

11th European Conference on Tourette Syndrome and Tic Disorders

Annual Meeting of the European Society
for the Study of Tourette Syndrome



ESSTS

ABSTRACTS



11th European Conference on Tourette Syndrome and Tic Disorders

Annual Meeting of the European Society for the Study of Tourette Syndrome



Copenhagen, DENMARK | June 13-15, 2018





The organising committee



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THANK YOU

To Suzanne Dobson, Seonaid Anderson and Pippa McClounan from Tourettes Action UK, for their invaluable logistics support and event coordination.





A SPECIAL THANK YOU

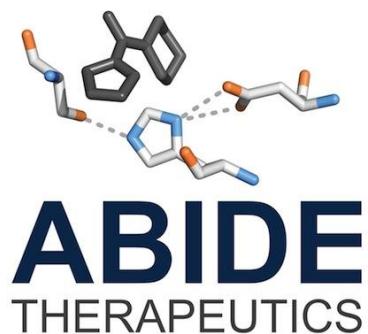
To the Danish Tourette Association, who have given financial support to this conference as a forum for the spread of knowledge and interchange of experience in the treatment of the Tourette syndrome, in accordance with the statutes of their association.



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PROGRAMME

JUNE 13th

MORNING

11:30 (open ended): Patients Associations Meeting

-Results of the Europe-wide survey among patients and their families on research topics, Dr. Seonaid Anderson, Research manager at Tourette's Action

-Closing the gap: easy ways we can improve the Quality of Life of those living with Tourette Syndrome by working together, Laura Beljaars, Board member Dutch Stichting Gilles de la Tourette

AFTERNOON

13:00-16:00

“Behavioural therapy for tic disorders: Where to next? Developing your toolkit.” (English):

-13:00: Developing your toolkit: a workshop on third wave approaches and supporting co-existing conditions in behavioural therapy.

Cara, Zsanett & Katrin

-14:00: Making the most of what you know: dissemination of treatment approaches.

Tara & Jolande

-15:00: Round table discussion and quiz.

Jolande, Katrin, Zsanett, Tara & Cara

Speakers:

-Zsanett Tarnok: Clinical psychologist/neuropsychologist at Vadaskert Child and Adolescent Psychiatry Budapest, Hungary.

-Tara Murphy: Consultant clinical psychologist, Great Ormond Street Hospital NHS Trust, London, United Kingdom

-Jolande van der Griendt: Jolande van de Griendt: Health psychologist/ cognitive behavioural therapist at TicXperts, the Netherlands

-Cara Verdellen: Clinical psychologist/behavioural therapist at TicXperts and at Parnassia Group/PsyQ Nijmegen, the Netherlands.

Oral presentations selected from abstracts:

01. Treatment of Tourette syndrome with attention training – a pilot study. Daniel Alvarez-Fischer

02. Online Remote Behavioural Intervention for Tics – ‘ORBIT’ Trial: protocol of an internal pilot study and single-blind randomised controlled trial. Charlotte L. Hall

03. Therapist- and parent-guided Internet-delivered behaviour therapy for pediatric Tourette’s Disorder: a pilot randomised controlled trial with long-term follow-up. Per Andrén

04. Group-based CBIT for adults with Tourette Syndrome or Chronic Tic Disorder – Preliminary Results. Morten Bekk



13:00-14:00 ENIGMA-TS progress update session

14:30-15:30 PANDAS/PANS interest group

15:45-16:30 Patient advocacy session

16:30-16:45 Welcome

Liselotte Skov (Paediatric Department, Herlev University Hospital, Herlev, Denmark), Kjeld Christensen (Danish Tourette Association) and Andreas Hartmann (chair ESSTS)

16:45-17:30 OPENING CEREMONY

Keynote Lecture: In the borderland of normality - tics as models of increased perception action binding.

Invited speaker: Alexander Münchau, Department of Pediatric and Adult Movement Disorders and Neuropsychiatry, Institute of Neurogenetics, Center for Brain, Behavior and Metabolism, University of Lübeck, Germany

18.30-19.30: Social arrangement: Canal tour with snacks

JUNE 14th

7:00-7:30 Running (5 km) along the beach (might be changed to a swim in the sea depending on the weather)

SESSION I

8:30-10:30 UPDATE ON ETIOLOGY (GENETICS – NON-GENETIC RISK FACTORS)

Co-Chairs: Peristera Paschou (Department of Biological Sciences, Purdue University, West Lafayette, IN, USA), Zeynep Tümer (Kennedy Center, Department of Clinical Genetics, The Juliane Marie Centre, Copenhagen University Hospital)

Invited Speakers:

08:30-09:00 Updates on large scale collaborative studies for Tourette Syndrome.

Peristera Paschou (Department of Biological Sciences, Purdue University, West Lafayette, IN, USA)

09:00-09:25 Structural variants and protein networks in Tourette Syndrome.

Zeynep Tümer (Kennedy Center, Department of Clinical Genetics, Copenhagen University Hospital, Denmark)

09:25-09:50 Genome-wide methylomic analysis of neonatal blood from Danish twins discordant for mental illness.

Shantel Weinsheimer (Institute of Biological Psychiatry, Copenhagen Mental Health Services, Denmark)





09:50-10:30 Oral presentations selected from submitted abstracts:

09:50-10:05 05. Genome-wide Association Study of Gilles de la Tourette Syndrome in a European cohort. Marianthi Georgitsi

10:05-10:20 06. Perinatal Risk Factors in Tourette's and Chronic Tic Disorders: A total population sibling comparison study. Gustaf Brander

10:20-10:30 07. Variants of the CNR1 gene in patients with Gilles de la Tourette syndrome. Natalia Szejko

10:30-11:00 COFFEE BREAK

SESSION II

11:00-13:00 IMMUNITY, ENVIRONMENT AND TIC DISORDERS

Co-Chairs: Davide Martino (University of Calgary, Calgary, Canada); Pieter Hoekstra (University of Groningen, Groningen, The Netherlands)

Invited Speakers:

11:00-11:45 Update on PANS and PANDAS.

Tanya Murphy (University of South Florida, St Petersburg, FL, US)

11:45-12:30 What are we learning about Tourette's from population-based studies?

The example of autoimmune diseases.

David Mataix-Cols (Karolinska Institutet, Stockholm, Sweden)

12:30-13:00 Oral presentations selected from submitted abstracts:

12:30-12:45 08. PANS/PANDAS in a Danish pediatric clinical cohort. Camilla Birgitte Sørensen

12:45-12:55 09. Self-reported symptoms in PANDAS: Development of a questionnaire for use in daily clinical practice. Louie Rogalla and Camilla Birgitte Sørensen

13:00-14:00 LUNCH

13:30-14:00 POSTER WALK (P1-P16)

SESSION III

14:00-16:00 NEUROBIOLOGY OF TOURETTE SYNDROME

Co-Chairs: Yulia Worbe (Faculté de Médecine, Sorbonne Université, Paris, France);

Christos Ganos (Department of Neurology, University Hospital Charité, Berlin, Germany)

Invited Speakers:

14:00-14:45 The Role of Dopamine in Tourette Syndrome: A Computational Account. Tiago Maia (Instituto de Medicina Molecular, Faculdade de Medicina, Universidade de Lisboa, Portugal)





14:45-15:30 Insights from animal models on the pathophysiology of tics and comorbid symptoms.

