

## Nationwide time trends in dispensed prescriptions of psychotropic medication for children and adolescents in Denmark

Steinhausen, Hans-Christoph E.; Bisgaard, Charlotte

*Publication date:*  
2014

*Document Version*  
Early version, also known as pre-print

[Link to publication from Aalborg University](#)

*Citation for published version (APA):*  
Steinhausen, H.-C. E., & Bisgaard, C. (2014). *Nationwide time trends in dispensed prescriptions of psychotropic medication for children and adolescents in Denmark*. Poster presented at NordCAP, Middelfart, Denmark.

### General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal -

### Take down policy

If you believe that this document breaches copyright please contact us at [vbn@aub.aau.dk](mailto:vbn@aub.aau.dk) providing details, and we will remove access to the work immediately and investigate your claim.



# **Nordic Child and Adolescent Psychiatric (NordCAP) Research Meeting**

*September, 10-11, 2014*

*Middelfart, Denmark*

## ***Convenor***

Prof. Hans-Christoph Steinhausen

## ***Representatives of the Nordic Countries***

Prof. Niels Bilenberg, Denmark

Prof. Kirsti Kumpulainen, Finland

Dr. Bertrand Lauth, Iceland

Dr. Kerstin Malmberg, Sweden

Dr. Torunn Stene Nøvik, Norway

Prof. Kerstin Jessica Plessen, Denmark

**Wednesday, September 10, 2014**

**9:00 – 10:30 Welcome and Keynote lecture:** Translational studies in child and adolescent psychiatry (Professor Jan Buitelaar, Nijmegen NL)

*10:30 - 11:00 Coffee break*

**11:00 - 12:30 Main theme 1: Schizophrenia and related problems**

- (1) Quetiapine versus aripiprazole in children and adolescents with psychosis - the randomised, blinded clinical Tolerability and Efficacy of Antipsychotics (TEA) trial. (Anne Katrine Pagsberg et al., Copenhagen)
- (2) The Danish High Risk and Resilience Study (Kerstin J. Plessen et al., Copenhagen; presenters: Kerstin J. Plessen and Anne A.E. Thorup, Copenhagen)
- (3) Overlapping and disease specific aspects of impulsivity in children and adolescents with schizophrenia spectrum disorders or Attention-Deficit/Hyperactivity Disorder (Jens Richardt Jepsen et al., Copenhagen)
- (4) Risk of diabetes in children and adolescents exposed to antipsychotics: a nationwide 12-year case-control study (René Ernst Nielsen et al., Aalborg; presenter: Hans-Christoph Steinhausen)

*12:30 – 14:00 Lunch*

**14:00 – 15:00 Poster session (see list of presentations at the end of the programme)**

**15:00 – 16:30 Main theme 2: Autism spectrum disorders**

- (1) The Roots of Autism and ADHD study Sweden (RATSS): the cognitive phenotype in discordant twins (Charlotte Willfors et al., Stockholm)
- (2) Association between siblings' psychiatric disorders and Autism Spectrum Disorders – A population-based study (Elina Jokiranta et al., Turku)
- (3) Neurocognitive alterations in ASD (Cathriona Cantio et al., Odense)
- (4) Time trends over 16 years in incidence rates of autism spectrum disorders across the lifespan based on nationwide Danish register data (Christina Mohr Jensen et al.; presenter: Marlene Briciet Lauritsen, Aalborg )

*16:30 - 17:00 Coffee break*

## **17:00 – 18:30 Depression and related problems**

- (1) The Youth and Mental Health Study - the development of depression symptoms from early adolescent to young adult age (Anne Mari Sund et al., Trondheim)
- (2) Time trends in lifetime incidence rates of first - time diagnosed bipolar and depressive disorders across 16 years in a Danish nationwide study (Christina Mohr Jensen et al., Aalborg)
- (3) Youth, suicide attempts and level of education – A Danish historical register based cohort study of the outcome of suicide attempt (Erik Christiansen, Odense)
- (4) Emergency psychiatric care for children and adolescents in Iceland (Bertrand Lauth, Reykjavik)

*20:00 Dinner/Social event*

**Thursday, September 11, 2014**

**9:00 – 10:30 Main theme 2: ADHD**

- (1) The development of WHO ICF core sets for ASD and ADHD (Elles de Schipper et al., Stockholm)
- (2) Validation of Diagnoses of Hyperkinetic Disorders in Children and Adolescents in the Danish Psychiatric Central Research Registry in 1995-2005 (Christina Mohr Jensen et al., Aalborg)
- (3) Polysomnography (PSG) and Multiple Sleep Latency Test (MSLT) in Children with ADHD (Anne Virring-Soerensen et al., Aarhus)
- (4) SAFARI (Study of Preschool ADHD Risk Indicators) (Niels Bilenberg et al., Odense)

*10:30 - 11:00 Coffee break*

**11:00 – 12:30 Main theme 3: Obsessive compulsive disorders**

- (1) The Nordic Long-term OCD Treatment Study (NordLOTS): Rationale and methods (Tord Ivarsson., Oslo)
- (2) The Nordic Long-term OCD Treatment Study (NordLOTS). Step 1: CBT outcome and predictors (Nor Christian Torp and Tord Ivarsson [presenter], Oslo)
- (3) Continued cognitive behavior therapy versus sertraline for children and adolescents with obsessive-compulsive disorder that were non-responders to cognitive behavior therapy - A randomized controlled trial (Gudmundur Skarphedinsson et al., Oslo)
- (4) The Genetic Aspects of Obsessive Compulsive Disorder (OCD) (Judith Becker Nissen et al., Aarhus)
- (5) Child and adolescent OCD symptom patterns: A factor analytic study (David Rurik Martinsson et al., Aarhus)
- (6) Discussant: Kerstin J. Plessen

*12:30 – 14:00 Lunch*

**14:00 – 15:30 Discussion groups and planning of next meeting**

15:30 End of the meeting

# List of poster presentations

*(listed alphabetically according to the surname of the first author)*

## **Dysregulation among infants and toddlers and development of mental health problems at 5-6 years. A longitudinal cohort study of risk and resilience factors for progression to ADHD**

Jette Asmussen, Niels Bilenberg

## **Social Cognition in Children and Adolescents with Anorexia Nervosa**

Mette Bentz, Jens Richardt Jepsen, Kerstin J. Plessen

## **Does type and debut of day-care influence early behavioral profile?**

Kristine Borg, Niels Bilenberg

## **Parental age and the risk of attention-deficit hyperactivity disorder (ADHD)**

Roshan Chudal, Petteri Joelson, Susanna Leivonen, Susanna Hinkka-Yli-Salomäki, David Gyllenberg, Venla Lehti, Alan S. Brown, Andre Sourander

## **Cognitive and Behavioral Control in Children with Tourette Syndrome**

Heike Eichele, Tom Eichele, Ingvar Bjelland, Marie Falstad Høvik, Lin Sørensen, Heidi van Wageningen, Marius Kalsås Worren, Kenneth Hugdahl, Kerstin J. Plessen

## **Visual perception, processing speed and short-term memory based on the theory of visual attention: deficits in 7 year-old children at high risk of developing schizophrenia or bipolar disorder in the Danish high risk and resilience study - VIA 7**

Nicoline Hemager, Jens Richardt Jepsen, Signe Vangkilde, Anne A. E. Thorup, Camilla Jerlang Christiani, Ditte Ellersgaard, Katrine Søborg Spang, Anne Ranning, Birgitte Klee Burton, Aja Greve, Ditte Lou Gantriis, Kate Kold Andreasen, Mette Skjærbæk, Anne Søndergaard, Marianne Melau, Ole Mors, Merete Nordentoft, Kerstin J. Plessen

## **The impact of individual factors on the efficacy and compliance of drug treatment of ADHD in children – Presentation of study design**

Tine Houmann, Kristine Kaalund Jørgensen, Marie Bang Hebsgaard, Henrik Berg Rasmussen, Pia Jeppesen, Anne Katrine Pagsberg, Kerstin J. Plessen

## **Time trends in incidence rates of diagnosed attention-deficit/hyperactivity disorder over sixteen years in a nationwide Danish registry study**

Christina Mohr Jensen, Hans-Christoph Steinhausen

## **Comorbid mental disorders in children and adolescents with attention-deficit/hyperactivity disorder in a large nationwide study**

Christina Mohr Jensen, Hans-Christoph Steinhausen

## **Maternal Smoking During Pregnancy as an Independent Risk Factor of Comorbid Attention-Deficit Hyperactivity Disorder and Conduct Disorder in a Nationwide Register-Based Study**

Petteri Joelsson, Roshan Chudal, Auli Suominen and Andre Sourander

## **The relationship between CES1 genotype and methylphenidate response in children with ADHD. Clinical characteristics of children included in INDICES WP 6.**

Kristine Kaalund-Jørgensen, Tine Houmann, Marie B Hebsgaard, Anne K. Pagsberg, Kerstin J Plessen, Jørgen H Dyrborg, Henrik B Rasmussen, Pia Jeppesen

**Motivation and its impact on self-regulatory control in children with Tourette syndrome**

Katrine Maigaard, Damian Herz, Lone Kelkjær, Liselotte Skov, Oliver James Hulme, Hartwig Roman Siebner, Kerstin J. Plessen

**High-dose treatment with stimulants - risk or benefit? Case reports in a Swedish clinical population**

Kerstin Malmberg, Ulrika Åhlund, Håkan Jarbin

**Cognitive behavioural group therapy in adolescents with ADHD**

Torunn Stene Nøvik, Anne Mari Sund, Per Hove Thomsen

**Performance monitoring and perfectionism in adolescents with current and adolescents with previous anorexia nervosa**

Tine Pedersen, Alessandro Calamuneri, Estelle Raffin, Norbert Brüggemann, Kristoffer Madsen, Julie Hagstrøm, Tim Dyrby, Mette Bentz, Hartwig Siebner, Kerstin J. Plessen

**Multisite pain and resilience factors in adolescents with behavioural and emotional problems: The Young-HUNT study.**

Marit Skrove, Pål Romundstad, Marit S. Indredavik

**Emotion regulation in children at high risk for bipolar disorder or schizophrenia**

Katrine Spang, Carsten Obel, Jens Richardt Jepsen, Anne Thorup, Nicoline Hemager, Anne Ranning, Ditte Ellersgaard, Birgitte Klee Burton, Camilla Christiani, Mette Skjærbæk, Anne Søndergaard, Aja Greve, Ditte Gantriis, Ole Mors, Merete Nordentoft, Kerstin J. Plessen

**Nationwide time trends in dispensed prescriptions of psychotropic medication for children and adolescents in Denmark**

Hans-Christoph Steinhausen, Charlotte Bisgaard

**Substance use disorders in association with attention-deficit/hyperactivity disorder, co-morbid mental disorders, and medication in a nationwide sample**

Hans-Christoph Steinhausen, Charlotte Bisgaard

**Family aggregation and risk factors in major mental disorders over three generations in a nation-wide study**

Hans-Christoph Steinhausen, Helle Jakobsen, Dorte Helenius, Charlotte Bisgaard, Povl Munk-Jørgensen, Kathleen Merikangas, Michael Strober

**Attachment, coping and depression in adolescence**

Anne Mari Sund, Tea Agerup, Stian Lydersen, Jan Wallander

**Sleep and daily functioning in children with ADHD**

Anne Virring Sørensen, Rikke Lambek, Lene Ruge Møller, Poul Jørgen Jennum, Per Hove Thomsen

**Characteristics of children with functional somatic symptoms referred to the child and adolescent mental health services**

Simone Tøt-Strate, Charlotte Ulrikka Rask, G. Dehlholm

# Abstracts

(listed alphabetically according to the surname of the first author)

## **Dysregulation among infants and toddlers and development of mental health problems at 5-6 years. A longitudinal cohort study of risk and resilience factors for progression to ADHD**

*Jette Asmussen, Niels Bilenberg*

**Objectives:** The main purpose of this study is to identify whether hereditary disposition in combination with a wide range of biological and social factors (prenatal, antenatal and in the beginning of life) are associated with a higher prevalence of dysregulation problems at age 2½ years. Children will be re-assessed at age 5 years to examine factors moderating outcome (ADHD and other mental disorders).

