. Furthermore, it will enhance continuity of care during the challenging transition from adolescent to adult psychiatric services by providing a standardized measure across age groups.

Poster 9

Cluster Analysis of Symptom Types, Severity, Age, Gender, and Comorbidity in Pediatric Obsessive-Compulsive Disorder

Orri Smárason^{1,2}, Robert R. Selles^{3,4}, <u>Davíð R. M. A.</u> <u>Højgaard⁵</u>, John R. Best^{3,4}, Karin Melin^{18,6}, Tord Ivarsson⁷, Per Hove Thomsen⁵, · Bernhard Weidle^{8,9}, Nicole Michelle McBride¹⁰, Eric A. Storch¹¹, Daniel Geller^{12,13}, Sabine Wilhelm^{12,13}, Lara J. Farrell¹⁴, Allison M. Waters¹⁴, Sharna Mathieu¹⁴, Noam Soreni^{15,16}, S. Evelyn Stewart^{17,3,4}, Gudmundur Skarphedinsson¹

¹Faculty of Psychology, University of Iceland, Reykjavik, Iceland ²Department of Child and Adolescent Psychiatry, Landspitali-The National University Hospital of Iceland, Reykjavik, Iceland

³University of British Columbia, Vancouver, BC, Canada

⁴BC Children's Hospital, Vancouver, BC, Canada

⁵Department of Child and Adolescent Psychiatry, Aarhus University Hospital, Psychiatry, Denmark

⁶Institute of Health and Care Sciences, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden

⁷University of Gothenburg, Gothenburg, Sweden

⁸Regional Center for Child Mental Health and Child Welfare, Norwegian

9St. Olavs University Hospital, Trondheim, Norway

¹⁰Embedded Preventive Behavioral Health Capability, III MEF, United States Marine Corps, Okinawa, Japan

¹¹Baylor College of Medicine, Houston, TX, USA

12Harvard Medical School, Boston, MA, USA

¹³Massachusetts General Hospital, Boston, MA, USA

¹⁴Griffith University, Queensland, Australia

¹⁵St. Joseph's Hospital, Hamilton, ON, Canada

¹⁶McMaster University, Hamilton, ON, Canada

¹⁷BC Mental Health and Substance Use Services, Burnaby, BC, Canada

¹⁸Region Västra Götaland, Department of Child and Adolescent Psychiatry, Sahlgrenska University Hospital, Gothenburg, Sweden

davmar@rm.dk

Abstract: Background: Obsessive-compulsive disorder (OCD) manifests in various ways and often co-occurs with other conditions, affecting about 70% of patients. This study aims to explore the underlying commonalities among OCD-affected children and adolescents in order to better conceptualize variations in disorder presentation.

Methods: Data from seven international programs focusing on pediatric OCD were pooled, comprising 830 cases aged 5-19, with 54% being female. The severity and types of OCD symptoms were assessed using the Children's Yale-Brown Obsessive-Compulsive Scale (CY-BOCS), while comorbid conditions were determined through diagnostic interviews. Dependent mixture modeling was employed to identify latent groups based on age, gender, symptom severity, type, and comorbidities.

Results: The modeling revealed four distinct clusters, primarily differentiated by symptom expression and comorbidity types. While fit indices for 3-7 clusters showed minimal variance, cluster characteristics remained largely consistent across different models, with additional smaller clusters in more complex models.

Conclusions: Integrating dimensional, developmental, and transdiagnostic information proved valuable in understanding OCD in children and adolescents. The identified clusters underscored the significance of contamination symptoms, associations between broader symptomatology and increased comorbidity, and the potential for intricate neurodevelopmental profiles. These clusters offer insights into potential adaptations for treatment approaches.

Poster 10

Mobile app-assisted behavioural treatment for children and adolescents with chronic tic disorders: - A pilot randomised controlled trial

<u>Maria Louise Jöhnk^{1,3}</u>, David Mataix-Cols², Per Hove Thomsen^{1,3}, Claus Sixtus Jensen^{3,4,5}, Judith Becker Nissen^{1,3}

¹Department of Child and Adolescent Psychiatry, Aarhus University Hospital (AUH), Denmark.

²Centre for Psychiatry Research, Department of Clinical Neuroscience, Karolinska Institutet and Stockholm Health Care Services, Region Stockholm, Sweden.