Izhar Bar-Gad (The Leslie and Susan Gonda Brain Research Center, Bar-Ilan University, Ramat-Gan, Israel)

15:30-16:00 Oral presentations selected from submitted abstracts (TBA)

15:30-15:45 010. Attention and inhibition in Tourette's Syndrome. Leanne Hockey

15:45-16:00 011. Involvement of the Endocannabinoid System in Tourette Syndrome: Evidence from an CSF Study. KW. Sühs

16:00-16:15 COFFEE BREAK

16:15-17:00 GENERAL ASSEMBLY MEETING

18:00-19:00 RECEPTION AT COPENHAGEN CITY HALL

From 19:30 DINNER IN TIVOLI

JUNE 15th

7:00-7:30 Running (5 km) along the beach (might be changed to a swim in the sea depending on the weather)

SESSION IV

8:30-10:00 COMORBIDITIES

Co-Chairs: Renata Rizzo (Department of Clinical and Experimental Medicine, Child and Adolescent Neurology and Psychiatry, Catania University, Catania, Italy), Kerstin Plessen (Child and Adolescent Mental Health Centre Copenhagen, Denmark & Division of Adolescent and Child Psychiatry, Department of Psychiatry, Lausanne University Hospital, Lausanne, Switzerland)

Invited Speakers:

08:30-09:00 Comorbidities in clinical versus non-clinical populations of children and adolescents with TS.

Elena Cravedi (Department of Child and Adolescent Psychiatry, Pitié-Salpêtrière Hospital, France & Pediatric Neurology Unit, University of Firenze, Florence, Italy)

09:00-09:30 Course of Tourette Syndrome and Comorbidities in a Large Prospective Clinical Study.

Camilla Groth (Paediatric Department, Herlev University Hospital, Herlev, Denmark).

09:30-10:00 Oral presentations selected from submitted abstracts:

09:30-09:45 012. Tic Disorders and its Association with Depression and Well-Being.

Feldman D

09:45-10:00 013. Predictors of adaptive behaviour in children with Tourette syndrome attending a specialist clinic. Chloe Taylor

10:00-10:30 COFFEE BREAK

SESSION V

10.30-12:15 TREATMENT

Co-Chairs: Danielle Cath (Department of Psychiatry and RGOC, University Medical Center Groningen, The Netherlands), Veit Roessner (Department of Child and Adolescent Psychiatry, Faculty of Medicine, TU Dresden, Dresden, Germany)

Invited Speakers:

10:30-11:00 Efficacy and safety of the cannabinoid modulator ABX-1431 in Tourette Syndrome: results from a phase 1b study.

Kirsten Müller-Vahl (Department of Psychiatry, Socialpsychiatry and Psychotherapy, Hannover Medical School, Hannover, Germany)

11:00-11:30 An update on deep brain stimulation on Tourette Syndrome.

Tom Foltynie (Sobell Department of Motor Neuroscience, UCL Institute of Neurology, National Hospital for Neurology and Neurosurgery, London, UK)

11:30-12:15 Oral presentations selected from submitted abstracts:

11:30-11:45 014. "Randomized Control Trial on the Efficacy of Habit Reversal Treatment Programme in Children and Adolescents - a Comparison With Resource Activation Treatment". Katrin Woitecki

11:45-12:00 015. Comprehensive Behavioral Intervention for Tics vs. Psychoeducational-Supportive treatments in group setting for children with chronic tic disorders: A randomized controlled trial. Sharon Zimmerman-Brenner

12:00-12:15 016. Effects of Cannabidiol on Mouse Head Twitch Response: Implications for Treatment of Children with Tourette syndrome. Sharon Anavi-Goffer

12:15-13:00 Keynote Lecture: Evidenced-Based and Emerging Treatments for Tourette Syndrome.

Invited speaker: Michael Bloch, Yale Child Study Center, Department of Psychiatry, Yale University, New Haven, CT, United States

13:00-14:00 LUNCH

13:25-14:00 POSTER WALK (P17-P33)



14:00-14:30 THE PROFESSOR MARY ROBERTSON AWARD

Efficacy of a Resource Activation Treatment in Children with Chronic Tic Disorders – A Within-Subject Analysis. Paula Viefhaus

SESSION VI

14:30-16:00 HOT TOPICS

Chair: Andrea Cavanna (Department of Neuropsychiatry, The Barberry National Centre for Mental Health, 25 Vincent Drive, Birmingham B15 2FG, UK), Nanette Mol Debes (Department of Paediatrics, Herlev University Hospital, Herlev, Denmark)

Discussion of hot topics and controversies from submitted abstracts of the meeting.

14:30-16:00 Oral presentations selected from submitted abstracts:

14:30-14:45. 017. Premonitory Urges Revisited: New Insights into the Location and Quality of Premonitory Urges. Ewgeni Jakubovski

14:45-15:00 018. A Strengths-Based Intervention for Complex Motor Stereotypies.

Amanda Maxwell

15:00-15:15 019. Misophonia in children with Tic Disorders. Sally Robinson

15:15-15:30 020. Association of Tourette's and Chronic Tic Disorders with metabolic and cardiovascular complications. Lorena Fernández de la Cruz

15:30-15:45 021. Impact of Tourette's and chronic tic disorders on objective indicators of educational attainment: A population-based sibling comparison study. Ana Pérez-Vigil

15:45-16:00 022. Exposure and Response prevention in a large Danish clinical cohort of children and adolescents with Tourette syndrome. Camilla Birgitte Sørensen

16:00-16:10 COFFEE BREAK

16:10-16:15 Prizes best poster presentation and best oral presentation

SESSION VII

16:15-17:30 CLINICAL ROUNDS

Co-Chairs: Liselotte Skov (Department of Paediatrics, Herlev University Hospital, Herlev, Denmark), Tammy Hedderly (Evelina London CH, GSTT, TANDEM Clinic., UK)

Clinical presentations and discussion of submitted cases.

17:30 CLOSING CEREMONY



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Selected oral presentations

O1. Treatment of Tourette syndrome with attention training – a pilot study

Anja Schaich¹, Valerie Brandt², Alena Senft¹, Christian Schiemenz³, Alexander Münchau⁴, Daniel Alvarez-Fischer^{1,3}

1 Department of Psychiatry and Psychotherapy, University Medical Center Schleswig-Holstein - Campus Lübeck, Germany; 2 Department of Psychology, Centre for Innovation in Mental Health, University of Southampton, Southampton, Hampshire, UK; 3 Institute of Neurogenetics, University of Lübeck, Lübeck, Germany; 4 Department of Pediatric and Adult Movement Disorders and Neuropsychiatry, Center of Brain, Behavior and Metabolism, University of Lübeck, Lübeck, Germany

Background:

Tourette syndrome (TS) is a childhood onset neuropsychiatric disorder characterized by multiple motor and vocal tics. Psychosocial interventions, such as comprehensive behavioral intervention for tics or habit reversal therapy are valuable tools for treating TS. A significant number of TS patients though do not benefit from these interventions. Recently published studies show that paying attention to tics increases whereas paying attention to other tasks decreases tic frequency.

Materials & Methods:

The aim was to study, as a proof of principle, whether Attention Training Technique (ATT), developed by Adrian Wells, can reduce tic frequency and severity and can improve quality of life in TS. To this end, three patients with TS under best medical treatment were allocated to a non-treatment baseline period of 4 weeks. Following the baseline period, patients received 6 weeks of ATT. Tic severity and frequency, as well as secondary outcome measures were assessed before and after baseline, after completion of ATT and 3 and 6 months later using the YGTSS (Yale Global Tic Severity Scale), the quality of life in Tourette syndrome scale (GTS-QoL), the revised version of the obsessive-compulsive inventory (OCI-R), the premonitory urge for tics scale (PUTS), and the modified Rush videotape rating scale at each time point. The latter was carried out by two independent blinded raters.