**Methods:** The children in this study are from the prospective Odense Child Cohort which includes 2500 pregnant women in the municipality of Odense in 2010 to 2012 and their families. During pregnancy and in the first 4 years, participants (mothers, fathers, and children) regularly respond to questionnaires and donate biological material. Additional data on social issues and child development is provided by visiting nurses and the municipality. Data on parental diagnosis and medication is taken from national registers. Information on child dysregulation and psychopathology is collected by use of the CBCL/c-TRF 1½-5 at the ages 2½- and 5 years.

We compare children with and without dysregulation on a broad range of variables to study the association of risk factors and outcome.

**Results:** Collection of data started in January 2010 and the complete data set up to 2½ years of age will be available for analysis in the summer of 2015. Preliminary results will be shown at the meeting.

**Discussion:** The strength of this study is that all information is collected prospectively from multiple informants and that there is biological material from each single child.

At 10 weeks of their pregnancy, all pregnant women in the municipal of Odense were invited to participate in the cohort and some 60 % accepted the invitation for participation in the study. Attrition analyses will consider any major systematic sample bias.

It is expected that the results of this study will provide information on associations between various risk factors and will point to resilience factors for the development of dysregulation problems in early childhood and of specific mental health problems at preschool age.

## **Social Cognition in Children and Adolescents with Anorexia Nervosa**

*Mette Bentz, Jens Richardt Jepsen, Kerstin J. Plessen*

**Objectives:** Social cognition has not yet been studied systematically in adolescents with anorexia nervosa. Our aim is to determine and describe the character of possible social cognitive deficits through neuropsychological testing of young people recovered from anorexia nervosa compared with patients in an acute phase of the disorder and with healthy controls.

**Methods:** We will test 30 participants in each group with a battery of standard clinical diagnostic mapping and a more general neuropsychological testing (IQ, executive functions), and with a set of 4 social cognitive tasks tapping into different subdomains of social cognition (emotional processing, social knowledge, attributional style, theory of mind). We will match participants according to age, intelligence and socioeconomic status on the group level

We hypothesize that recovered AN-patients show a social cognitive performance that falls between currently ill patients and healthy controls. We further hypothesize that if AN-patients and recovered patients show signs of social cognitive deficits then these deficits will correlate with reduced mental flexibility and superior detail processing.

**Results:** Data collection will end by September 2014. We will present preliminary results of data analyses.

**Discussion:** The existing literature suggests that subtle social cognitive deficits persist in adults recovered from AN. If this finding is confirmed in recovered adolescents, this will point to the notion that impairment in this domain may be a trait feature of individuals with AN, and may help to understand underlying factors of the disorder. However, with our analyses we cannot disentangle pre-existing traits in vulnerable young people from changes that may express as an impairment representing a consequence of having had the disorder.

If on the other hand this study does not confirm in adolescents the deficits found in recovered adults in other studies, this will support a view on such deficits as illness-related consequences and warrant further investigation into the developmental path of these deficits.



## Does type and debut of day-care influence early behavioral profile?

*Kristine Borg, Niels Bilenberg*

**Objectives:** ADHD is the most prevalent childhood psychiatric disorder and there is a great need for identification of possible causal factors.

The aetiology of ADHD is far from clear, especially in the child's early years the causes of ADHD or early signs of ADHD seem poor understood.

In Denmark children spend 33 hours/week in an institution and the average age of debut is a little before age one year.

We study the association between the type and debut of day-care in relation to the development of early signs of ADHD in infants. By comparing the CBCL:1½-5 and C-TRF-responses at age 2-3 y with institutional data, and other already known risk factors, the aim of this project is to examine the association between day-care career and debut of early signs of ADHD.

**Methods:** In a cross-sectional study (birth cohort) ADHD symptoms in 2-3-year-old toddlers are collected by use of CBCL 1½-5 and the C-TRF (N is about 1,500). The children's behavioural profile, including early signs of ADHD is compared with data about the type and debut of day-care for each child from Odense Kommune (OK). Only the first part of the cohort has been analysed – and the presentation include 478 children with CBCL 1½-5 answers and 287 children with both CBCL 1½-5 and CTR-F answers.

**Results** (preliminary): So far the results show no significant association between the types of day-care and Total Problem Score ( $p=0,087$ ) or ADHD score ( $p=0,089$ ). Also, no significant association between the age of debut,  $\pm 1$  year, and total problem score ( $p=0,252$ ) or ADHD score were found ( $p=0,294$ ).

**Discussion:** We found no significant association between types of day-care, age at day-care-debut and ADHD score.

Further analyses will stratify for parent educational level and for information about psychiatric disorders.

## Cognitive Alterations In Autism Spectrum Disorders (ASD)

*Cathriona Cantio, S. White, G. Madsen, Jens Richardt Jepsen, Niels Bilenberg*

**Objectives:** Cognitive deficits in children with Autism Spectrum Disorders (ASD) are well known. The objective of this study was to look at cognitive subgroups and examine how cognition may be associated with core autistic behaviours.

**Methods:** Forty children diagnosed with an ASD together with 38 neurotypically developed (NTD) children were all tested with a comprehensive 4-hour neuropsychological battery covering the cognitive domains: Theory of Mind (ToM), Executive Functions (EF) and Central Coherence (CC). All children were aged between 8 and 12 years and had IQs between 75 and 145. Core ASD symptoms were assessed with the ADOS and ADI-R, and comorbid symptoms were rated by parents (CBCL) and teachers (TRF).

**Results:** We found that the ASD and NTD groups differed significantly on the ToM-composite and EF-composite but not on the CC-composite. No correlations between these three composites were found. The ASD cases were divided into (relatively) good and poor performers on each of the 3 cognitive composites and these groups were compared. The poor ToM-group showed greater parent-reported anxiety and internalizing behaviour but did not differ from the good ToM-group in terms of their ASD symptoms. The poor EF-group displayed more severe verbal and non-verbal communication symptoms on the ADI-R, as well as greater difficulties using non-verbal means to regulate social interactions and more severe stereotyped and repetitive motor mannerisms. Surprisingly, this group also presented with fewer conduct problems according to both teacher and parent ratings.

**Discussion:** ToM and EF alterations are characteristic of individuals with ASD and differentiate this population from NTD individuals. However, there also appears to be cognitive heterogeneity within the autism spectrum, with only a proportion of individuals displaying each cognitive abnormality. EF difficulties appear to predict ASD symptoms whilst ToM difficulties predict comorbid symptoms.

### Youth, suicide attempts and level of education – A Danish historical register based cohort study of the outcome of suicide attempt

*Erik Christiansen*

**Objectives:** The literature provides us with evidence, that poor school performance in adolescence is associated with raised risk for suicide attempts. The aim of this study was to estimate the unbiased effect from suicide attempt on level of education in early adulthood.

**Methods:** We used a cohort design of all individuals born in Denmark, in the period 1983-1989 and who had finished 9 years of primary school. A total of 355,725 offspring were included. Historical register data and extended Cox proportional hazard model were used to estimate associations. The outcome factor was a dichotomized factor of “secondary education”.

**Results:** Suicide attempters were significantly less likely to finish a secondary education before the age of 29 years. Crude estimate of hazard ratio (HR) was 0.377 and adjusted HR 0,877. The association was analysed in specific subgroups and it seems that suicide attempt is not an independent risk factor for not finishing a secondary education in youth with mental illness.

**Discussion:** A suicide attempt is an indicator for subsequent low level of education in youth. The significant difference in crude and adjusted HR indicates that association between suicide attempts and low level of education is confounded by other factors, as mental illness, parental level of education etc. Undiagnosed mental illness might bias our results.

### Parental age and the risk of attention-deficit hyperactivity disorder (ADHD)

*Roshan Chudal, Petteri Joelson, Susanna Leivonen, Susanna Hinkka-Yli-Salomäki, David Gyllenberg, Venla Lehti, Alan S. Brown, Andre Sourander*

**Objectives:** The aim of this study is to explore the association between both paternal and maternal age in relation to ADHD.

**Methods:** In this nested case-control study, we identified 10,425 ADHD cases born in Finland during 1991-2005 and diagnosed between 1995 and 2011 and 40,141 controls matched on sex, date and place of birth, from nationwide population based registers. Conditional logistic regression was used to examine the association adjusting for potential confounding due to parental psychiatric history, maternal socio-economic status, marital status, maternal smoking during pregnancy, number of previous births and birth weight for gestational age.

**Results:** An association was seen between young parental age and the risk of ADHD. In addition, a decreased risk was seen with increasing maternal age. Fathers younger than 20 years had a 55 % increased risk of having offspring with ADHD as compared to fathers aged 25-29 years. Mothers of the same age group had 41 % increased risk.

**Discussion:** ADHD was associated with having both fathers and mothers young at the time of birth. Advanced paternal age was not associated with offspring ADHD, but advanced maternal age was inversely associated with ADHD. These findings, when considered in context of the effects of parental age on other psychiatric conditions suggest that the changing demographics of parenthood may have varying influence on different mental health outcomes.

## Cognitive and Behavioral Control in Children with Tourette Syndrome

Heike Eichele, T. Eichele, I Bjelland, M. F Høvik, L. Sørensen, H. van Wagoningen, M.K. Worren, K Hugdahl, Kerstin Plessen

**Objectives:** TS is a neurodevelopmental disorder characterized by vocal and motor tics with an onset of tics at the age of around six years and a maximum of motor and vocal tics at ten to twelve years of age, whereas tics gradually tend to decline in their intensity during or after puberty. Circumstantial evidence from neuropsychological studies and from studies using structural Magnetic Resonance Imaging (sMRI) suggests that this decline of symptoms relates to the development of self-regulatory control in adolescents during that age period; thus we hypothesize that Cognitive control is an important factor for the clinical impact of tics in children with Tourette Syndrome (TS). To this end, we measured brain activity with electrophysiology related to cognitive control in 25 children with TS compared with 35 healthy control children and 40 children with ADHD aged 8-12 years at time of inclusion.

**Methods:** Participants performed a PC-based modified Eriksen-Flanker task while recording EEG. On compatible trials, arrows pointed to the same direction (<<<<<<<, >>>>>>>). On incompatible trials flanker arrows and target arrow pointed to different directions. (<<<<<<<, >>>>>>>). Participants were instructed to respond to the direction of the target arrow while ignoring the flanker arrows by pressing the left or right mouse button.

Brain activity was continuously recorded from 34 scalp EEG channels. Channels from each dataset were subjected to temporal ICA using infomax, implemented in EEGLAB, estimated 30 components after PCA compression. In order to cluster components for further analysis and identify the most relevant to conflict and error processing, we used automated sorting routines.

**Results:** We expect differences in single trial event - related EEG responses, namely that the stimulus-locked N2 and the response-locked error-related negativity (ERN) differ between children with TS, children with ADHD, and healthy peers. The within-group variability of these measures will correlate with symptom load and neuropsychological features indicative of control functions and will give an indication of underlying neurobiological group differences that may be due to adaptive phenomena in the TS group with the aim to suppress their tics.

**Discussion:** Strategies for analyses and preliminary results will be discussed at the poster presentation.

## Visual perception, processing speed and short-term memory based on the Theory of Visual Attention: Deficits in 7 year-old children at high risk of developing schizophrenia or bipolar disorder in The Danish High Risk and Resilience Study - VIA 7

Nicoline Hemager, Jens Richardt Jepsen, Signe Vangkilde, Anne A. E. Thorup, Camilla Jerlang Christiani, Ditte Ellersgaard, Katrine Søborg Spang, Anne Ranning, Birgitte Klee Burton, Aja Greve, Ditte Lou Gantriis, Kate Kold Andreasen, Mette Skjærbæk, Anne Søndergaard, Marianne Melau, Ole Mors, Merete Nordentoft, Kerstin J. Plessen

**Objectives:** The aim of this sub study is to measure attentional functioning - specifically visual processing speed and capacity of visual short-term memory - in children at genetic high risk for developing schizophrenia (SZ) or bipolar disorder (BD).