³Department of Clinical Medicine, Aarhus University (AU), Denmark ⁴Department of Paediatrics and Adolescent Medicine, (AUH), Denmark

⁵Research Centre for Emergency Medicine, (AUH), Denmark <u>maria.joehnk@viborg.rm.dk</u>

Abstract: Background: Chronic tic disorders are neurodevelopmental disorders that occur relatively

frequently in childhood. Tics can have a significant impact on the child, both academically and socially. Clinical guidelines recommend behaviour therapy as the primary approach, but limited resources may pose challenges to its implementation. International research suggests that digital interventions may be effective in treating tic disorders, although additional clinical trials are necessary to confirm these findings.

Methods: This is a pilot study preceding a randomised clinical superiority trial comparing the efficacy of appassisted tic training versus app-assisted tic learning. The study evaluates the feasibility and acceptability of the app-based treatment and participants are randomized to either this treatment or treatment delivered by video sessions. Both interventions implement strategies from the well-documented manual "Nix to tics," utilising a combination of Habit Reversal Training (HRT) and Exposure and Response Prevention (ERP). Thirty participants aged between 9 and 17 years were included, fourteen of these were assigned to the app-treatment group while the remaining sixteen were assigned to the videoconferencing group. Two participants dropped out of each group.

Results: The study indicates that the recruitment process is feasible and with satisfactory adherence to the treatment. A clinically significant reduction in total tic severity score was observed in both groups, and the acceptability of the app intervention indicates satisfaction with the treatment itself and the outcome. Furthermore, data was used for power calculations in the randomised clinical superiority trial.

Poster 11

Distinguishing internalizing, disinhibited, or antagonistic self-damaging behaviors: Testing a HiTOP-informed latent structural model of selfdamaging behaviors in two community samples

<u>Jesper Nørgaard Kjær</u>¹, Brianna J. Turner², Andrew Switzer², Paweena Sukhawathanakul², Megan Ames² ¹Psychosis Research Unit, Aarhus University Hospital - Psychiatry,

Aarhus, Denmark

²Department of Psychology, University of Victoria, Victoria, Canada jespka@rm.dk

Abstract: Self-damaging behaviors (SDB) commonly co-occur, share etiologies and motivations, and respond to similar interventions, yet are often treated as distinct or unrelated phenomena. Theoretical models seek parsimony by organizing subtypes of SDB, for instance according to their potential for injury, intended outcomes, or associations with dimensions of psychopathology.

We used confirmatory factor analysis to compare these models in two community samples of adolescents (N=557) and first-year university students (N=704). In both samples, fit indices favored a Hierarchical Taxonomy of Psychopathology (HiTOP) informed model, with one higher-order "dysregulated behavior" factor and three lower-order factors that characterized SDB subtypes: internalizing, disinhibited externalizing, and antagonistic externalizing.

To validate this best fitting model, we examined differential associations between latent SDB scores, self-reported personality traits, and performance on a computerized approach/avoidance task. As expected, internalizing SDB had a medium negative association with emotional stability and medium positive association with

negative urgency, and small positive associations with fun-seeking, behavioral inhibition, extraversion, and lack of perseverance. Disinhibited externalizing SDB had a medium positive associations with fun-seeking, small positive associations with extraversion, negative urgency, sensation seeking, and lack of premeditation, and small negative associations with agreeableness and behavioral inhibition. Antagonistic externalizing SDB had medium positive associations with sensation seeking and fun-seeking, small positive associations with negative urgency, drive, extraversion, and taskbased approach motivation, and small negative associations with conscientiousness, reward responsivity, and behavioral inhibition.

Results support the potential of a HiTOP-informed model to advance research and treatment of co-occurring SDB.

Poster 12

eLi12: A new method to estimate 12-hour lithium levels: An early health economic assessment on optimizing lithium treatment via eLi12

<u>Ole Köhler-Forsberg</u>^{1,2},*; Christian L. Kraft³, MD; Camilla R. Birch⁴; Lars H. Ehlers⁴

¹Psychosis Research Unit, Aarhus University Hospital - Psychiatry, Denmark

²Department of Clinical Medicine, Aarhus University, Denmark

³Departments of Affective Disorders, Aarhus University Hospital - Psychiatry, Denmark

⁴Nordic Institute of Health Economics (NIHE), Aarhus, Denmark <u>karkoe@rm.dk</u>

Abstract: 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 mixedcosting 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.