Results and Conclusions:

All three participants experienced a reduction of tic frequency, severity and global impairment from baseline to post intervention. Overall impairment rating in YGTSS showed a maximal reduction of $43\% \pm 4\%$. Global severity score reduced to 42% of baseline values. Interestingly, values of PUTS remained unchanged. Additionally, quality of life was improved in all patients (maximal reduction $60\% \pm 1\%$ compared to baseline values). Also, scores in ADHD and OCD scale reduced in the same range. However, a resurgence of symptoms back to baseline levels was observed in one patient after 6 months upon discontinuation of ATT.

In this case series, ATT effectively reduced tic frequency and severity in patients with TS. Results must be interpreted with caution given the small number of patients. This notwithstanding, further studies including randomized controlled trials appear warranted.



O2. Online Remote Behavioural Intervention for Tics – ‘ORBIT’ Trial: protocol of an internal pilot study and single-blind randomised controlled trial

Charlotte L Hall¹, Emin Hadziosmanovic¹, E Bethan Davies¹, Tara Murphy², Per Andrén³, Sophie Bennett², Amber Evans², Charlotte Sanderson², Joseph Kilgariff⁴, Liam Chamberlain⁴, Kareem Khan¹, Cris Glazebrook¹, Isobel Heyman² and Chris Hollis^{1,4} on behalf of the ORBIT Trial team

¹University of Nottingham, Nottingham, UK; ²Great Ormond Street Hospital for Children NHS Foundation Trust, London, UK; ³Centre for Psychiatry Research, Department of Clinical Neuroscience, Karolinska Institutet, Stockholm, Sweden; ⁴Nottinghamshire Healthcare NHS Foundation Trust, Nottingham, UK

Background:

Tourette syndrome is a common, disabling childhood-onset neurodevelopmental condition. Recent guidelines recommend that behavioural therapy should be offered as first-line treatment for children with tics. However, there are very few tic-trained therapists and many patients cannot access appropriate care. Internet-delivered behaviour therapy for tics could increase the availability of evidence based treatment. This method of delivery has been piloted with promising results (Andrén et al., manuscript in prep2018) but currently lacks randomised controlled trial evidence. This trial investigates whether Internet-delivered behavioural interventions for tics can reduce severity of symptoms.

Materials & Methods:

This parallel-group, single-blind, randomised controlled superiority trial will recruit children and young people (aged 9-17 years-old) with chronic tic disorders over an 18-month period recruited within the United Kingdom. Participants will be randomised to receive 10-weeks treatment of either online, remotely-delivered, therapist-supported behavioural therapy for tics, or online, remotely-delivered, therapist-supported education on tics. Participants will be followed-up at mid-treatment, 3-, 6-, 12-, and 18-month post-randomisation. There is an internal pilot in the 9th month to assess whether recruitment, engagement with the intervention and retention to the trial are sufficient to allow the trial to progress and provide a definitive answer on effectiveness.

The primary outcome is reduction in tics as measured on the Yale Total Tic Severity Score from the Yale Global Tic Severity Scale. Secondary outcomes include quality of life, a cost-effectiveness analysis, optimising of the intervention design, identification of the barriers and facilitators to implementation. An integrated process evaluation will analyse quantitative and qualitative data in order to fully explore implementation of the intervention.

Results and Conclusions:

The findings will inform clinicians and healthcare providers about the clinical and cost effectiveness of Internet delivered treatment for children and young people with tics.

This research was funded by the NIHR Health Technology Assessment (ref 16/19/02). The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health.



O3. Therapist- and parent-guided Internet-delivered behaviour therapy for paediatric Tourette's Disorder: a pilot randomised controlled trial with long-term follow-up

Per Andrén^{1,2}, Kristina Aspvall^{1,2}, Lorena Fernández de la Cruz¹, Paulina Wiktor³, Sofia Romano³, Erik Andersson¹, Tara Murphy^{4,5}, Kayoko Isomura^{1,2}, Eva Serlachius^{1,2}, and David Mataix-Cols^{1,2}

¹Centre for Psychiatry Research, Department of Clinical Neuroscience, Karolinska Institutet, Stockholm, Sweden; ²Stockholm Health Care Services, Stockholm County Council, Sweden; ³Department of Clinical Neuroscience, Division of Psychology, Karolinska Institutet, Stockholm, Sweden;

⁴Tourette Syndrome Clinic, Great Ormond Street Hospital for Children NHS Foundation Trust, London, UK; ⁵Institute of Child Health, University College London, UK

Background:

Behaviour therapy (BT) for Tourette's Disorder (TD) and Persistent Motor or Vocal Tic Disorder (PTD) is rarely available. We evaluated the feasibility of adapting two existing BT protocols for TD/PTD (habit reversal training [HRT] and exposure and response prevention [ERP]) into a therapist- and parent-guided online self-help format.

Materials & Methods:

Twenty-three young people with TD/PTD, aged 8-16, were randomly assigned to one of two 10-week therapist- and parent-guided Internet-delivered programmes (called BIP TIC HRT and BIP TIC ERP). Blinded evaluators rated symptoms at baseline, post-treatment, and 3-month follow-up (primary endpoint). All participants were naturally followed-up to 12 months after treatment. The primary outcome measure was the Yale Global Tic Severity Scale (YGTSS).

Results and Conclusions:

Patients and parents rated the interventions as highly acceptable, credible, and satisfactory. While both interventions resulted in reduced tic-related impairment, parent-rated tic severity, and improved quality of life, only BIP TIC ERP resulted in a significant improvement on the primary outcome measure. Within-group effect sizes and responder rates were, respectively: $d=1.12$ and 75% for BIP TIC ERP, and $d=0.50$ and 55% for BIP TIC HRT. The therapeutic gains were maintained up to 12 months after the end of the treatment. Adverse events were rare in both groups. The average therapist support time was around 25 minutes per participant per week. To conclude, Internet-delivered BT has the potential to greatly increase access to evidence-based treatment for young people with TD/PTD. Further evaluation of the efficacy and cost-effectiveness of this treatment is warranted.

ClinicalTrials.gov Identifier: NCT02864589

O4. Group-based CBIT for adults with Tourette Syndrome or Chronic Tic Disorder – Preliminary Results

Morten Bekk¹, Erna Marie Moen², Anniken Andersen², Karet Jacobsen Meland², Benjamin Hummelen³

¹ Regional Resource Centre for Autism, ADHD, Tourette Syndrome and Narcolepsy, Oslo University Hospital; ² Outpatient clinic for OCD-related Disorders, Oslo University Hospital; ³ Section for Treatment Research, Department of Research and Development, Clinic Mental Health and Addiction, Oslo University Hospital



Background:

Tourette Syndrome (TS) is a serious medical condition characterized by motor and vocal tics, which may have a considerable negative impact on social functioning and quality of life. TS is associated with comorbid disorders such as ADHD, OCD, anxiety, depression, and impulsive behaviour⁽¹⁾.

Comprehensive Behavioural Intervention for Tics (CBIT) is a well-documented, individualized treatment of tics⁽²⁾, and consists of four elements: psychoeducation, habit reversal training (HRT), functional analyses, and relaxation exercises⁽³⁾.

A number of studies have shown that CBIT, administered as individual therapy, is an effective treatment for TS in adults. CBIT delivered in groups might be even more effective and more cost-effective. Group-based treatment with HRT has been shown to be beneficial for youth with TS^(4,5,6). However, the effectiveness of this treatment approach has not been tested yet for adults.

Aims:

The aim of the current study is to evaluate treatment outcome of CBIT for adult patients with TS or Chronic Tics Disorder (CTD). Therapy is delivered in groups, conducted at ordinary outpatient settings. The primary outcome is reduction of tics, and the secondary outcome is increased tic-specific quality of life, e.g., better (increased) function, less social anxiety, increased social activity.