**Methods:** We are establishing a stratified cohort of 500 children aged 7 with either 0, 1 or 2 parents with SZ or BD. In this sub study of 30 children from each of the three subgroups we assessed visual attention using the instrument TVA-based Whole Report based on Bundesen's Theory of Visual Attention.

**Results:** Data collection in this sub study has been completed by April 2014 and data analyses will commence in May 2014.

**Discussion:** We expect that children at genetic high risk for SZ will show more severe impairments compared with children at genetic high risk for BD. Whereas the latter group may show more deficits in visual attention than children of parents without BD and SZ.

## The impact of individual factors on the efficacy and compliance of drug treatment of ADHD in children – Presentation of study design

*Tine Houmann, Kristine Kaalund Jørgensen, Marie Bang Hebsgaard, Henrik Berg Rasmussen, Pia Jeppesen, Anne Katrine Pagsberg, Kerstin J. Plessen*

**Objectives:** Despite of a significant effect of methylphenidate (MPH) on ADHD core symptoms, behaviour and learning, clinical studies indicate that adherence to treatment is poor. Parental reports of inadequate treatment effectiveness or adverse effects are often stated as reasons for discontinuation of medication, but overall, our knowledge of factors associated with treatment efficacy and adherence is limited. Deficient emotional self-regulation (emotional dysregulation), is often a problem in ADHD, and may be a significant marker of impairment and MPH treatment failure. Emotional dysregulation (ED) is characterized by a specific profile on the Child Behavior Checklist (CBCL). In several studies ED has been associated with more severe psychopathology and impairment, comorbidity, psychosocial disadvantage, inappropriate parenting, a worse prognosis, and increased family load of ADHD. The significance of ED for efficacy and compliance of drug treatment in ADHD in children has not yet been investigated. The aim of this study thus is to investigate ED and other factors within the child or the family context that moderate the effect of MPH treatment.

### *Hypotheses*

1. MPH treatment of ADHD is less effective at short- and long term follow up (12 weeks and 2-3 years), in children with ED
2. Severity of ADHD core symptoms and impairment in daily functioning at baseline, and socio-economic status, ADHD and other mental health problems in parents or siblings predict treatment adherence at short and long term follow up of index child
3. Severity of ADHD core symptoms and impairment in daily functioning at baseline, predict MPH treatment effect at 12 weeks follow up.

The significance of gender, age and comorbidity will be assessed in a cluster analysis.

**Methods:** The design is a longitudinal, naturalistic study of a clinical population of 225 drug naïve children in the age between 7-12 years, who begin a first MPH-treatment for ADHD under close monitoring of beneficial and adverse effects, and participate in the INDICES WP6 study at the Centre for Child and Adolescent Mental Health, the Capital Region of Denmark. Diagnostic assessment includes a diagnostic interview (K-SADS), questionnaires (CBCL, WFIRS, ADHD -RS) and a test of attention and impulsivity (TOVA test).

Follow-up after 12 weeks include: ADHD-DSM-IV-RS, CGI-severity, CGI-improvement, CGI-efficacy, ADHD-RS, WFIRS, TOVA, side effect rating scale. We plan to conduct a long-term follow up, 2-3 years after the participants complete the INDICES WP6 study, including ADHD-RS (parent and teacher), CBCL, WFIRS, collection of data from the Danish Register of Medical Product Statistics, regarding ADHD medication purchased by the participants in the follow-up period.

To date a number of 178 children have been recruited for The INDICES WP6 study.

**Results:** None yet

## The Nordic Long-term OCD Treatment Study (NordLOTS): Design, rationale, procedures and methods

*Tord Ivarsson*

**Objectives:** To describe the rationale behind the study including the design, research methods, procedures, and the data capture system and to report on the vicissitudes of running large-scale multi-centre studies.

**Methods:** State of the art measures like the KSADS, CY-BOCS, genetics sampling etc.

**Results:** We included 269 young people with OCD and treated them with manual based CBT. A separate talk will provide particulars on treatment and predictors. Non-responders were randomized to continued CBT or to treatment with sertraline. Outcome data will be presented in another separate talk. Our follow-up scheme to study the durability of gains will be described and some preliminary data will be reported.

**Discussion:** The NordLOTS is the biggest OCD study to date, and the strengths and limitations will be discussed briefly. Following the presentations of data a more detailed discussion will address the issue how NordLOTS findings fit into the current knowledge on OCD in children and adolescents

## Time trends in lifetime incidence rates of first - time diagnosed bipolar and depressive disorders across 16 years in a Danish nationwide study

*Christina Mohr Jensen, Hans-Christoph Steinhausen*

**Objectives:** Studies of time trends in incidence rates of bipolar disorders and depression based on representative large samples are rare and there is limited knowledge about the effect of sex and age. This study sought to establish potential trends in the diagnosed incidence of affective disorders based on nationwide psychiatric registry data.

**Methods:** The Danish Psychiatric Central Research Registry (DPCRR) was used to identify incident diagnosed cases with bipolar disorder, and depression at the ages 4-65 from 1995-2010. Furthermore, yearly census data was obtained from Statistics Denmark. Age and sex adjusted incidence rates per 100.000 person-years were calculated and incidence rates were adjusted for time trends in the total number of people seen in psychiatry in separate analyses. Time trends were analyzed using Joinpoint regression analysis via calculating annual percent changes and optimal number of join points in the data.

**Results:** A total of 96.185 persons had an incidence of at least one affective disorder. Incidence rates increased for bipolar disorder from 11.5 to 24.5 per 100.000 person years (PY) and for depression from 86.2 to 189.7 per 100.000 (PY). For both disorders the annual percent change was identified to be 5.4-5.7. There were no differences in time trends for the two sexes. For both bipolar disorder and for depressive disorders, time trends were most pronounced for younger persons up to 29 years of age. A sizeable part of the increasing incidence rates could be attributed to an increase in the total number of persons diagnosed in psychiatry.

**Discussion:** Time trends in incidence rates were similar for bipolar disorder and depressive disorders across sixteen years in this nationwide representative Danish study and reflected to a large extent a general increase of diagnosed mental disorders.

## Time Trends in Incidence rates of diagnosed Attention-Deficit/Hyperactivity Disorder over Sixteen Years in a Nationwide Danish Registry Study

*Christina Mohr Jensen, Hans-Christoph Steinhausen*

**Objectives:** To investigate time trends in incidence rates of first-time diagnosed Attention Deficit/Hyperactivity Disorder (ADHD) in a nationwide sample aged 4-65 years over 16 years and identify potential contributing factors to these time trends such as general trends in the number of patients receiving psychiatric services for any psychiatric disorder, age and sex.

**Methods:** Incidence rates of first-time diagnosed ADHD based on ICD-10 criteria in Danish psychiatric hospitals per 100,000 person years (PY) were calculated for the total population, the two sexes, and four age groups using data from the Danish Psychiatric Central Research Registry (DPCRR) and annual census data from Statistics Denmark. Time trends and the role of contributing factors were analysed and identified using Joinpoint regression procedures by calculating Annual Percent Changes (APC) for the time period 1995-2010

**Results:** A total of 20,281 patients were diagnosed with ADHD and 249,607 patients were seen in Danish psychiatry for any of the psychiatric disorders. Incidence rates of diagnosed ADHD increased 12.5 fold from 6.8 to 98.8 per 100,000 PY during the study period. After adjusting the incidence rates for the trend observed in psychiatry for patients seen with any psychiatric disorder, incidence rates were still increasing, but were down-sized to a 7.4-fold increase and increased from 7.3 to 58.3 per 100,000 PY. Joinpoint analysis suggested that incidence rates for diagnosed ADHD rapidly increased from 1998 to 2002, peaked from 2002 to 2008, and slowed down from 2008 to 2010. Contributing factors related to the increased rates of patients diagnosed with ADHD apart from the general increase in patients seen in psychiatry for any psychiatric disorder was an increased awareness and recognition of ADHD in females, adolescents, and adults.

**Discussion:** Results support the notion of increasing incidence rates of diagnosed ADHD across the sixteen years of observation. Contributing factors are a general increase in the number of patients seen in the Danish psychiatric clinics over the years, and an increased focus on females, adolescents and adults with ADHD in the clinics.

Since ADHD is a relatively recent diagnosis in the psychiatric nosology, the social awareness of ADHD in both sexes and across the lifespan has developed only in the more recent past and due to a relatively small number of persons in the population being diagnosed, it seems premature to conclude that at present ADHD is over-diagnosed.



## Comorbid mental disorders in children and adolescents with Attention-Deficit/Hyperactivity Disorder in a large nationwide study

Christina Mohr Jensen, Hans-Christoph Steinhausen

**Objectives:** The objectives of the present study are (1) to study the entire spectrum of concurrent mental comorbidities diagnosed according to ICD-10 criteria in a large cohort of newly diagnosed patients with ADHD, (2) the identification of potential differences by sex and age at first diagnosis in this pattern of comorbidities, and (3) the study of the associations among these various comorbid disorders

**Methods:** Data from the Danish Psychiatric Central Research Registry (DPCRR) was used to identify all patients aged 4-17 with a first-time diagnosis of Hyperkinetic Disorder (ICD-10: F90) in the time period 1995-2010. Concurrent comorbidity was defined as primary or secondary diagnoses given 3 months +/- the date of first-time ADHD diagnosis. Medians and interquartile ranges (IQR) for the age of onset are presented. The effect of sex on the risk of the various comorbid disorders was analyzed using logistic regression models controlled for age at diagnosis. Investigation of associations among comorbid disorders were analyzed using logistic regression models controlled for the presence of other comorbidity, age at ADHD diagnosis and separate analyses were performed for the two sexes.

**Results:** A total of 14.825 patients were identified (79.4 % males) with a mean age of 9.8 (SD 3.5). In the population 48 % had non-comorbid ADHD, 52% had at least one comorbid disorder and 26.2% two or more disorders. The most frequent comorbid mental disorders were Conduct disorders (CD) (16.5%), Specific disorders of development (15.4%), Autism spectrum disorders (ASD) (12.4%), intellectual disabilities (7.9%).

After controlling for age, males with ADHD were at increased risk for most neurodevelopmental disorders such as ASD (Odds Ratio [OR] 1.4, 95% Confidence Interval [CI] 1.2-1.6) and specific disorders of development (OR 1.3, 95%CI 1.1-1.5) and for CD (OR 1.4, 95%CI 1.3-1.6). Females with ADHD were at increased risk for a range of mental disorders including depressive disorders (OR 2.4, 95% CI 1.9-3.2), anxiety disorders (OR 1.7, 95% CI 1.3-2.3), eating disorders (OR 8.0, 95%CI 4.3-14.8), and intellectual disability (OR 1.3, 95% CI 1.11-1.5). The emergence of comorbid disorders was developmentally sensitive as shown by the median ages IQR for the age at first time diagnosis for the various disorders. After controlling for the effect of age, sex, and the presence of other comorbid disorders, positive and negative associations were detected between various comorbid mental disorders.

For instance, intellectual disability (OR 2.5, 95%CI 2.2-2.9) and tic disorder (OR 1.9, 95%CI 1.6-2.4) was positively associated with ASD and CD was negatively associated with ASD (OR 0.6, 95%CI 0.5-0.7).

**Discussion:** This nationwide registry-based study documented that concurrent comorbid mental disorders in ADHD are frequent and dependent on the sex and age of the patient. The analysis of associations between the various comorbid disorders identified several clusters highlighting the various differential developmental trajectories seen in patients with ADHD.

The study shows that particular attention should be given to patients with comorbid developmental disorders such as ASD and intellectual disability in future longitudinal studies or clinical trials because these patients constitute a large but often excluded study population. These patients might follow a different course than patients without these comorbid disorders.