Poster 13

Five-factor personality traits and Functional Somatic Disorders: a systematic review and metaanalysis

<u>Thomas Tandrup Lamm</u>^{1,2}, Victoria Von Schrottenberg³, Anneline Rauch^{1,2}, Bo Bach⁴, Heidi Frølund Pedersen^{1,2}, Mette Rask^{1,2}, Eva Ørnbøl^{1,2}, Kaare Bro Wellnitz^{1,2}, Lisbeth Frostholm^{1,2}

¹Research Clinic for Functional Disorders and Psychosomatics, Aarhus University Hospital,

²Department of Clinical Medicine, Aarhus University

³Institute of General Practice and Health Services Research, Technische Universität München

⁴Center for Personality Disorder Research, Region Zealand <u>THLAMM@rm.dk</u>

Abstract: Background: Personality traits are assumed to play an important role for Functional Somatic Disorders (FSD), but existing reviews use narrow operationalizations of FSD, incongruent personality measures, and have several methodological limitations. Objectives: The aim of the current study is to conduct a systematic review and meta-analysis of the association between Five-factor model (FFM) personality traits and FSD.

Methods: Data were drawn from systematic searches in PsycInfo, PubMed and Embase. Studies had to include

eligible FSD group(s), eligible control group(s) and assess FFM traits. Results were analyzed using randomeffects models, and heterogeneity explored using subgroup analyses.

Results: A total of k=6692 records were screened, and k=52 included. Analyses showed that compared to healthy/unspecified controls, FSD cases were higher on neuroticism (k=46, g=.72) and lower on extraversion (k=31, g= -.41) and agreeableness (k=15, g= -.22). Compared to somatically ill controls, FSD cases were higher on neuroticism (k=9, g=0.26) and agreeableness (k=4, g=.43), but did not differ on extraversion (k=6, g=-.17). No differences were found for conscientiousness and openness. Significant heterogeneity was observed for most comparisons, and was only moderated by the method used to define FSD. Only 3 studies included psychiatric controls. These studies examined associations for neuroticism but heterogeneity was too high to draw conclusions.

Conclusion: Significant differences on neuroticism, agreeableness, and extraversion were found when comparing FSD cases with healthy/unspecified and somatic controls. This review illustrates the need for more knowledge the causal role and clinical impact of FFM traits for FSD.

Poster 14

Decoding Addiction Through DNA Methylation and Neuroimaging: A Longitudinal Study on Developmental Predisposition

<u>Leonardo Melo Rothmann</u>¹, Alexandre Rosa Franco^{2,3,4}, Simon Fristed Eskildsen⁵, Per Qvist⁶, Rodrigo Grassi-Oliveira1⁷

¹Aarhus University - Translational Neuropsychiatry Unit (Denmark) ²New York University (United States of America)

³Child Mind Institute (United States of America)

⁴Nathan S Kline Institute for Psychiatric Research (United States of America)

⁵Aarhus University - Center of Functionally Integrative Neuroscience (Denmark)

⁶Aarhus University - Department of Biomedicine (Denmark) ⁷Pontifical Catholic University of Rio Grande do Sul (Brazil) <u>leo@clin.au.dk</u>

Abstract: Substance Use Disorders (SUDs) exhibit consistent MRI changes in gray and white matter, along with marked alterations in DNA methylation, possibly linked to addiction severity and early life stress. Current research often uses limited techniques and data extraction methods. Determining the roles of DNA methylation and neural markers, whether as predictors, moderators, or mediators, is crucial for advancing research. The Neuroimaging Epigenetics approach aims to bridge these gaps by exploring epigenetic markers' relationship with in vivo brain activity and their potential to predict behavioral tendencies. Unraveling

the developmental routes to addiction via neuroimaging and epigenetic findings is essential to develop hypothesis[1]driven inquiries and illuminate future research directions. We aim to create models (Signature and Mechanism Model) using the Neuroimaging Epigenetics approach by connecting blood DNA methylation to specific brain regions and clinical aspects of SUD. Our investigation will analyze these outcomes from dimensional and categorical perspectives to enable tailored risk assessment and informed interventions. We hypothesize that certain methylation sites are intricately linked with specific neural networks in our SUD participants, influencing functional and structural aspects. We suggest that susceptibility to SUD arises from epigenetic variations and neural changes during youth, with adult influences accentuating these vulnerabilities. The first step will be based on the Coccaine Study (Figure 1A), a unique longitudinal biopsychosocial study of Brazilian adults with Cocaine Use Disorder (CUD) to investigate neurobiological changes in CUD over time with an ongoing second wave. The second step will be based on the Brazilian High-Risk Cohort Study (BHRC) (Figure 1B). BHRC is a rich longitudinal biopsychosocial dataset of schoolage children (now adults) from Brazil that aims to investigate trajectories of psychopathology and neurodevelopment. BHRC has three waves of data collection. BHRC and Coccaine performed a comprehensive cognitive, clinical, and environmental assessment. Moreover, Magnetic Resonance Imaging (MRI) and blood samples were collected in all sessions.