Methods:

Participants are assessed with Yale Global Severity Scale (YGTSS), Adult Tics Questionnaire (ATQ), The Gilles de la Tourette syndrome –Quality of Life Scale (GTS-QoL) by pre-treatment, post-treatment after eight sessions, after three booster sessions, and after one year. Comorbid disorders were assessed at baseline by Yale-Brown Obsessive-Compulsive Scale (YBOCS) and Adult ADHD Self-report Scale v1.1. (ASRS v1.1.). Therapy is manualized and comprises eight structured sessions and three follow-up booster sessions⁽³⁾.

The first groups were small (three or four participants and two therapists) but it will be considered to increase the number of group members to at least four participants. By spring 2018, a total of seven different treatment groups had finished a minimum of eight structured sessions. At the time being, 23 participants are included in the study, with an age range of 20 to 69 years, 10 women and 13 men.

Results and conclusion:

The study is still in progress, but preliminary clinical experience indicate: Decreased frequencies of tics, and learning and mastering competitive responses caused increased experience of control of tics. Increased experience of control also contributed to decreased symptoms of social anxiety and increased participation in social daily life and activities.

Effects of participation in group-based treatment: Participants emphasize that group participation has been of significant importance for change and has resulted in a reduction of shame and social insecurity; a greater understanding and knowledge about Tourette Syndrome, tics and oneself; improved self-esteem and self-accept. In addition, participation in group therapy had positive significance for the individual patient's motivation to carry out HRT.

CBIT administered in groups offer, in addition to HRT, a context for the participants to exchange experiences, provide mutual support, and offer solutions to tic-related problems and other life challenges. The therapists contribute to facilitate these mutual exchanges by asking explorative questions, and by using the functional analyses in the CBIT-manual.

All participants emphasize that meeting other adults with tics was one of the most valuable aspects of the treatment and point out aspects such as exchanging experiences and getting recognition. Being together with others with tics also facilitated feelings of security and openness.



The preliminary experiences of administrating CBIT in groups for adults with TS or CTD seems promising.

O5. Genome-wide Association Study of Gilles de la Tourette Syndrome in a European cohort

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Background:

Being a complex disorder, Gilles de la Tourette Syndrome (GTS) etiology is determined by both environmental and genetic factors. The genetic contribution in GTS is under intensive research through several international consortia, and although a few genes, such as *SLTRK1*, *AADAC*, *NRXN1*, *CNTN6* and *IMMP2L* have been often associated with GTS in a few cases, the causative genes largely underlying GTS pathophysiology remain unknown.

Materials & Methods:

Here, we report on a genome-wide association study using single nucleotide polymorphisms over 1,490 GTS cases and 12,039 population-matched controls collected from different European nations, genotyped on various Illumina chips. To account for different genotyping platform issues and potential discrepancies, we performed imputation on each platform separately before merging the data. Ancestry matching of imputed data was done by merging the cohort with 1000genomes genotype data and projecting it on top principal components as calculated from Principal Component Analysis, followed by removal of population outliers. Next, quality control-filtered, merged, imputed data were subjected to logistic regression analysis using PLINK.

Results and Conclusions:

Of particular interest among the top statistically significant hits associated with GTS, are genes previously implicated in schizophrenia and major depressive disorder, with a biological role in neurogenesis and axonal growth and guidance of motor and sensory neurons. These genomic variants warrant further investigation in order to shed light into the genetic background of GTS. Meta-analysis of our results with GWAS data from other consortia is expected to reveal new interesting candidates and point to biological pathways underlying the disorder.

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O6. Perinatal Risk Factors in Tourette's and Chronic Tic Disorders: A total population sibling comparison study

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Background:

Family and molecular genetic studies suggest that Tourette's disorder (TD) and chronic tic disorders (CTD) are both familial and highly heritable conditions. There is growing evidence that environmental factors are also important in the etiology of these disorders, with at least 23% of the variance being explained by non-shared environmental factors. Adverse perinatal events may increase the risk of Tourette's and chronic tic disorders (TD/CTD), but previous studies have been unable to control for unmeasured environmental and genetic confounding. We aimed to prospectively investigate potential perinatal risk factors for TD/CTD, taking unmeasured factors shared between full siblings into account.

Materials & Methods:

A population-based birth cohort, consisting of all singletons born in Sweden in 1973–2003, was followed until December 2013. A total of 3 026 861 individuals were identified, 5597 of which had a registered TD/CTD diagnosis. We then studied differentially exposed full siblings from 947 942 families; of these, 3563 families included siblings that were discordant for TD/CTD. We performed Cox regression analyses to estimate hazard ratios (HR) and 95% confidence intervals (CI) of the association between perinatal factors and TD/CTD. Perinatal data were collected from the Medical Birth Register and TD/CTD diagnoses were collected from the National Patient Register, using a previously validated algorithm.

Results & conclusions:

In the fully adjusted models, impaired fetal growth, preterm birth, breech presentation and cesarean section were associated with a higher risk of TD/CTD, largely independent from shared family confounders and measured covariates. Maternal smoking during pregnancy was associated with risk of TD/CTD in a dose–response manner but the association was no longer statistically significant in the sibling comparison models or after the exclusion of comorbid attention-deficit/hyperactivity disorder. A dose–response relationship between the number of adverse perinatal events and increased risk for TD/CTD was also observed, with hazard ratios ranging from 1.41 (95% confidence interval (CI): 1.33–1.50) for one event to 2.42 (95% CI: 1.65–3.53) for five or more events. These results pave the way for future gene by environment interaction and epigenetic studies in TD/CTD.

O7. Variants of the *CNR1* gene in patients with Gilles de la Tourette syndrome

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Background:

Gilles de la Tourette syndrome (GTS) is a neuropsychiatric disease of unknown etiology, although major role of genetic factors has been established. Variants of *CNR1* gene encoding the central cannabinoid receptor (CB1) are supposed to be the risk factor for the developing of some neurodevelopmental diseases. Moreover, usage of cannabinoid drugs may alleviate tics. Our aim was to test the association of selected *CNR1* gene variants with GTS.

Materials & Methods:

The study group comprised of 257 patients aged 6-59 (mean: 23.9 ± 11.8 years; 199 males, 77.4%). The control group consisted of 279 healthy persons aged 13-54 (mean: 22.6 ± 3.4 years; 213 males, 76.3%). Four single nucleotide polymorphisms (SNPs) in *CNR1* were selected: rs2023239, rs2180619, rs806379, rs1049353 based on minor allele frequency in general population (MAF>15%). These variants were genotyped using a real-time quantitative polymerase chain reaction system (TaqMan SNP genotyping assay).

Results and Conclusions:

We found significant association of GTS clinical phenotype with rs2023239 variant. Minor allele C and genotype CT frequency were found significantly more often in GTS patients compared to controls ($p=0.003$ and $p=0.001$, respectively). There were no statistically significant results for rs806379, rs1049353 and rs2180619 variants. Our findings suggest that rs2023239 polymorphism of the *CNR1* gene is a risk factor of GTS in Polish population. Abnormal endocannabinoid transmission is suspected to be one of the causes in pathogenesis of GTS.

O8. PANS/PANDAS in a Danish pediatric clinical cohort

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Background:

Pediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections (PANDAS) and Pediatric Acute-onset Neuropsychiatric Syndrome (PANS) have been suggested to be a result of a disordered immune response after an infection causing neuropsychiatric symptoms. An association with a group A beta-hemolytic streptococcus (GAS) infection is suggested in PANDAS and with other infectious agents in PANS. Although the diagnosis PANDAS/PANS has been controversial, more focus has come on the diagnosis, pathophysiology and treatment during the recent years.

Materials and Methods:

We reviewed patient charts of 15 pediatric patients with suspected PANS/PANDAS from the Danish National Tourette syndrome clinic; charts were reviewed for demographics, symptoms, examinations, treatment, and outcome.