## Time Trends Over 16 Years in Incidence-Rates of Autism Spectrum Disorders Across the Lifespan Based on Nationwide Danish Register Data

Christina Mohr Jensen, Hans-Christoph Steinhausen  
Marlene Briciet Lauritsen

**Objectives:** The aim of this study was to investigate nationwide time trends in the diagnosed incidence rates of Autism spectrum disorder according to ICD-10 criteria, including all relevant diagnostic subgroups, in the Danish population aged 0–65 years from 1995 to 2010 and to analyze the effect of sex and age.

**Methods:** Data on the numbers of incident cases diagnosed for the first time with ASD was obtained from the Danish Psychiatric Central Research Registry (DPCRR). Using these data, all patients with an ICD-10 diagnosis of childhood autism (F84.0), atypical autism (F84.1-84.12), Asperger's syndrome (F84.5) or other/unspecified pervasive developmental disorders (PDD-NOS) (F84.8-84.9) were identified. Yearly census data was obtained from Statistics Denmark. This data was used to calculate the annual incidence rates per 100,000 person years (PY). To evaluate time trends, data was fitted using non-linear least square procedures to obtain an estimate of the annual growth rate (regression coefficients).

**Results:** A total of 14,997 individuals were diagnosed for the first time with ASD from 1995 to 2010 including the following sub-diagnoses: childhood autism N = 4,099, atypical autism N = 1,806, Asperger's syndrome N = 4,691, PDD-NOS N = 6,262. Incidence rates for ASD increased from 9.0 to 38.6 per 100,000 person years during the 16-year period. The incidence rates per 100,000 PY increased from 2.0 to 11.0 for childhood autism, from 0.5 to 4.1 for atypical autism, from 2.7 to 11.7 in Asperger's syndrome, and from 2.8 to 17.3 per 100,000 PY for PDD-NOS. Major time trends were observed for adolescents and adults, females and for the milder diagnoses within the autism spectrum such as PDD-NOS and Asperger's syndrome.

**Discussion:** Increasing incidence rates were observed in the study period from 1995 to 2010 for total ASD and diagnostic subgroups and are in line with findings in other studies. We found that the increase in incidence for most diagnoses was highest in the older age groups, in particular in the age band of 14–20 years. Furthermore, a large increase was found for females and the increase was highest for Asperger's syndrome and PDD-NOS.



## Validation of Diagnoses of Hyperkinetic Disorders in Children and Adolescents in the Danish Psychiatric Central Research Registry in 1995-2005

*Christina Mohr Jensen, Susanne Vinkel Koch, Hans-Christoph Steinhausen*

**Objectives:** The purpose of the present study is to investigate the validity of diagnoses of Hyperkinetic Disorders (HD) in the Danish Central Psychiatric Research Registry (DPCRR) in children and adolescents (aged 4-15 yrs.) in a nationwide Danish sample in 1995-2005.

**Methods:** Out of a total cohort of N=4967 diagnosed with HD in the DPCRR aged 4-15 years in 1995-2005, a random sample of N=389 children and adolescents was drawn from the registry and the patient files were retrieved. This sample covered all regions of Denmark in a representative way. The sample was identified using a random sample function of the Statistical Package for the Social Sciences (SPSS) to maximize objectivity. Patient files were investigated and scored for the presence of symptoms and associated features according to ICD-10 criteria for HD (F90) and conduct disorder/oppositional defiant disorder (CD/ODD) (F91). The study material included the complete medical files of the patient, i.e., anamnesis, psychological and somatic assessments, test and, questionnaire findings, reports, discharge letters etc. To ensure validity and reliability of the extracted data, 50% of the retrieved patient files were co-rated by a specialist in child and adolescent psychiatry who was blind to the discharge diagnoses of the patients. Statistical procedures included positive predictive analyses and the calculation of inter-rater reliability.

**Results:** Out of the total validation sample of N= 389 patients diagnosed with HD, N=373 (95.9%) of the patient files were identified whereas the remaining 16 patient files (4.1%) were missing in the various hospital archives. Preliminary results of the validation study in N=81 (20.8%) showed a good validity of DPCRR diagnoses for HD with N=77 (95.1%) meeting criteria for HD (F90) or Inattention disorder (F98.8c). In N=2 (2.5%) a diagnosis of HD was not warranted and in another N=2 (2.5%) a lack of information in the patient file made it impossible to establish certainty of the diagnoses. Of the N=77 identified as having HD, the diagnosis was evaluated as certain for N=65 (84.4%) as likely for N=11 (14.3%) and as uncertain for N=1 (1.3%). The validity of the subtypes of HD could not be established in N= 31(40.3%) and a general under-reporting of Hyperkinetic Conduct Disorder (F90.1) (HD+CD/ODD) and of Inattention Disorder (F98.8c) was identified among patients diagnosed with Hyperkinetic Disorder F90.0.

**Discussion:** So far, the preliminary findings of this ongoing study indicate that the diagnoses of HD in the DPCRR for children and adolescents aged 4-15 and diagnosed in 1995-2005 are valid and fulfilling ICD-10 criteria. Thus, data on patients with HD in this age group and time period may be used in future registry studies without any major risk of misclassification bias. However, the validation of the remaining data and reliability analyses are needed before firm and final conclusions can be made.

### Overlapping and disease specific aspects of impulsivity in children and adolescents with schizophrenia spectrum disorders or Attention-Deficit/Hyperactivity Disorder

*Jens Richardt Møllegaard Jepsen, Jacob Rydkjær, Birgitte Fagerlund, Anne Katrine Pagsberg, Bob Oranje, Birte Yding Glenthøj,*

**Objectives:** To identify disease specific and overlapping aspects of impulsivity in children and adolescents with early-onset schizophrenia spectrum disorders or ADHD.

**Methods:** Motor impulsivity (Stop Signal Task), reflection impulsivity (Information Sampling Task), and trait impulsivity (Barratt Impulsiveness Scale) are compared between three groups of children and adolescents between 12 and 17 years of age: patients with early-onset schizophrenia spectrum disorders (N=29), patients with ADHD (N=29), and healthy controls (N=45).

**Results:** Preliminary results: Reflection impulsivity is significantly increased in patients with ADHD but not in early-onset schizophrenia spectrum disorder patients who perform non-significantly different from the healthy controls in the decreased win condition.

**Discussion:** Reduced information sampling in children and adolescents with ADHD may reflect an inability to delay their decision making to gather more information in a condition with a conflict between reward and certainty. The reduced information sampling may also reflect an increased conviction in the decision at a point of relative uncertainty.

### Maternal Smoking During Pregnancy as an Independent Risk Factor of Comorbid Attention-Deficit Hyperactivity Disorder and Conduct Disorder in a Nationwide Register-Based Study

*Petteri Joelsson, Roshan Chudal, Auli Suominen and Andre Sourander*

**Objectives:** The aim of the study is to investigate whether the connection between maternal smoking during pregnancy (MSDP) and ADHD is stronger with comorbid conduct (CD) disorder than without conduct disorder.

**Methods:** The study is based on a nested case-control design. The cases (N=10,132) consisted of all Finnish citizens born between January 1, 1991 and December 31st, 2005 and who were diagnosed with hyperkinetic disorder (ICD-10: F90.X or ICD-9: 314.X) by December 31, 2011 according to the Finnish Hospital Discharge Register (FHDR). Information about comorbid CD was also obtained from FHDR. For every case there were four controls matched by sex, date of birth (+/- 30 days) and place of birth (N=40,141). The information of MSDP was obtained from the Finnish Maternal Birth Register.

**Results:** According to preliminary results, the association between MSDP and ADHD with comorbid CD is significantly stronger than without comorbid CD. Statistical significance remained after adjusting the results with confounders. Conclusive results will be completed during summer 2014.

**Discussion:** The high comorbidity rate of ADHD and CD has previously been suggested to be explained with shared genetical factors. The results of this study indicate the comorbidity to be a result of also shared prenatal risk factors.

### **Association between siblings' psychiatric disorders and Autism Spectrum Disorders – A population-based study**

*Elina Jokiranta, Keely Cheslack-Postava,  
Auli Suominen, David Gyllenberg, Dan Sucksdorff,  
Roshan Chudal, Susanna Leivonen, Alan S. Brown,  
Andre Sourander*

**Objectives:** Autism spectrum disorders (ASD) cluster in the families. However, the familial clustering of other psychiatric disorders than ASD remains to be established.

The aim of the study is to examine the association between siblings' psychiatric disorders and ASD after adjusting for covariates.

**Methods:** The cohort includes 4705 children born between 1987 and 2005, diagnosed at the end of 2007 with childhood autism, Asperger's syndrome or pervasive developmental disorders/ pervasive developmental disorders – not otherwise specified (PDD-NOS). Cases were ascertained from the Finnish Hospital Discharge Register. Each case was matched to four controls by sex, date of birth, place of birth, and residence in Finland. Controls were selected from the Finnish Medical Birth Register. Cases' and controls' siblings were born between 1977 and 2005 and diagnosed with psychiatric disorder between 1987 and 2009. Siblings were identified through Finnish Central Population Register. Generalized linear mixed models were used to assess the associations between siblings' psychiatric disorders and ASD after controlling with covariates.

**Results:** Several psychiatric disorders were more common among cases' siblings than among controls' siblings.

**Discussion:** ASD and other psychiatric disorders cluster in the families. These findings may suggest shared common etiologic factors between these psychiatric disorders.

### **The relationship between CES1 genotype and methylphenidate response in children with ADHD**

Clinical characteristics of children included in INDICES WP 6.

*Kristine Kaalund-Jørgensen, Tine Houmann, Marie B Hebsgaard, Anne K Pagsberg, Kerstin J Plessen, Jørgen H Dyrborg, Henrik B Rasmussen, Pia Jeppesen*

**Objectives:** The aim is to investigate the associations between CES1 genotype and the beneficial and adverse effects of treatment with MPH in children between 7 and 12 years old, recently diagnosed with ADHD.

**Methods:** A total of 15- 20 % of the children with Attention Deficit Hyperactivity Disorder (ADHD) do not experience a clinically significant, beneficial response to treatment with methylphenidate (MPH) and discontinuation of treatment occurs in 2-10% due to adverse drug reactions. Several studies have found evidence for genetic variations underlying these variations in MPH treatment response. Carboxylesterase 1 (CES1) is a key enzyme in the metabolism of MPH. Clinical and preclinical studies indicate that polymorphisms in the CES1 gene may be responsible for some of the individual variations in MPH treatment response. Recent data from a collaborative study have revealed duplication of the CES1 gene at frequencies of approximately 0.20 in Europe. Gene duplication may give rise to increased rate of metabolism of CES1 dependent drugs including MPH.

The observational study is carried out at the Centre for Child and Adolescent Mental Health in The Capital of Region Denmark in 2012-2014. A total of 225 drug-naïve children are included and followed in a twelve week study with step-wise dose escalation of MPH. Based on weekly assessment of beneficial and adverse effects. Given Informed Consent from the parents, we also collect saliva sample for the CES1 genotyping and a blood sample for measurement of the MPH concentration.

The primary measure of outcome will be the rate and degree of normalization on the ADHD-DSM-IV-RS adjusted for sex and age. ADHD-DSM-IV-RS is a clinician rated 18-item ADHD Rating Scale rated every week. The secondary measures include ADHD-RS from parents and teachers and Clinical Global Impression (CGI) every four weeks (CGI-severity, CGI-efficacy, CGI-improvement). Changes after 12 weeks of treatment in scores on the computerized, Test Of Variables Attention (TOVA) and on Weis Functional Impairment Rating Scale (WFIRS). The secondary measures also include adverse drug effects every week and discontinuation of treatment.

**Results:** The data collection will be completed by November 2014. The preliminary data will be presented on the study population, including demographic characteristic, type and severity of ADHD, co-morbid mental disorders and daily and social functioning measured by W-FIRS.