Poster 15

Infancy predictors of functional somatic symptoms in pre- and late adolescence

Lina Münker^{1,2,3}, Martin Køster Rimvall^{4,5}, Lisbeth Frostholm^{2,3}, Eva Ørnbøl^{2,3}, Kaare Bro Wellnitz^{2,3}, Pia Jeppesen^{4,5,6}, Judith Rosmalen⁷, Charlotte Ulrikka Rask^{1,3}

¹Department of Child and Adolescent Psychiatry, Aarhus University Hospital Psychiatry, Denmark

²Department of Functional Disorders and Psychosomatics, Aarhus University Hospital, Denmark

³Department of Clinical Medicine, Aarhus University, Denmark

⁴Department of Child and Adolescent Psychiatry, Copenhagen University Hospital - Psychiatry Region Zealand, Roskilde, Denmark ⁵Child and Adolescent Mental Health Centre, Copenhagen University Hospital - Mental Health Services CPH, Copenhagen, Denmark

⁶Department of Clinical Medicine, Faculty of Health and Medical Sciences, University of Copenhagen, Denmark

⁷University of Groningen, University Medical Center Groningen, Departments of Psychiatry and Internal medicine, Groningen, Netherlands

linamu@rm.dk

Abstract: Purpose: Childhood vulnerabilities and early familial adversity might contribute to the development of Functional somatic symptoms in youth. Physiological

regulatory problems, including problems in the area of sleeping, feeding, and tactile reactivity, have been associated with impairing FSS at the preschool age. We aimed to extend findings by examining not only the association of physiological regulatory problems, but also emotion dysregulation and contact problems in infancy with FSS in pre- and late adolescence.

Methods: Standardized behavioral assessments in infancy and self-report questionnaire data in adolescence 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 regression analyses were performed to examine the association between infancy factors and FSS in pre- and late adolescence.

Results: Only infancy physiological regulatory problems were significantly associated with preadolescent FSS (b = 0.38, 95% CI [0.14, 0.62]) also when accounting for maternal postpartum psychiatric illness and family adversity. This association was attenuated and became non-significant for late adolescent FSS.

Conclusion: Infancy physiological regulatory problems may represent early signs of a dysregulated stress system, and might play an important role in the etiology of FSS from an early age. Implications for early FSS prevention could include testing parent-mediated interventions to promote infants' regulation of sleep, feeding and tactile reactivity.

Poster 16

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

<u>Laura Amalie Poulsen Dam</u>^{1,2}, Stina Lou^{2,3}, Eva Skovslund Nielsen^{1,2}, Karen Hansen Kallesøe¹, Helene Søgaard Singh², Marianne Bonnert^{4,5}, Maria Lalouni⁴, Charlotte Ulrikka Rask^{1,2}

¹Department of Child and Adolescent Psychiatry, Aarhus University Hospital Psychiatry, Denmark.

²Department of Clinical Medicine, Aarhus University, Denmark.

³DEFACTUM, Central Denmark Region, Denmark.

⁴Department of Clinical Neuroscience, Karolinska Institute, Sweden. ⁵Department of Medical Epidemiology and Biostatistics, Karolinska Institute, Sweden.

laurdm@rm.dk

Abstract: Abstract not available.

Poster 17

IMMUNE ACTIVATION PRECEDES THE SYNAPTIC VESICLE GLYCOPROTEIN 2A DENSITY LOSS IN THE STRIATUM OF A PREFORMED FIBRIL MOUSE MODEL

<u>Caroline Cristiano Real</u>^{1,2}, Majken B Thomsen^{1,2}, Benny Bang-Andersen³, Florence Sotty⁴, Anne M Landau^{1,2}

¹Department of Nuclear Medicine and PET, Department of Clinical Medicine, Aarhus University, Aarhus, Denmark.

²Translational Neuropsychiatry Unit, Department of Clinical Medicine, Aarhus University, Aarhus, Denmark.