Results and conclusions:



11 patients met full criteria for either PANDAS or PANS. Four patients did not fulfill all diagnostic criteria due to age at onset, absence of GAS infection and/or sub-acute onset of symptoms. Most reported symptoms were tics (86.7%), sleep disturbance (66.7%), behavioral disturbances (60.0%), anxiety (53.3%), motoric control abnormalities (53.3%), Obsessive Compulsive Disorder (OCD) (40.0%) and eating restrictions (20.0%). Streptolysin-O antibody and streptococcus throat culture were taken in 13 patients, and tests were positive in respectively 61.5% and 38.4%. Anti-neuronal antibody titers were taken in 14 patients, a minimum of one titer was positive in 92.8%; Calmodulin-dependent kinase II and Anti-beta-tubulin were most often positive. Acute antibiotic (AB) treatment was given to all patients and had an effect in 73.3%. Prophylactic AB was given to 53.3% of patients and had an effect in all patients. Besides AB, some patients were treated with steroid, intravenous immunoglobulin, non-steroidal anti-inflammatory drug, tonsillectomy and standard psychiatric treatment.

Further research with inclusion of more patients with suspected PANS/PANDAS are needed to discuss the usefulness of the existing diagnostic criteria, the pathophysiology, examination, and treatment.

O9. Self-reported symptoms in PANDAS: Development of a questionnaire for use in daily clinical practice.

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Background:

Pediatric Autoimmune Neuropsychiatric Disorders Associated With Streptococcal Infections (PANDAS) was defined in 1998 as motoric and psychiatric symptoms, with an acute onset post a streptococcal infection and thereafter a fluctuating course of illness, most likely correlating with subsequent infections. Since then, efforts have been made in regards to define not only the criteria, but also the co-morbidities and symptoms unique for this illness. 20 years later, the knowledge concerning pathophysiology and diagnostic criteria of PANDAS are far from well-known and are still subjects of discussion.

Materials & Methods:

Through a systematic review of literature concerning the symptoms and comorbidities tied to PANDAS, a questionnaire has been developed in an attempt to differentiate PANDAS from other movement- and/or psychiatric disorders, to assess symptoms severity and monitor effect of treatment, thereby unveiling traits unique for PANDAS. In this pilot study, the questionnaire was tested on 10 children with suspected PANDAS, and 10 children diagnosed with Tourette syndrome.

Results and Conclusions:

As data collection is ongoing, the results will be presented at the conference. The questionnaire used in the pilot study is in Danish, but will at the conference be presented in an English version. We expect to be able to present a PANDAS questionnaire that can be implemented directly in the clinic. If the questionnaire is proven useful in the clinic, our aim is to get it validated and used broadly for diagnosis and illness monitoring.



O10. Attention and inhibition in Tourette's Syndrome

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Background:

Disrupted inhibitory processing may explain why people with Tourette's syndrome (TS) have difficulty with tic control. As tics can be distractable, impaired attentional mechanisms may also play a role. We studied attention and inhibition in the same people with TS.

Materials & Methods:

16 healthy volunteers (HV: 35.82 ± 14.31 yrs; 11 male) and 30 adults with TS (36.73 ± 14.20 yrs; 20 male) underwent: CANTAB cognitive testing to assess inhibitory control and attention; a test of interoceptive awareness (heartbeat mental tracking); and paired pulse transcranial magnetic stimulation (TMS) short-interval intracortical inhibition (SICI) and short afferent inhibition (SAI) to assess inhibitory neurophysiology. Independent t-tests were used to compare groups.

Results:

In TS, significant reductions were found for: interoceptive awareness (TS: mean 0.75 SD 0.17 , HV: mean 0.63 SD 0.16 ; $t(45) = 2.34, p < 0.05$), SICI when a conditioning TMS pulse was delivered 3ms prior to the onset of the test TMS pulse (normalised MEPs, TS: mean 0.33 SD 0.23 , HV: mean 0.65 SD 0.46 ; $t(43) = -2.58, p < 0.005$) and SAI when a conditioning sensory stimulus (median nerve) preceded a test TMS pulse at time points corresponding to the N20 somatosensory evoked potential, $N20 \pm 2$ ms, 4ms and 6ms (normalised MEPs, all $p < 0.05$). There were no significant differences on CANTAB tasks of sustained attention, planning and spatial working memory (all $p > 0.05$). On the Intra Extra Dimensional task, a test of rule acquisition and reversal, TS showed a specific impairment in shifting attention to a novel stimulus dimension that was previously incorrect, as indicated by significantly more extradimensional shift errors (TS: mean 8.5 SD 9.2 ; HV: mean 3.3 SD 5.5 ; $t(44) = -2.05, p < 0.05$). In the Stop Signal Reaction Time (SSRT) Task, testing inhibition of a planned response, the SSRT during the last half of the task was significantly longer (TS: mean 190.11 SD 51.99 ; HV: mean 164.15 , SD 30.35 ; $t(45) = -1.88, p < 0.05$).

Conclusions:

Deficits in cortical inhibition and inhibiting an already activated motor response were found. Impairments in switching attention in order to suppress inappropriate, habitual responses and inaccurately attending to internal autonomic events were also shown. Together impaired inhibition and attention may explain the difficulty in tic control.

O11. Involvement of the Endocannabinoid System in Tourette Syndrome: Evidence from an CSF Study

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Background:

In Tourette-Syndrome (TS) several lines of evidence suggest an involvement of cortico-striato-thalamo-cortical regulatory circuits and disturbed dopaminergic transmission. However, basal ganglia neurons express a high density of central cannabinoid (CB1) receptors indicating a paramount role of the endocannabinoid system (ECS) in movement control. In TS, it is suggested that exocannabinoids such as tetrahydrocannabinol (THC) as well as modulation of endocannabinoids improves tics and comorbidities. Therefore, an endocannabinoid hypothesis has been suggested in TS. In the presented work we focused on specific changes of the main ligands of the ECS, anandamide (AEA) and 2-arachidonoylglycerol (2-AG) within the cerebrospinal fluid (CSF) in adults with TS.

Materials & Methods:

Endocannabinoids including AEA, 2-AG and arachidonic acids (AA) were extracted from CSF using a standardized liquid-liquid extraction method. A multiplex quantitative assay based on liquid chromatography/multiple reaction monitoring (LC/MRM) was used to quantitatively determine endocannabinoid levels. The endocannabinoid values were normalized to CSF volume. Patients with TS were thoroughly clinically characterized including established assessments for tics and comorbidities and MRI. As a control group 18 age- and sex matched patients with normal pressure hydrocephalus or idiopathic intracranial hypertension were included.

Results and Conclusions:

20 adult patients with TS were included (median age=36.1 ± 14.34 SD, range, 19 - 64 years). MRI did not reveal any significant abnormalities. CSF standard measurements displayed no pleocytosis, slightly dysfunctional blood-CSF-barrier in 4/20 patients using QAlb. Compared to the control group, concentrations of all endocannabinoids were significantly elevated in patients with TS: AA: 40.47 ± 4.44 vs 16.29 ± 1.76 pmol/ml (p <0.0001), 2-AG: 0.18 ± 0.024 vs 0.073 ± 0.01 (p= 0.0003), and AEA: 2.94 ± 0.34, n=20 1.29 ± 0.13 (p= 0.0001)

Despite the small sample size owed to the invasive nature of the lumbar puncture, our data clearly indicate a dysregulation in the ECS in TS. Yet, seemingly contradictory to the beneficial clinical effects of cannabinoids, we assume that the elevation of endocannabinoid levels might be best explained by a counter-regulation due to a dysfunctional ESC in TS.