## Emergency psychiatric care for children and adolescents in Iceland

Bertrand Lauth, Helen Sif Sævarsdóttir, Urður Njarðvík and Guðrún Bryndís Guðmundsdóttir

**Objectives:** In many European countries as well as in Australia and North America, a large and still increasing number of children and adolescents have been seeking help for acute psychiatric problems in the recent past. Policy questions have been raised concerning the necessary development of emergency mental health care. Given the dramatically increasing number of requests in Iceland, a retrospective study is being conducted to determine the demographic and associated factors, and the clinical characteristics of children and youth presented in 2013 for acute psychiatric problems including the context of the request and the level of care which has been finally recommended. Comparisons will be made with available data from 2008 before the onset of the economical crisis.

**Methods: Participants:** All children and adolescent who presented for emergency mental health services at the outpatient clinic of the Department of Child and Adolescent Psychiatry of the National University Hospital of Iceland during the years 2008 (about 150 patients) and 2013 (more than 300 patients).

**Method:** Two experienced child and adolescent psychiatrists assisted by a clinical assistant review the clinical charts using a systematic and standardized method of collecting information. The patients had been evaluated using routine non-structured psychiatric evaluations and several rating-scales and ICD-10 diagnoses had been assigned under the supervision of child and adolescent psychiatrists. Information has been collected about important risk factors, source and context of requests, as well as about treatment provided and level of care recommended. Special attention is paid to patients who were admitted to the inpatient unit.

**Results:** The data collection is on-going. Preliminary results will be presented and compared with available data from other countries.

**Discussion:** Best practices have yet to be established for child and adolescent emergency mental health services which must begin with a good understanding of the individuals who present for such services. The study results will be discussed with the intent of making recommendations on the standardization of emergency psychiatric care.

## Changes in Psychiatric Problems Among 8-Year-Old Children: A 24-Year Time-Trend Study

Lotta Lempinen, Andre Sourander

**Objectives:** To study how psychiatric problems have changed among 8-year-old children during 24 years at four time points: 1989, 1999, 2005 and 2013.

**Methods:** Information was gathered at four time points from parents and teachers using Rutter's questionnaires. The design, methods, and samples were similar at all four time points.

The sample size was about 1000 8-year-old children at each time point. The participation rates were 96% in 1989, 86% in 1999, 84% in 2005, and 85% in 2013.

**Results:** Preliminary results show that between 1989 and 2013 there were no significant changes in parent and teacher reported mean total problem scores. When comparing changes in specific symptom scales between years 1989 and 2013 there was a significant decrease in conduct symptoms among boys and a significant decrease in emotional symptoms among boys and girls according to parent reports.

**Discussion:** According to the preliminary results of this study, the changes in psychiatric symptoms have been quite limited during 24 years.

## Motivation and its Impact on Self-Regulatory Control in Children with Tourette syndrome

*Katrine Maigaard, Damian Herz, Lone Kelkjær, Liselotte Skov, Oliver James Hulme, Hartwig Roman Siebner, Kerstin J. Plessen*

**Objectives:** This fMRI study is an investigation of the effects of motivation on the inhibition of prepotent motor responses in children with Tourette Syndrome (TS).

TS is defined by the combination of motor and vocal tics. The disorder starts in childhood and symptoms typically decrease during puberty, concurrent to the emergence of enhanced self-regulatory control.

TS involves anatomic and functional disturbances in the cortico-striatal circuitry, parts of which connect the prefrontal cortex to the basal ganglia. These circuits are involved in reinforcement learning. Previous studies have shown that individuals with TS are sensitive to positive reinforcement, and that treatment with dopamine receptor antagonists bluntens this sensitivity. This could be the result of a bias in the cortico-striatal circuits, a bias that could lead to tic formation due to excessive reinforcement of motor sequences. However, altered reward sensitivity could also be exploited in effective treatments of this disorder.

**Methods:** In our study we include a total of 120 children: children with TS, children with TS and ADHD, children with ADHD, and children without neuropsychiatric disorders ( $n = 30$  in all four groups). After thorough clinical characterisation, we use fMRI to assess functional brain activity during an experimental task that introduces response inhibition at a high and a low level of motivation. The task is a modified Simon task, contrasting conditions of low external motivation (no reward prospect) and high external motivation (prospect of reward for correct responses). We aim to map task-related changes in activity and connectivity in brain networks of self-regulatory control to investigate how these networks are influenced by motivation.

**Results:** We hypothesise that children with TS will have an altered speed-accuracy trade-off in the Simon task, leading to slower reaction times to maintain high accuracy. In the presence of reward, children with TS will show shorter reaction times without an increase in error rate relative to the other diagnostic group.

Furthermore, children with TS will display a stronger task-related activation of the ventral striatum and an increased coupling between the ventral striatum and task-related medial and lateral prefrontal networks as opposed to task-related activation of the Simon task without reinforcement.

**Discussion:** Improving our knowledge of motivational processes in fronto-striatal circuits will allow us to better understand how disturbances in the development of those circuits contribute to difficulties associated with childhood neuropsychiatric disorders, and improve the treatments of these conditions.



## High-dose treatment with stimulants - risk or benefit? Case reports in a Swedish clinical population

Kerstin Malmberg, Ulrika Åhlund, Håkan Jarbin

The risks to increase methylphenidate treatment to high dose seem to be limited while the benefits are greater. This also shows that the dose- response curve is individual.

**Objectives:** Through case studies find individuals that have been on high-dose treatment with methylphenidate, where high dose is defined as the daily doses of methylphenidate 90 mg or 2 mg / kg. Examine the benefits and risk with high dose methylphenidate.

**Methods:** The material included 10 individuals treated with high-dose methylphenidate at three Child and Adolescent clinics in Sweden, Halland, Skåne and Stockholm. Case studies done by medical record review and conversations with therapists

**Results:** All 10 individuals have severe ADHD combined type and 9 of 10 individuals are boys. Their age was between 8,11 and 18,4 years (March 2014). Comorbidity were mild mental retardation (n = 3), oppositional defiant disorder (n = 3), anxiety disorders (n = 2 ), depression (n = 2) and early trauma (n = 2). The daily dose of methylphenidate has been median 126 ( 100-240 ) mg which weight - related median 2.9 (1.2 to 6.3 ) mg / kg. All but one is simultaneously treated with other psychotropic drugs. The individuals have been on high-dose of methylphenidate between 1,6 and 4,5 years. All individuals have improved much / very much of high dose treatment and C- GAS increased 12.5 (7-17) during treatment. Side effects were gastrointestinal symptoms in 9 individuals, mostly loss of appetite (n = 7). Other side effects were insomnia (n = 4), tachycardia / palpitations (n = 2), and hypertension (n = 1). Age-related BMI increased by 2.6 ( -0.2 - +6.5 ) units. Age-related length has decreased 0.15 SD (-1.3 - +1.0 ) and 3 of the individuals have lost more than 0.5 SD in length, and all those were on treatment with the combination of atomoxetine and methylphenidate.

**Discussion:** The results are limited by a selected material of individuals on high- dose methylphenidate during long-term follow-up. Relatively large functional improvement can be explained by the majority of the patients tested had great difficulty in functioning at baseline. Careful monitoring of growth and vital signs is necessary. Growth retardation seems to be the most common long term side effect and combination treatment with atomoxetine may cause an increased risk. Five individuals have concomitant neuroleptic treatment which may explain increased BMI. Cardiovascular events were fewer than expected. There are patients in whom the recommended maximum dose is clearly on the low side, which must be identified and dosage adjusted according to clinical observation.

### **Risk of diabetes in children and adolescents exposed to antipsychotics: a nationwide 12-year case-control study**

*René Ernst Nielsen, Mathilde Frahm Laursen, Ditte Lammers Vernal, Charlotte Bisgaard, Hans-Christoph Steinhausen, Christoph U. Correll*

**Objectives:** In this study, we aimed to investigate the effects of exposure to antipsychotic drug treatment, as well as psychiatric diagnosis on the risk and rate of developing type II diabetes, defined as prescription of an oral antidiabetic drug, in a large, nationwide, child and adolescent population located in Denmark.

**Methods:** We conducted a longitudinal register linkage case control study of type II diabetes, defined as prescription of an oral antidiabetic drug, in all child and adolescent hospital-based psychiatric patients diagnosed in Denmark from 01.01.1999-31.06.2010, a period chosen to allow full data retrieval from all registers used.

**Results:** We compared the risk of diabetes in 48,299 psychiatrically ill youth. Of 7,253 youth exposed to antipsychotics, 52 (0.72%; 95% CI: 0.52% - 0.91%) developed type 2 diabetes. Of 41,046 youth without exposure to antipsychotics, 111 (0.27%; 95% CI: 0.22%-0.32%) developed type 2 diabetes. In a logistic regression analysis, type 2 diabetes development was associated with antipsychotic drug exposure (odds ratio [OR] 1.60; 95% CI 1.08 - 2.36,  $p < 0.05$ ) female sex, (OR 4.48; 95% CI 2.90 - 6.91,  $p < 0.001$ ) and older age at first psychiatric diagnosis (OR 1.19; 95% CI 1.12 - 1.27,  $p < 0.001$ ), but not with psychiatric diagnosis. In a Cox-regression analysis, shorter time to type 2 diabetes onset was associated with female sex (Hazard Ratio (HR) 4.83; 95% CI 3.05–7.66,  $p < 0.001$ ), and older age at first psychiatric diagnosis (HR 1.19; 95% CI 1.12-1.28,  $p < 0.001$ ), while antipsychotic exposure (HR) 1.41; 95% CI 0.92-2.16,  $p = 0.11$ ) trended towards increasing the rate of diabetes.

**Discussion:** Altogether, these findings raise considerable concern about the increased use of antipsychotics in children and adolescents, especially in young populations and for aggressive and disruptive behavior disorders, conditions that are all too infrequently treated with non-pharmacologic interventions, despite clear guidance to do so. Thus, the current study shows that antipsychotic drug treatment increases the frequency of type 2 diabetes development, as shown in the regression, in conjunction with fixed risk factors (older age at psychiatric diagnosis and female gender). The clinical importance of these findings is underscored by studies that have shown increased morbidity and mortality associated with an earlier onset of type II diabetes.

### **The Genetic Aspects of Obsessive Compulsive Disorder (OCD)**

*Judith Becker Nissen, Per Hove Thomsen, Henriette Nørmølle Buttenschøn, Ole Mors, Tord Ivarsson, Elias Eriksson*

**Objectives:** This presentation from the NordLOTS project will focus on the genetics methods used in the study.

**Methods:** Children and adolescents included in the NordLOTS study were asked to participate in the genetic study. With informed consent saliva probes were achieved from both the patients and their parents. Every family filled out a genogram concerning the occurrence of OCD, tic disorder, depression and anxiety disorders in the family.

**Results:** The study is ongoing and examining the importance of selected neurotransmitter systems and their mutual influence in relation to OCD. The results will be preliminary.

**Discussion:** OCD is a heterogeneous condition with regard to clinical presentation, comorbidity, and treatment response. Evidence for a strong genetic component has been shown by both twin and family studies as well as by segregation analyses. Neuroimaging and neuro-functional studies have shown the impact of neurotransmitters such as serotonin, dopamine and glutamate. Association studies have suggested a potential role for genes which are relevant in these neurotransmitter systems by contributing to susceptibility to OCD.



### Child and Adolescent OCD Symptom Patterns: A Factor Analytic Study

*D. Martinsson, E.L. Mortensen, T. Ivarsson, R. Valderhaug, K.A. Hybel, G. Skarphedinsson, K. Dahl, N.C. Torp, A. Lewin, K. Melin, E. Storch, E. de Haan, (J. Piacentini), (M. Grados), J. Nissen, P.H. Thomsen*

**Objectives:** To investigate OCD symptom structure in children and adolescents in order to identify OCD subtypes.

A few studies have tried to identify symptom based subtypes of OCD in Children and Adolescents, and found it to contain 4-5 factors. There are several reasons for the different number of factors found such as different methods and limited sample sizes. Therefore, this study based on a large sample will be a valuable addition to the previous studies.