³Medicinal Chemistry and Translational DMPK, H. Lundbeck A/S, 9 Ottiliavej, Copenhagen-Valby, Denmark.

⁴Neuroscience Research, H. Lundbeck A/S, 9 Ottiliavej, Copenhagen-Valby, Denmark.

caroline.real@clin.au.dk

Abstract: Not available.

Poster 18

Long-term risk of psychiatric disorders following neonatal, invasive Group B Streptococcus disease. A population-based cohort study

<u>Malene Risager Lykke¹</u>, Henrik Toft Sørensen¹, Joy Elisabeth Lawn², Erzsébet Horváth-Puhó¹

¹Department of Clinical Epidemiology, Aarhus University and Aarhus University Hospital, Aarhus, Denmark.

²Faculty of Epidemiology and Population Health, London School of Hygiene & Tropical Medicine, London, United Kingdom. mrl@clin.au.dk

Abstract Background: Long-term data om neurodevelopmental outcomes following neonatal, invasive Group B Streptococcus disease (iGBS) is sparse. We aimed to examine the association between infant iGBS (sepsis or meningitis) and the risk of psychiatric disorders (PDs) until adolescents.

Methods: We conducted a population-based cohort study using health care data from 1997 through 2018 in Denmark. Exposed children had hospital-diagnosed iGBS during the first 89 days of their life. A general population comparison cohort was randomly sampled and matched 10:1 to the exposed cohort by sex, year of birth and gestational age.

PDs were defined by the International Classification of Diseases, Tenth Revision codes (ICD-10-codes). Cumulative risk (CR) of PD was calculated by treating death as a competing event. Cox proportional hazards regression was used to compute hazard ratios (HRs) and the associated 95% confidence intervals (CIs).

Results: The CR of PDs after 18 years of follow-up from index date was 20.4% (95% CI 17.6 – 23.4) for the iGBS cohort compared to 15.4% (95% CI 14.6 – 16.2) in the comparison cohort. 13% of the exposed children had more than one PD registered after 18 years of follow up.

iGBS disease was associated with increased risk of nervous and stress-related disorders (HR 1.75 (95% CI 1.37-2.24)), intellectual disabilities (HR 1.54 (95% CI 0.98-2.42), mental developmental disorders (HR 1.31 (95% CI 1.02-1.71)) and behavioral and emotional disorders (HR 1.46 (95% CI 1.18 - 1.81)). Premature born children affected by iGBS had an IR of 14.97 PY (10.56–19.02) compared to 10.59 PY (95% CI 9.46–11.72) for the comparison cohort members born premature after 18 years of follow-up. The HR was 1.40 (95% CI 1.03-1.90). The risk of PD between mothers with a low educational level and mothers with a high educational level was nearly 25%.

Conclusion: Invasive Group B Streptococcus disease is associated with a long-term increased risk of mental health disorders in later childhood. Premature birth, and low maternal education modified the association.

Poster 19

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

<u>Eleni Sia</u>¹, Pedro Henrique Gobira¹, Samia Joca², Cristiana Cruceanu³, Timothy Bredy⁴, Rodrigo Grassi-Oliveira¹

¹Translational Neuropsychiatry Unit, Aarhus University, Denmark ²Department of Biomedicine, Aarhus University, Denmark

³Karolinska Institutet, Sweden

⁴Queensland Brain Institute, Australia esia@clin.au.dk

Abstract: 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. Δ 9-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 Δ 9-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 animal and brain organoids models. We will implement a whole genome single cell-approach to explore epigenetic modifications within neurons in the PFC and Hippocampus in both models. 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. The extent of the phenotypic and molecular profile differentiation between male and females will also be explored offering a better understanding of the relevant sex-dependent neurobiological pathways.

Poster 20

Internet-CBT for children and adolescents with functional abdominal pain disorders: Insights from a single-case experimental design study

<u>Eva Skovslund Nielsen</u>^{1,2}, Karen Hansen Kallesøe¹, Maria Lalouni³, Anders Helles Carlsen¹, Lisbeth Frostholm^{1,4}; Marianne Bonnert³; Charlotte Ulrikka Rask^{1,2}

¹Department of Child and Adolescent Psychiatry, Aarhus University Hospital Psychiatry

²Department of Clinical Medicine, Aarhus University

³Department of Clinical Neuroscience, Karolinska Institutet

⁴The Research Clinic for Functional Disorders and Psychosomatics, Aarhus University Hospital

eniels@rm.dk

Abstract: Not available.