O12. Tic Disorders and its Association with Depression and Well-Being

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Background:

The impact of tics disorders (TD) on patients' well-being can be quite variable, ranging from minimal to severe, depending on their psychosocial and physical impact and on psychiatric comorbidities. Among comorbidities depression has been shown to have higher prevalence in both adults and children with TD^{11,35}. However comparing with the major comorbidities, depression in this population is relatively understudied. The aim of the present study is to focus on depression and its effects on well-being of children with tic disorders. More specifically, this study aims to investigate whether depression would moderate the relationship between tic severity and well-being in children with tic disorders



Materials & Methods:

Fifty children with tics between the age of 7 to 16 years ($M=11.57$, $SD=2.66$) were examined by clinical interview and self-report questionnaires regarding depression (MFQ: Mood and Feelings Questionnaire), tic disorders (YGTSS: Yale Global Tic Severity Scale), obsessive compulsive disorders (CY-BOCS: Childrens Yale–Brown Obsessive Compulsive Scale), Wellbeing-Quality of life (QOL: KINDL questionnaire) and Well-being -Difficulties in life (part of SDQ: strength and difficulties in life questionnaire).

Results and Conclusions:

The majority of the patients (63.3%) had between mild and moderate tics. Only 6.12% of the patients suffered from a Major Depression. A significant positive correlation was found between depression and YGTSS score and tics impairment but not with total tics severity. On well-being measures, QOL was negatively and significantly correlated with all tic measures. Difficulties in life were positively and significantly associated with total tic severity and YGTSS scores. Depressive symptoms moderated the relationship between tic severity and tic impairment so that a stronger correlation between tics severity and tic impairment was observed in participants with elevated depressive symptoms. However, depressive symptoms did not moderate the relationship between tic severity and other well-being measures (QOL, SDQ)

To conclude, this study presents important findings related to depression and well being in children with tic disorders and Tourette syndrome. Also, a series of testable hypotheses useful for future TD research was developed that, if replicated, will have a number of clinical implications.

O13. Predictors of adaptive behaviour in children with Tourette syndrome attending a specialist clinic

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Background:

Tourette Syndrome (TS) is a neurological condition affecting 0.3-0.9% of school-age children in the general population¹. TS has high rates of psychiatric comorbidity including Attention Deficit Hyperactivity Disorder (ADHD)², Anxiety and Obsessive-Compulsive Disorder (OCD)³, perhaps underpinned by shared genetic and neurobiological substrates including disruptions to corticostriatal-thalamocortical circuits⁴.

As well as elevated rates of psychiatric comorbidity, children with TS have increased likelihood of specific learning disorders⁵ and cognitive difficulties⁶. Research in TS populations highlights cognitive difficulties in processing speed, fine motor co-ordination, performance IQ, socialisation, executive functioning, and adaptive behaviours⁷.

There is a paucity of research investigating the adaptive functioning of young-people with TS. Adaptive behaviours refer to a person's ability to manage everyday life demands and personal independence skills relative to their expected age group; these include a wide range of skills such as communication, self-care, social skills, self-direction, and academic skills⁸. It is important to identify these deficits to better support children with TS in developing these skills in the future.

To date no studies have examined how neuropsychological function and presence of commonly co-occurring disorders predict level of adaptive behaviour in a TS sample. The current study aimed to investigate predictors of adaptive functioning of children with a diagnosis of TS within a UK sample.

Materials and Methods:

60 children and adolescents were selected from a specialist Tourette syndrome clinic in the UK attending between 2011 and 2014. This study used a cross sectional research design, with independent variables including IQ, measured using the Wechsler Intelligence Scale for Children – 4th Edition, and participants' diagnosis (TS; TS+ADHD; TS+Anxiety; TS+OCD) diagnosed by a Multidisciplinary Clinical Team. Adaptive functioning was the dependent variable measured using the Vineland Adaptive Behaviour Scales – 2nd Edition. Regression analyses assessing predictors of adaptive functioning and Mann Whitney U tests to identify differences between TS subgroups were completed.

Results and Conclusions:

The sample comprised the following diagnoses: 22 children TS only, 18 TS+ADHD, seven TS+OCD, five TS+Anxiety, seven TS+2 comorbid diagnoses and one TS+3 comorbid diagnoses. Across the groups, two participants had additional LD diagnoses and 29 had Specific Learning Disorders.

A diagnosis of ADHD was a predictor for level of adaptive functioning ($p=0.035$) and accounted for 18% of the variance in scores. Participants with 2 comorbid diagnoses had the lowest adaptive functioning scores of all TS subgroups.

Executive Functioning scores on subscales 'Emotional Control' and 'Organisation of Materials', measured using the Behavior Rating Inventory of Executive Function, also predicted level of adaptive functioning ($p=0.0001$) accounting for 28% of the variance in scores.

Psychiatric comorbidity and Executive Functioning difficulties are independent predictors of adaptive behaviour within TS populations. Poor emotional control and impaired organisation of materials are particularly important predictors of difficulties with adaptive functioning, and should be considered when designing support for children with TS. Executive Functioning was the strongest predictor of adaptive functioning in this sample and findings from this study are consistent with previous findings of a relationship between ADHD, Executive Function and emotional regulation^{9,10}. Clinical implications and suggestions for further research are discussed.

O14. "Randomized Control Trial on the Efficacy of Habit Reversal Treatment Programme in Children and Adolescents - a Comparison With Resource Activation Treatment"

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Background:



The main purpose of this study is to evaluate the efficacy of a habit reversal based treatment program (THICS, Woitecki & Döpfner, 2015) compared to an intervention aimed at the activation of resources (STARK, Perri et al., 2014) for children and adolescents aged 8 to 19 years with tic disorders.

Materials & Methods:

N=44 patients were randomized to one of the two groups after a 8 weeks diagnostic phase (T0-T1). Both groups had a 16 session treatment (T1-T3). Multiple outcome measures assessed by clinicians, parents and patients were used to measure the effects of the treatment on tic symptoms. Additionally, impairment/subjective burden ratings and the self-efficacy to control tics were assessed. An analysis of variance with repeated measures comparing both groups was analyzed.

Results and Conclusions:

Comparing both groups by analyzing the YGTSS, no intervention was superior. Tics reduced during both interventions. Tic ratings done by parents and patients also showed no differences between interventions, but a tic-reduction overall. During clinical observation done by therapists during therapy session the THICS-group showed a significant greater reduction of tics than the STARK-group. Also controllability of the tics rated by patients themselves improved in the THICS group significantly more than in the STARK group. Overall patients and parents were satisfied with treatment outcome. Interventions based on behavioral therapy can be used to reduce tics effectively and increase controllability of the tics by patients. A significantly greater tic reduction through symptom orientated interventions as habit reversal training could not be shown clearly for all outcome measures. There are tendencies that show superiority but activation of resources should not be neglected in treatment of tic-patients.

O15. Comprehensive Behavioral Intervention for Tics vs. Psychoeducational-Supportive treatments in group setting for children with chronic tic disorders: A randomized controlled trial.

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Background:

Comprehensive Behavioral Intervention for Tics (CBIT) by individual delivery is effective in reducing tic severity for chronic tic disorders and Tourette syndrome (TS), as well as improving psychosocial functioning and co-occurring psychiatric symptoms. Group-based delivery may provide additional benefits, such as social support. Group based treatments are effective in treating psychological conditions; however limited data exists for managed of chronic tics. We initiated a randomized controlled trial investigating the efficacy of CBIT and Psychoeducational -supportive (PES) treatments in group setting on tics and on psychosocial functioning and tic-related psychiatric symptoms.