**Methods:** Exploratory factor analysis will be applied to the Children's Yale-Brown Obsessive-Compulsive Scale (CY-BOCS) symptom checklist items in order to reveal any latent factor structure. The relation between specific factors and co-morbid disorders will be examined. Data for 696 children and adolescents with OCD is already collected and the final sample is expected to be around 850 subjects, collected from 24 different research units in Europe and USA. This study is a part of the Nordic Long-Term OCD Treatment Study (NordLOTS).

**Results:** Work in progress. Preliminary results will be available at the time of presentation.

**Discussion:** Our study is unique in that it includes individual CY-BOCS checklist items and it is thus possible that our results will refine or go beyond the "classical" factors in the original publication. The importance of our findings for studies on OCD genetics and pathogenesis of symptoms will be discussed.

### Cognitive Behavioural Group Therapy in Adolescents with ADHD

*Torunn Stene Nøvik, Anne Mari Sund, Per Hove Thomsen*

**Objectives:** Cognitive Behavioural Therapy (CBT) has demonstrated benefit for adults with ADHD, however studies in adolescents are lacking. CBT may especially be beneficial for improving planning and organization skills and self esteem, and reducing emotional problems. We have recently conducted a pilot study of a 12-week treatment programme in adolescents with ADHD 15-17 years of age, based on the Young-Bramham group treatment programme (Young & Bramham, 2012). A treatment study is being planned, in which the objective is to examine if adolescents aged 14-17 years who receive Cognitive Behavioural Group Therapy in addition to medication and psychoeducation (Treatment-As-Usual, TAU), obtain greater improvement in ADHD symptoms, functioning and Quality of Life (QoL) than adolescents who receive TAU only.

**Methods:** Adolescents diagnosed with ADHD in the two CAP outpatient units in Trondheim will receive medication and psychoeducation. After a further assessment, the patients will be randomised to 12 weeks of group CBT or TAU (follow-up of medical treatment).

ADHD symptoms, psychosocial functioning, and QoL will be assessed with the ADHD-RS, the Weiss Functional Impairment Rating Scale (W-FIRS), and Inventar zur Erfassung der Lebensqualität bei Kinder und Jugendlichen (ILC). Executive functioning will be examined with the BRIEF, while self-esteem and self-efficacy will be assessed with the Rosenberg Self-Esteem Scale and the General Perceived Self-Efficacy Scale. Sleep will be assessed with the Adolescent sleep wake scale. Subjects will be reassessed at the end of treatment and after three months.

**Results:** Results pertaining to the pilot study will be presented.

**Discussion:** CBT group treatment was well received and is feasible in the population of adolescents with ADHD. Thus, further research is warranted.

**Quetiapine versus aripiprazole in children and adolescents with psychosis - the randomised, blinded clinical Tolerability and Efficacy of Antipsychotics (TEA) trial**

*Anne Katrine Pagsberg, Pia Jeppesen, Dea Gowers Klauber, Karsten Gjessing Jensen, Ditte Rudå, Marie Stentebjerg-Olesen, Peter Jantzen, Simone Rasmussen, Eva Ann-Sofie Saldeen, Maj-Britt Glenn Lauritsen, Niels Bilenberg, Anne Dorte Stenstrøm, Jesper Pedersen, Louise Nyvang, Sarah Madsen, Christian Gluud, Maria Skoog, Jørn Wetterslev, Christoph U Correll, Jens Richardt M. Jepsen, Birgitte Fagerlund, Anders Fink-Jensen*

**Objectives:** The main objective of the TEA trial is to compare the benefits and harms of quetiapine versus aripiprazole in children and adolescents with psychosis in order to inform rational, effective and safe treatment selections.

**Methods:** Patients aged 12-17 years with psychosis, antipsychotic-naïve or treated for a limited period are 1:1 randomised to a 12- week, double-blind intervention with quetiapine versus aripiprazole. Effects on psychopathology, cognition, health-related quality of life, and adverse events are assessed 2, 4, and 12 weeks after randomisation. The primary outcome is change in the positive symptom score of the Positive and Negative Syndrome Scale. The recruitment period is 2010-2014.

**Results:** A total of 113 patients were randomized to the intervention. Baseline clinical data describing the participants will be presented.

**Discussion:** It will be discussed whether the clinical profile of the trial participants reflects a representative sample of early onset psychosis (EOP).

## Performance Monitoring and Perfectionism in Adolescents with Current and Adolescents with Previous Anorexia Nervosa

*Tine Pedersen, Alessandro Calamuneri, Estelle Raffin, Norbert Brüggemann, Kristoffer Madsen, Julie Hagstrøm, Tim Dyrby, Mette Bentz, Hartwig Siebner, Kerstin J. Plessen*

**Objectives:** Perfectionistic behavior and a constant alertness towards avoiding making mistakes are prominent traits in individuals with Anorexia Nervosa (AN). Excessive control of behavior seems to play an important role in the development and maintenance of AN, but knowledge concerning underlying vulnerability and personality traits is limited. Surprisingly, only few studies have examined the neurobiological measures in young people with AN and most have focused on how patients exert exaggerated control over primal and salient hunger cues. The present study that maps the feature of performance monitoring in AN may help to further illuminate the patients' over-perfectionistic behavior, and give clues as to whether perfectionism is present only in episodes of illness with considerable loss of weight or whether it persists after recovery and rather represents a trait abnormality.

**Methods:** In this study, we examine performance monitoring to assess the association between perfectionistic traits and neurobiological measures, gained with the means of functional Magnetic Resonance Imaging (fMRI). Neurobiological factors can be difficult to map in patients who are underweight, given underlying physiological changes as a result of the weight loss. We thus compare a group of 30 recovered adolescents with a previous diagnosis of AN, 30 adolescents who currently receive treatment for AN, and 30 healthy controls, matched for age, socioeconomic status, and IQ.

We use fMRI to investigate whether activation in the cingulo-opercular system – the core network for performance monitoring – differs on a trial-by-trial basis, especially in individuals exerting perfectionistic behavior.

**Results:** We are still recruiting participants for the study. Our hypotheses suggest that adolescents recovered from AN and adolescents with AN will show an increased tendency to avoid errors and an increased ability to correct for errors compared to healthy controls. We hypothesize that perfectionism will correlate with increased performance monitoring, as a behavioral trait, during a cognitive demanding task.

The results of the study will bring about, whether neurobiological correlates are present in recovered and currently ill adolescents and thus whether traits of perfectionism persist.

**Discussion:** Family-based treatment is the only form of evidence-based treatment for children and adolescents with AN but not all patients profit from this kind of treatment. If large subgroups of patients and recovered patients have heightened levels of perfectionism, this will help us understand the poorer response to treatment and contribute to our knowledge of how to individually adjust treatment.

This study extends evidence from previous studies, because the design will allow us to discriminate individual features in the subjects, which are due to acute illness and underweight, from more stable traits of perfectionism.

This study, however, does not include individuals before the onset of AN, which still is a critical limitation. To our knowledge, this is the first study to examine mechanisms of perfectionism and performance monitoring in both young patients with AN and recovered patients by using brain mapping.

### **The Danish High Risk and Resilience Study–VIA 7**

*Kerstin J. Plessen, Anne A. E. Thorup, Jens Richardt Jepsen, Nicoline Hemager, Camilla Jerlang Christiani, Anne Ranning, Aja Greve, Ditte Gantriis, Birgitte Klee Burton, Ditte Ellersgaard, Katrine Søborg Spang, Mette Skjærbæk, Ole Mors, Merete Nordentoft*

**Objectives:** The overall objective of this study is to map genetic liability, psychiatric symptoms and environmental influences in a large cohort of 7-year-old children at high genetic risk for developing schizophrenia or bipolar disorder compared with a group of healthy controls in a longitudinal perspective. Abundant literature documents the genetic vulnerability in children of individuals with schizophrenia and with bipolar disorder. Recently a possible genetic overlap between the two disorders has been suggested. However, neither developmental pathways of psychopathology in children at risk, nor the implications of specific resilience factors have been assessed sufficiently in a crossdiagnostic perspective.

**Methods:** We will examine 200 children with a parent with schizophrenia, 100 children with a parent with bipolar disorder and 200 controls (defined as not diagnosed with SZ or BP) as well as their parents when the child is 7, 11 and 15 years of age. We will use a wide range of validated interviews and questionnaires, but also direct observations, cognitive tests and biological specimens to map clinical symptoms, motor and social development, intelligence and cognition, resilience factors, and finally the environment and emotional climate at home. We currently recruit participants via Danish Registers to establish a representative cohort and make sure that those children at high risk and controls are matched on gender, age and community.

**Results:** Hypotheses: Based on earlier literature, we hypothesize that children at a high risk for bipolar disorder and for schizophrenia will show higher rates of psychiatric disturbances at age 7. Moreover, we expect that children at high risk will show impairments of underlying developmental traits, such as delayed motor development and impaired coordination, and poorer cognitive function and social cognition.

**Discussion:** This study will map the development of psychopathology in children at high risk. We will focus on underlying potential endophenotypes in a crossdiagnostic perspective and map the maturation of endophenotypes to understand the trajectories of psychopathology.

Moreover, we aim to document resilience factors, such as intelligence, emotional regulation, quality of life, parent involvement and familial interaction patterns, to analyze the implications of resilience factors for dimensions of development.

Finally, the Danish registers offer a unique possibility to use data from registries to further explore the influence of risk factors and their interaction with genetic and clinical measures in this national cohort.

## The development of WHO ICF core sets for ASD and ADHD

*Elles de Schipper, Sven Bölte*

**Objectives:** The WHO's International Classification of Functioning, Disability and Health (ICF) provides a comprehensive, universally accepted framework for the description of functioning in relation to health conditions. ICF Core Sets are shortlists of ICF categories that are selected to capture those aspects of functioning that are most relevant when describing a person with a specific condition. The objective of the present project is to develop ICF Core Sets for ASD and ADHD, following a rigorous scientific process that was developed by WHO and the ICF Research Branch.

**Methods:** The development process involves four preparatory studies: a systematic review, an expert survey, a qualitative focus group study, and a clinical cross-sectional study. Evidence from these studies will be presented to a group of experts at an international consensus conference, where they will follow a formal decision-making process to arrive at a consensus on the ICF categories to be included in the ICF Core Sets for ASD and ADHD.

**Results:** A short introduction to the development process will be given, along with a presentation of results from the first two of the preparatory studies: (1) the systematic literature review which captures the research perspective on ability and disability in ASD and ADHD; and (2) the international expert survey, capturing the opinion leader perspective. Results consist of ICF categories that have been found to be specifically relevant to ASD and ADHD, and the frequency with which they have been identified in the presented studies.

**Discussion:** ICF Core Sets for ASD and ADHD are being developed with the goal of providing useful standards for research and clinical practice, and to generate a common language for ability and disability in ASD and ADHD in different areas of life and across the lifespan. Results from the studies will be discussed in relation to ASD and ADHD and in terms of their contribution to the ICF Core Sets development process.

## A naturalistic RCT study of neurofeedback and working memory training in ADHD ("KITE")

*Seija Sirviö, Sven Bölte*

**Objectives:** The aim of the study is to evaluate whether neurocognitive training methods improves core symptoms of ADHD.

**Methods:** 200 children and adolescents with ADHD, aged 9 to 17 years, will participate in this study. They are randomized into four groups; two groups with different forms of neurofeedback (NF), a working memory (WM) group and a control group in conjunction with treatment as usual (TAU) such as drug treatment. Children/adolescents visit the clinic five times per week for five weeks in a total of 25 training sessions (about 50 minutes per occasion).

Pre-, post- and six months follow-up assessments are made by self-, parents- and teachers estimates, psychometric tests and neurophysiological measurements.

**Results:** First children/adolescents were enrolled in the study in September 2013. The results will be analysed and published at the estimated end of the study in 2016.