Materials and Methods:

Children aged 9-15 years diagnosed with TS or Chronic Motor Tics were recruited through the pediatric movement disorders clinic at Tel Aviv Sourasky Medical Center and were randomized to receive PES or CBIT treatment. In each arm, six groups of 4-7 children participated in 8 weekly sessions of group treatment delivered by two clinicians for each group, with additional 3 monthly booster sessions. Parent educational-supportive groups (5 sessions) ran in parallel. Individual sessions were converted into group sessions previously (Zimmerman- Brenner, Rachamim, Murphy). PES protocol was a modification of the original protocol (Murphy & Heyman), discussing TS and other related issues.

Primary outcome was defined as improvement in the Yale Global Tic Severity Scale (YGTSS). Secondary measures included child's beliefs about his/her tics, anxiety, depression and self-esteem. All measures were assessed at 3 evaluation points: Pretreatment, after 8 sessions (post-acute phase treatment), and at 3 month follow up.

Results and conclusions:

61 children (age 8-15, 45 boys) were randomized to receive CBIT (27 children) or PES (28 children). 46 (23 in each group) completed 5 or more meetings and thus eligible for analysis. Significant decrease in YGTSS motor tic severity score was found when comparing pre vs. post-treatment in both CBIT (12.3 ± 5.1 vs 9.74 ± 6.8 , $p=0.008$) and PES (14.0 ± 3.5 vs 8.0 ± 5.1 , $p=0.00014$) with no difference between groups ($p=.333$). This decrease remained significant at follow up in the CBIT (10.9 ± 6.1 $p=0.001$) but not in PES (14.1 ± 4.3 $p=0.69$) showing significant difference between groups ($p=0.049$). Increase in YGTSS vocal tic severity score was found when comparing pre vs. post-treatment in both CBIT (10.6 ± 6.5 vs 21.8 ± 11.2 , $p<0.00001$) and PES groups (8.0 ± 4.6 vs 21.9 ± 8.0 , $p<0.00001$) with no difference between groups. Assessment at 3 month follow up showed a decrease ($t2/t3$ $p<0.00001$) back to pre-treatment scores ($t1/t3$ $p=0.088$) in both groups. The Parent Tic Questionnaire showed improvement with CBIT not noted in PES, while other secondary measures were similarly improved after treatment in both groups. Consistent with a previous pilot study, the current research showed that both CBIT and PES group interventions are associated with a reduction in motor tic severity in children (with CBIT having a lasting effect during follow up), while vocal tics were noted to worsen in this setting. Consistent with other studies, CBIT did not provide additional improvement for secondary outcomes compared to PES. Group delivery for chronic tic disorders can be considered a good alternative to individual delivery, however further investigations are recommended.

O16. Effects of Cannabidiol on Mouse Head Twitch Response: Implications for Treatment of Children with Tourette syndrome

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Background:

It has been documented that administration of 2,5 dimethoxy-4-iodoamphetamine (DOI), a potent agonist of the serotonin 5-HT_{2A}/5-HT_{2C} receptors, increases head twitch response in adult mice. DOI-induced head twitch response has been proposed to model motor tics of Tourette syndrome. Studies have previously shown that the delta-9-tetrahydrocannabinol (Δ^9 -THC), the principle psychoactive cannabinoid of *Cannabis sativa*, reduces DOI-induced head twitch response. These results are further supported by clinical reports describing a significant amelioration of symptoms



when cannabis was used by patients with Tourette syndrome. However, the effect of cannabidiol (CBD), the main non-psychoactive cannabinoid of *Cannabis sativa*, in the mouse DOI model of Tourette syndrome has not yet been investigated. In addition, the onset of Tourette syndrome is in children, therefore, the effects of CBD in the DOI model are yet to be studied in juvenile mice.

Materials & Methods:

The behaviour of juvenile C57BL/6J male mice was tested in the presence or absence of DOI. The number of head twitches and the frequency of grooming behaviour were recorded in the open field cage.

Results:

Our results show that DOI induces dose-dependent head twitch response and increased grooming behaviour in juvenile C57BL/6J male mice, resembling the onset of motor tics in children with Tourette syndrome.

CBD had a small, but significant, reversal effect on head twitch response. However, CBD had no effect on DOI-induced grooming behaviour.

Surprisingly, CBD alone significantly increased the head twitch response in healthy juvenile mice.

Conclusions:

These results show that CBD cannot effectively reverse motor-like tics and compulsive-like behaviour that are mediated by 5-HT_{2A}/5-HT_{2C} receptors in a juvenile DOI model. These results suggest that CBD may not effectively treat motor tics in children and may even exacerbate tics in a population of patients.

Acknowledgments

The Research Grant Award, Tourette Association of America (SAG). Kamin Award, Officer of Chief Science, Ministry of Science and Technology, Israel (SAG).

O17. Premonitory Urges Revisited: New Insights into the Location and Quality of Premonitory Urges

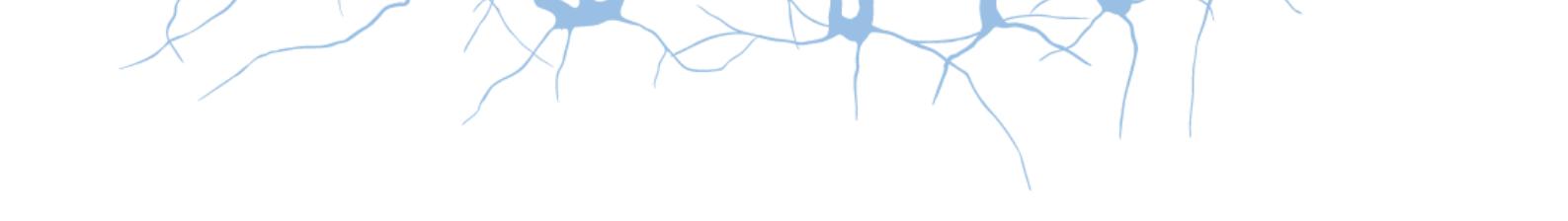
Ewgeni Jakubovski¹, Jana Essing¹, Nikolas Psathakis¹, Sinan Necdet Cevirme¹, Kirsten Müller-Vahl¹

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Background:

One of the main characteristic of the psychopathology of tics is a commonly reported sensation that precedes a tic – the premonitory urge (PU). The frequency and location of PU were firstly investigated by Leckman et al. (1993). In this frequently cited work, PU were shown to be a common phenomenon and a heat map was provided indicating the body areas with the most frequently experienced PU. From this heat map it is suggested that PU are distributed asymmetrically with a considerable degree of PU in areas where tics are rather rare (such as the feet). Interestingly, to date no attempts have been made to replicate this work. We carried out a first replication study in order to validate the precise location and quality of PU.

Methods:



We constructed an online survey using the SoSciSurvey online platform to investigate the quality and location of PU with the following features: 1) current tics were assessed via the checklist of the Yale Global Tic Severity Scale (YGTSS), 2) for each tic, information on the PU was collected, such as: precise location on a body drawing similar to the one used by Leckman et al., lateralization, and sensational quality. The statistical analysis was carried out with SPSS.

Results:

292 patients participated in our online survey (221 m, 71 f). PU were experienced by 73.0% of the patients. Complex (motor and vocal) tics were more frequently accompanied by a PU than simple tics (78.6% vs 68.9%). In motor tics, the PU was most frequently described as a feeling of tension; in complex tics, as a non-just-right feeling. In the majority of cases, a PU was experienced in the body area of the tic. The most commonly affected body areas were the front, the cheeks and the mouth. The majority of tics occurred symmetrically on both lateral body sides (75%), asymmetrical tics affected both sides similarly (13% right, 12.3% left). In 58.6% of the cases PU were experienced on both body sides, with the right body side being slightly more affected (10.6% vs. 6.8%).