**Discussion:** There is a great need to find effective treatment options for children with ADHD.

Non-pharmacological interventions as NF and WMt are put forward as promising methods. This study will try out NF and WM-training and will also examine the feasibility of neurocognitive training in a child and adolescent psychiatric clinic.

### Continued cognitive behavior therapy versus sertraline for children and adolescents with obsessive-compulsive disorder that were non-responders to cognitive behavior therapy - A randomized controlled trial

Gudmundur Skarphedinsson, Bernhard Weidle, Per Hove Thomsen, Kitty Dahl, Nor Christian Torp, Judith B. Nissen, Karin Holmgren Melin, Katja Hybel, Robert Valderhaug, Tore Wentzel-Larsen, Scott N. Compton, Tord Ivarsson

**Objectives:** To investigate the effectiveness of sertraline (SRT) versus continued CBT in children and adolescents that did not respond to an initial course of CBT.

**Background:** Expert guidelines recommend cognitive-behavior therapy (CBT) as a first line treatment in pediatric obsessive-compulsive disorder (OCD) and the addition of selective serotonin reuptake inhibitors (SSRI) when CBT is not effective. However, the recommendations for CBT non-responders are not supported by empirical data.

**Methods:** Randomized controlled trial (RCT) conducted in five sites in Denmark, Sweden and Norway. 54 children and adolescents, aged 7-17 years, with DSM-IV primary OCD were randomized to SRT or continued CBT for sixteen weeks. These participants had been classified as non-responders to CBT following 14 weekly sessions. Primary outcomes were the CY-BOCS total score and clinical response (CY-BOCS<16). The study was a part of the Nordic Long-Term OCD Treatment Study (NordLOTS).

**Results:** Intent-to-treat sample included 50 participants, mean age 14.0 (SD=2.7) and 48% (n=24) males.

Twenty-one of 28 participants (75%) completed continued CBT and 15 of 22 participants (69.2%) completed SRT. Planned pairwise comparison of the CY-BOCS total score did not reveal a significant difference between the treatments ( $p=.351$ ) nor in response rates. Within-group effect sizes were large and significant across both treatments.

**Discussion:** Large within-group effect sizes suggest that continued treatment for CBT non-responders is beneficial. However, there were no significant between group differences in SRT or continued CBT at post-treatment.

### Multisite pain and resilience factors in adolescents with behavioural and emotional problems: The Young-HUNT study.

Marit Skrove, Pål Romundstad, Marit S. Indredavik

**Objectives:** The objective of the study was to assess the prevalence of chronic multisite pain with high disability in adolescents with behavioural or emotional problems, and to investigate if resilience factors could attenuate the associations between psychiatric symptoms and chronic multisite pain.

**Methods:** The study used data from a large cross-sectional population-based study in Norway, the Nord-Trøndelag Health Study (HUNT 3: 2006-2008) and included 7070 adolescents aged 13 to 19 years. To measure psychiatric symptoms we used 14 questions regarding the adolescent's schoolfunctioning (conduct problems and attention problems), the SCL-5 (anxiety and depression) and six items from the SPAI-C (social anxiety). Chronic multisite pain was defined as pain at least once a week during the last three months, with high score on a disability index, occurring in three or more locations. Resilience factors were measured by eight items from the Resilience Scale for Adolescents (READ).

**Results:** The prevalence of chronic multisite pain increased with increasing scores symptoms in all four symptom groups of psychiatric symptoms and was higher for girls than for boys ( $p<0.001$ ). For adolescents with high scores (>85%) for symptoms of attention or conduct problems, anxiety/depression or social anxiety, the prevalence of chronic multisite pain ranged from 22.8 to 31.0% for girls and from 8.8 to 19.0% for boys. High scores for attention problems or anxiety/depression showed the strongest associations with multisite pain in both girls and boys (OR 8.4-15.4). Resilience factors showed a marked attenuating effect on the associations between psychiatric symptoms and chronic multisite pain.

**Discussion:** Few previous studies have reported on the prevalence of chronic multisite pain in unselected populations of adolescents with behavioural or emotional problems.

The relationship between psychiatric symptoms and chronic pain may be bidirectional and the causal explanations are multifactorial. In this study one out of three girls and one out of five boys reporting high scores on symptoms of behavioural or emotional problems had chronic multisite pain.

Resilience factors markedly attenuated the associations between psychiatric symptoms and multisite pain. Hence, adolescents with high scores for resilience factors are less likely to experience chronic pain, even if they have psychiatric symptoms. Psychiatrists should be careful to assess and treat comorbid chronic pain in adolescents with behavioural or emotional problems.



### Emotion regulation in children at high risk for bipolar disorder or schizophrenia

*Katrine Spang, Carsten Obel, Jens Richardt Jepsen, Anne Thorup, Nicoline Hemager, Anne Ranning, Ditte Ellersgaard, Birgitte Klee Burton, Camilla Christiani, Mette Skjærbæk, Anne Søndergaard, Aja Greve, Ditte Gantriis, Ole Mors, Merete Nordentoft, Kerstin J. Plessen*

**Objectives:** The ability of emotional regulation has an important predictive value for the development of mental health problems during lifespan. The main objective of this sub-study thus is to investigate this ability in children of parents with bipolar disorder (BP) and to compare these abilities with children of parents with schizophrenia (SZ) and children of healthy controls (HC).

**Methods:** The study is part of The Danish High Risk and Resilience Study – VIA 7. We will establish a stratified cohort of 500 children, age 7, with one, two, or none parents with SZ or BD. The three cohorts have been invited on the background of information derived from the Danish Civil Registration System and the Danish Psychiatric Central Register.

Emotion regulation is not consensually defined and at present no direct test of emotion regulation exists. We will assess the ability to regulate emotions primarily with questionnaires, asking parents, teachers and children about their emotional reactions and social abilities in their everyday life. In addition, we will use data from cognitive tests and an emotion recognition task to directly assess the general capacity of self-regulation and the ability to recognize emotions on pictures with an affective content. Finally, the direct test will be used to validate data derived from questionnaires.

We hypothesize that children at high risk for bipolar disorder will be more impaired in their ability to regulate emotions than the control group and children at risk for schizophrenia. The results from this study will contribute to better characterize the specific problems in children with parents with BP and thereby open new avenues for early interventions that directly target this capacity.

**Results:** Data collection started December 2012. We have included 162 families by January 2014 and 101 families have completed the test-battery.

### Substance use disorders in association with attention-deficit/hyperactivity disorder, co-morbid mental disorders, and medication in a nationwide sample

*Hans-Christoph Steinhausen, Charlotte Bisgaard*

**Objectives:** The association of substance use disorders (SUD) with attention-deficit disorder (ADHD), co-morbid mental disorders, and medication has only been studied in isolation and in rather small samples. Thus, the issue was re-analyzed in a representative nationwide sample.

**Methods:** Data were based on four Danish national registers covering a total of 20,742 patients with ADHD, their dispensed medications, co-morbid mental disorders, and associated SUD between 1994 and 2010. The analyses considered the risk of various medications (methyl-phenidate only, antidepressants only, antipsychotic only, mixed medication) in comparison to a control group of non-medicated patients with ADHD, various co-morbid disorders, duration of medication, age at diagnosis, year of birth, and sex for developing SUD.

**Results:** The observation period of the cohort ranged between 2.25 and 66.21 years and the prevalence for SUD was 9.51%. The SUD rates were significantly higher prior to, compared to following the onset of medication in the methylphenidate and the mixed medication subgroup, whereas they were significantly higher following onset of medication in the antidepressants and the antipsychotics subgroups. However, the SUD rates were significantly higher in all drug conditions except for methylphenidate after onset of medication compared to the non-medicated subgroup.

Risk factors obtained by regression analysis did not include methylphenidate but did include antidepressants, antipsychotics, and mixed medications, in combination with co-morbid mood, anxiety, personality, and conduct disorders, and older age at diagnosis.

Longer duration of medication and female sex were protective factors.

**Discussion:** This representative study based on a large nationwide psychiatric sample provides solid evidence into the patterns of SUD in patients with ADHD based on medication use and comorbidities.

## Nationwide time trends in dispensed prescriptions of psychotropic medication for children and adolescents in Denmark

*Hans-Christoph Steinhausen, Charlotte Bisgaard*

**Objectives:** The analysis of time trends in dispensed prescriptions of psychotropic medications for children and adolescents in Denmark.

**Methods:** The entire data set of the Danish prescription register covering stimulants, antidepressants, antipsychotics, and anxiolytics used in children and adolescents over a 15-year time span from 1996 to 2010 was analyzed.

Both non-adjusted age-standardized prevalence rates and adjusted age-standardized prevalence rates considering the increase in patient numbers over time were calculated, and time trends were assessed based on 105 908 patient-years.

**Results:** For stimulants, antidepressants, and antipsychotics, the non-adjusted prevalence rates increased significantly. These trends were strongest for the stimulants. However, all adjusted prevalence rates were much lower with the anxiolytics even declining significantly.

The prevalence rates of stimulants and antipsychotics were significantly higher among males than females, whereas females received significantly more antidepressants. The increase in prescription rates for both antidepressants and antipsychotics was mainly due to increased use among the 14- to 17-year-olds.

Stratification by diagnoses revealed significantly increasing prevalence rates of dispensed antidepressants and antipsychotics in six major diagnostic indications.

**Discussion:** Although increasing, the unadjusted Danish prevalence rates of dispensed prescriptions of psychotropics for children and adolescents are still lower than in many other Western countries.

## Systematic quantitative analysis of the long-term outcome of autism spectrum disorders

*Hans-Christoph Steinhausen, Christina Mohr Jensen  
Charlotte Bisgaard, Marlene Briciet Lauritsen*

**Objectives:** The study of the long-term adult outcome of ASD.

**Methods:** Based on a systematic literature search, we performed quantitative calculations of the outcome data of those studies that used a classification of good, fair, poor and very poor outcomes and have been published in the years 1967-2013.

**Results:** In a total of xx outcome studies suitable for analysis, we found that among a total of N=xxx patients on average xx percent had a good, xx1 percent had a fair, xx percent had a poor, and xx percent had a very poor outcome. Prognostic factors included level of intellectual and language impairment.

**Discussion:** There was some evidence that in the more recent studies the outcome of ASD has improved significantly.

However, the positive changes in outcome over time are still rather small. Furthermore, the outcome has been less favorable in rather homogenous samples containing patients with a diagnosis of infantile autism only as compared to samples with a wider definition of ASD.



## Family Aggregation and Risk Factors in Major Mental Disorders over Three-Generations in a Nation-wide Study

*Hans-Christoph Steinhausen, Helle Jakobsen, Dorte Helenius, Charlotte Bisgaard, Povl Munk-Jørgensen, Kathleen Merikangas, Michael Strober*

**Objectives:** The study of the family aggregation and further risk factors in schizophrenia (SZ), bipolar disorders (BP), depression (DEP), anxiety disorders (ANX), obsessive compulsive disorders (OCD), substance use disorders (SUD), and anorexia disorders (AN) in a large nationwide sample covering three generations.

**Methods:** Data on all patients aged 1 - 18 years collected in the Danish Psychiatric Central Research Register (DPCRR) with first psychiatric contact from 1.4.1969 to 9.6.1985, their parents, siblings, and offspring. Life-time follow-up period from 1.4.1969 – 29.6.2004 (35 years), later extended to 10.12.2009 (40 years). Matched case-control design with three times larger control groups who did not have a psychiatric record during childhood and adolescence, their parents, siblings and offspring.

Analyses of mental disorders according to ICD-8 (1969-1994) and ICD-10 (since 1994). Further risk factors included sex, parental age at birth, year of birth, and region.

Statistical analyses included frequency comparisons, calculations of effects sizes, conditional logistic regression analysis, and various mixed regression models.

**Results:** A series of studies in the various disorders provided further evidence of the high family aggregation of all major mental disorders (SZ, BD, DEP, ANX, OCD, SUD, AN).

The explained total variance of the disease manifestation by family aggregation varies by disorder: substance use disorders: 27%, schizophrenia: 23%, bipolar disorders: 20%, depression: 17%, anxiety disorders: 12%, obsessive compulsive disorders: 6%, and anorexia nervosa: <1%

Higher paternal age at birth is a risk factor only in SZ. Higher maternal age is a risk factor only in OCD (first report). Male sex is a risk factor for SZ, female sex is a risk factor for BD, DEP, ANX, OCD.

There are period effects in the SZ, DEP, ANX, OCD samples (more recent years of birth contain more risks).

Living in the capital implies a higher risk for SZ, DEP, ANX, OCD, SUD. Age at diagnosis in any of the disorders had no differential effect on the family load. Case relatives did not develop the event earlier than control relatives.

**Discussion:** These findings point to family transmission as a highly relevant factor in the aetiology of most of the major mental disorders. The varying amount of explained variance of the disease manifestation by family aggregation is most likely reflecting varying heritability rates in different disorders. This issue needs further studies which are ongoing. Whereas parental age was not a substantial risk factor, the varying sex patterns were very much in accordance with preceding studies and clinical expertise. There was no proof of the hypothesis that early manifestation of any of the major disorders reflects a stronger vulnerability. The way how metropolitan life circumstances transmit into mental disorders needs further studies.

### **The Youth and Mental Health Study - the development of depression symptoms from early adolescence to young adult age**

Anne Mari Sund, Johannes Foss Sigurdson,  
Anne Mari Undheim, Lars Wichstrøm

**Objectives:** Study the development of depressive symptoms in a population sample from early adolescence to young adult age, and factors possibly moderating this development.

**Methods:** A large representative sample (N=2464) was recruited and assessed on self-reported demographics and psychosocial adjustment in two counties in Mid-Norway in 1998 (T<sub>1</sub>), mean age 13.7 years, 88.0% response rate and 1999/2000 (T<sub>2</sub>), mean age 14.9 years, 4.3% attrition. The participants were assessed again at a follow-up in 2012 (T<sub>4</sub>) (N=1266, 51% response rate) with a respondent mean age of 27.2, with the following instruments repeated at all time-points:

*The Mood and Feelings Questionnaire*, a 34 items questionnaire aiming to assess the affective, melancholic, vegetative, cognitive and suicidal aspects of depression.

*The Coping with Depression Scale*: a 21 items questionnaire made for the present study aiming to assess ruminating, problem solving, distracting and social coping with depression.

**Results:** The analyses of the longitudinal data will be performed using descriptive statistics and mixed model statistics.

**Discussion:** The results will possibly demonstrate which adolescents who are more at risk and who are less at risk for lasting or increasing high levels of depressive symptom level over a 12-13 years timespan. Further, possible protective mechanisms like early coping styles will be studied. The results might inform mental health workers and preventive public agencies.

### **Attachment, coping and depression in adolescence**

Anne Mari Sund, Tea Agerup, Stian Lydersen,  
Jan Wallander

**Objectives:** To study the associations of self-reported maternal, paternal and peer attachment with a life-time diagnosis of depression among 15 year olds. Also a possible mediating role of coping for these associations was studied.

**Methods:** From a representative sample of 2464 adolescents, participating in the Youth and Mental Health study in Mid-Norway, after a screening procedure with the MFQ (The Mood and Feelings Questionnaire), 345 adolescents (72.5% girls, mean age 15 years) completed the K-SADS-PL (Kiddie-Schedule for Affective Disorders and Schizophrenia-Present and Lifetime interview) to assess depressive disorders. 159 adolescents received a life-time depression diagnosis (minor or major). Attachment separately for mother, father, and peers was measured with the self-report IPPA (Inventory for Parent and Peer Attachment).

Coping was measured by the Coping Inventory for Stressful Situations (CISS), addressing emotional coping, problem solving coping and distraction.

**Results:** Binary logistic regression using gender and age as covariates showed an association between attachment relationships with both mother, father and with peers and a lifetime depression diagnosis. A positive association between emotional coping and depression was found. When analyzing attachments and coping multivariately, the effect of attachment with mother on depression weakened marginally and disappeared for father and peers. This indicated that the effect of attachment was partly mediated through adolescent emotional coping strategies, i.e. a tendency to react with anger, low mood, self-reproach and getting upset in stressful situations.

**Discussion:** The results suggest that attachment relationships with parents may play a role in the occurrence of depression in adolescents, as well as that adolescent emotional coping might mediate these relationships. This information might inform clinical work with adolescents.

## Polysomnography (PSG) and Multiple Sleep Latency Test (MSLT) in Children with ADHD

Anne Virring Sørensen, Rikke Lambek, Lene Ruge Møller, Poul Jørgen Jennum, Per Hove Thomsen<sup>1</sup>

**Objectives:** To report the objective measures of sleep by PSG and MSLT in children referred for attention problems (age 6-13). Objective measures were related to questionnaire measures and data were stratified for ADHD-presentations and sub-types.

**Methods:** A case-control study, based on questionnaires and ambulatory objective measures: DAWBA, Children's sleep habits questionnaire, PSG and MSLT.

**Results:** Sleep (subjective and objective) was assessed in 78 children with ADHD and in 25 controls. Several objective sleep measures differed in children with ADHD compared to controls. There were no significant differences between ADHD presentations and various types of additional comorbidity.

**Discussion:** The observed differences in sleep parameters in the present study differ from findings of preceding studies. However, the small sample sizes both in the present study (n=15) using ambulatory PSG and in the largest study based on 34 patients using both PSG and MSLT have to be taken into account. The main discussion will focus on how sleep may be related to the aetiology of ADHD.

## Sleep and daily functioning in children with ADHD

Anne Virring Sørensen, Rikke Lambek, Lene Ruge Møller, Poul Jørgen Jennum, Per Hove Thomsen

**Objectives:** To describe the relation between reported sleep problems and daily functioning in consecutively referred children (age 6-13) throughout two years. Stratifying for ADHD-presentations and sub-types.

**Methods:** A case-control study, and a cross-sectional design based on questionnaires: DAWBA, Children's sleep habits questionnaire, Weiss functional impairment rating scale

**Results:** Sleep problems were assessed in 397 children.

We found a moderate positive correlation between sleep problems and impaired functioning in both children with ADHD and in typically developed children. Sleep problems did not differ significantly in various presentations and subtypes of ADHD. Children with ADHD and a comorbid internalising or autistic disorder had the highest sleep problem score.

**Discussion:** Sleep affects all children in the same manner regardless of diagnoses. Further issues of discussion pertain to the lacking differences between various ADHD-presentations, the impact of additional co-morbid diagnoses, and measurement effects by parental report.

### Characteristics of children with functional somatic symptoms referred to the Child and Adolescent Mental Health Services

Simone Tøt – Strate, Charlotte Ulrikka Rask,  
G. Dehlholm

**Objectives:** The main aim of this study was to characterize children with medically unexplained or functional somatic symptoms (FSS) referred to The Child and Adolescent Mental Health Services (CAMHS) with regard to clinical and anamnestic characteristics. A secondary aim was to investigate if reasons for referral reflect the few recommendations described in international literature.

**Methods:** As a first step 248 children were included. All were hospitalized at the paediatric department, Odense University Hospital, Denmark during year 2012 and received discharge ICD-10 diagnoses possible related to functional symptoms (index diagnoses) and/or were referred to the CAMHS with one of index diagnoses. Based on an evaluation of the discharge summaries performed by two child and adolescent psychiatrists and one paediatrician, these children were categorised as having no, possible or definitely FSS (combined kappa 0, 74). The final study sample consisted of all children who were evaluated as having definitely FSS (N=60) of which a subgroup was referred to the CAMHS (n=16). Medical records of the referred (n=16) and the non-referred group (n=44) were evaluated by a standardised medical record review which was specifically developed for this study. Referred children were compared to non-referred children with regard to various anamnestic and clinical characteristics by means of univariate analyses ( $\chi^2$  and Fisher's exact test).

**Results:** The mean age of children was 11.12 yrs (range: 6-16), with no statistically significant difference between the two groups ( $p=0.223$ ). Compared to the non-referred children, the referred children presented to a higher degree a multisymptomatic picture ( $p=0.012$ ) which was more dominated by neurological symptoms ( $p=0.032$ ) and had longer symptom duration ( $p=0.048$ ) as well as a higher use of health care resources in the paediatric setting (more clinical investigations during admission ( $\geq 3$ ,  $p=0.002$ ) and longer duration of admission ( $\geq 2$  weeks,  $p=0.021$ )). The paediatricians gave several reasons for their referral of children with FSS to the CAMHS. Number of reasons specified in each referral ranged from one (19%), two (19%), three (59%) to four (12%), with inadequate treatment response in the paediatric setting being the most frequent.

**Discussion:** Multisymptomatic presentation, long-term duration of symptoms and a higher use of health care resources in the paediatric setting may be characteristic of children with FSS referred to the CAMHS. It seems that the paediatricians in this particular Danish setting give various reasons for referral of children with FSS to the CAMHS, which corresponds quite well to the few recommendations given in the current literature.

Together with future larger studies performed across several paediatric departments and in different countries, the present results may be useful in the development of more specific guidelines for referral of children with FSS to the CAMHS.

**The Nordic Long-term OCD Treatment Study (NordLOTS): Step 1 CBT outcome and predictors**  
*Nor Christian Torp, Tord Ivarsson*

**Objectives:** To describe the outcome of manual - based CBT (14 sessions) in 269 children and adolescents with OCD. Moreover, predictors of outcome will be described

**Methods:** Both semi-structured interviews (KSADS and CY-BOCS) as well as dimensional measures of symptom severity and co-morbidities.

**Results:** More than 70% of the patients responded well to treatment. Outcome was predicted by OCD severity and impairment and by some co-morbid diagnoses as well as by dimensional measures of externalizing and internalising symptom severity.

**Discussion:** The NordLOTS is the biggest OCD study to date, and the outcome from manualised CBT was better than expected. Moreover, the statistical power was sufficient to show new and partly different predictors of outcome than has been showed previously.

**The Roots of Autism and ADHD study Sweden (RATSS): the cognitive phenotype in discordant twins**

*Charlotte Willfors, Lina Poltrago, Steve Berggren, Christina Coco, Henrik Anckarsäter, Paul Lichtenstein, Angelica Ronald and Sven Bölte*

**Objectives:** The study of differences between monozygotic (MZ) twin pairs with respect to Attention Deficits Hyperactivity Disorders (ADHD) and Autism Spectrum Disorders (ASD) may provide novel leads to disentangle the environmental contribution driving these phenotypes. The aim of this study is to examine non-shared environmental influences on 1) executive function in dimensionally defined ADHD, and 2) central coherence/attention to details in dimensionally defined ASD.

**Methods:** Two studies included in the broader RATSS-program will be presented and discussed.

Study one included 27 MZ twin pairs being moderately to substantially discordant for ADHD traits as assessed by the Attention Problem (AP) scale of the Child Behavior Checklist/Adult Behavior Checklist. In this study, the twins completed the Wisconsin Card Sorting Test (WCST) for cognitive flexibility and Tower Test (TT) for foresighted planning.

Study two included 23 MZ pairs being moderately to substantially discordant for ASD traits as assessed by Social Responsiveness Scale (SRS) and Autism Quotient (AQ). The abilities of attention to details and visual central coherence were assessed with Fragmented Picture Test and Embedded Figure Test.

**Results:** The analyses revealed a link between ADHD on one hand, and inhibitory control on the other hand, mediated by non-shared environmental factors. In the ASD discordant pairs, the results showed an association between ASD traits and impaired visual central coherence, and the link was affected by non-shared environmental factors.

**Discussion:** Our findings confirm previous research suggesting both ASD and ADHD to be quantitative extremes on continuums.

The results suggest executive functions to be a cognitive marker of ADHD traits, and visual central coherence to be a marker for ASD traits. Both these abilities seem to be affected by non-shared environment.