Conclusions:

Our data (i) replicated the results of Leckman et al. in showing that PU is a very common phenomenon in patients with tics, (ii) supplemented the results of Leckman et al. by showing that PU are linked to the body area of the tic and are unlikely to be experienced in an unrelated body area and by showing that complex tics are more likely associated with PU than simple tics.

O18. A Strengths-Based Intervention for Complex Motor Stereotypies

Dr Amanda Maxwell (Clinical Psychologist)¹, Dr Tamsin Owen (Clinical Psychologist)¹, Victoria Turner (Assistant Psychologist), and Dr Tammy Hedderly (Consultant Paediatric Neurologist)¹.

¹ Tic and Neurodevelopmental Movement Service (TANDeM), Children's Neurosciences Centre, Evelina London Children's Hospital, Guy's and St Thomas' NHS Foundation Trust, London

Background:

Complex Motor Stereotypies (CMS) are repetitive, rhythmic and seemingly purposeless movements that occur in children with neurodevelopmental and neurological conditions as well as typically developing children. CMS are described as enjoyable and at times functionally useful but can also impair daily functioning. There is little evidence for pharmacological treatment of stereotypies and few effective behavioural interventions reported in the literature (Miller et al., 2006; Specht et al, 2017). We report on a strengths-based child behavioural intervention delivered in group and individual format. The aim of this intervention was to increase the children's control over their movements and teach privatization and acceptance with the aim to improve quality of life.

Method:

Eight children aged between 8-12 years with CMS participated in a 4 hour group intervention. Six of the children were then offered 4 individual follow-up sessions. Five children attended a 4 month follow-up intervention group. The intervention included: psychoeducation, functional analysis of the movements and replacement behaviours, competing responses and response prevention strategies, and promoting functional aspects of the movements. The Stereotypy Severity Scale (SSS), parent and self-report Paediatric Quality of Life Inventory (PedsQL) and a measure of

perceived control of movements were completed at a pre and post intervention visit and again at a 4 month follow-up.

Results and Conclusions:

Five of 7 children showed a reduction on the SSS Total Score after treatment (group pre mean = 32.5, post mean = 26.2). At the 4 month follow-up, 4 of 5 who attended the group showed a further reduction in SSS Total Score compared with the pre-treatment result (group follow-up mean = 17.2). At 4 month follow-up, all 5 children reported having a greater control over their movements.. Qualitative feedback indicated that children and parents both found the intervention to be beneficial, and the group format had been particularly useful in normalising stereotyped movements and sharing strategies. In conclusion the findings indicate that a strengths-based approach is acceptable and enjoyable to children and their families and can increase perceived control and decrease severity of the stereotyped movements and global impairment.

O19. Misophonia in children with Tic Disorders

Dr Sally Robinson (Paediatric Clinical Neuropsychologist)¹, Dr Tammy Hedderly (Consultant Paediatric Neurologist)¹, Dr Giulia Conte (MD)², Dr Osman Malik (Consultant Child and Adolescent Psychiatrist)¹ and Prof. Francesco Cardona (Professor of Child and Adolescent Neuropsychiatry)²

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Background:

Misophonia is a condition characterised by the dislike or hatred (miso) of specific sounds (phonia) that results in an extreme emotional response. There has been growing interest in misophonia, with emerging evidence from neurodevelopmental populations and on-going debate regarding psychiatric classification and the mechanisms underlying this phenomenon. We hypothesize that misophonia is an underestimated condition in children with tic disorders, possibly contributing to the frequent emotional distress and anger outbursts described in these patients, which leads to a poorer quality of life and may worsen tic severity.

Materials & Methods:

We report 12 patients (aged 7 to 18 years) with tic disorders and misophonia undergoing follow-up at the Department of Paediatrics and Child Neuropsychiatry at University La Sapienza of Rome, Italy (Cases 1-6) or the Tic and Neurodevelopmental Movement service (TANDEM) at Evelina London Children's Hospital, UK (Cases 7-12). Nine patients were males, 11 had co-morbid difficulties, which included 10 with anxiety difficulties, 8 with OCD/obsessive-compulsive traits and 3 with ADHD. Misophonia was classified as a selective aversive response in accordance with the criteria proposed by Schröder, et al., (2013), diagnosed by clinical interview.

Results and Conclusions:

The mean age of misophonic onset was 10 years. Family member specificity was commonly reported (83%) and most frequent trigger sounds were specific words (50%) and oral/nasal sounds (42%). Typical behavioural reactions were anger outbursts (58%), followed by an increase in tics (42%), trigger avoidance (33%), trigger repetition (25%) and self-injurious behaviour (17%). No

single treatment was effective, with some responding to cognitive behavioural therapies and others to pharmacological support.

These cases highlight that, for some, misophonia contributes to emotional distress, episodic rage attacks and tic exacerbation. It is conjectured that attentional processing biases may contribute to the increased salience of aversive sounds (possibly as part of a conditioned response), with difficulties disengaging attentional focus contributing to emotional dysregulation and tic exacerbation. Misophonia should be considered as part of a comprehensive clinical assessment in patients with tic disorders, as successful management leads to improvements in quality of life.

O20. Association of Tourette's and Chronic Tic Disorders with metabolic and cardiovascular complications

Lorena Fernández de la Cruz, Gustaf Brander, Kayoko Isomura, Zheng Chang, Ralf Kuja-Halkola, Catarina Almqvist, Henrik Larsson, David Mataix-Cols

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Background:

Persons with neuropsychiatric disorders are at increased risk of cardiometabolic complications, but there is little data concerning Tourette's and chronic tic disorders (TD/CTD).

Material and methods:

This population-based study included 14,045,026 individuals living in Sweden between 1973-2013. Using the Swedish National Patient Register and previously validated International and Statistical Classification of Diseases, Tenth Revision codes, we identified 7,804 individuals diagnosed with TD/CTD. Cox proportional hazard regression analyses investigated the risk of cardiometabolic complications in individuals with TD/CTD patients. Additionally, we explored the effect of antipsychotics in this risk.

Results and conclusions:

Individuals with TD/CTD had higher risk of any metabolic and cardiovascular complications, compared to the general population (adjusted hazard ratio [aHR]=2.19; 95% CI=2.09–2.30). Specifically, TD/CTD individuals had higher risks for obesity (aHR=2.76; 95% CI=2.47–3.09), circulatory system diseases (aHR=2.02; 95% CI=1.92–2.13), and type 2 diabetes mellitus (aHR=1.67; 95% CI=1.42–1.96). The risks were already evident from childhood and were significantly reduced with the exclusion of comorbid attention-deficit/hyperactivity disorder (aHR=1.60; 95% CI=1.50–1.71), while excluding other comorbidities did not significantly affect the results. In sibling comparison analyses, the risk for metabolic and cardiovascular complications was reduced but remained significant (aHR=1.52; 95% CI=1.38-1.68). Compared to TD/CTD patients not on antipsychotics, patients on longer duration of antipsychotic treatment (>1 year) had lower risks of metabolic and cardiovascular complications. TD/CTD are associated with a substantial risk of metabolic and cardiovascular complications. This highlights the importance of carefully monitoring cardiometabolic health in patients with TD/CTD across the lifespan.

This work was funded by a research grant from Tourettes Action awarded to Dr Fernández de la Cruz (grant reference TALFC17).

O21. Impact of Tourette's and chronic tic disorders on objective indicators of educational attainment: A population-based sibling comparison study

Ana Pérez-Vigil, MD^{1*}, Lorena Fernández de la Cruz, PhD¹, Gustaf Brander, MSc¹, Kayoko Isomura, MD, PhD^{1,2}, Andreas Jangmo, MSc³, Ralf Kuja-Halkola, PhD³, Eva Hesselmark BSc¹, Brian M. D'Onofrio, PhD^{3,4}, Henrik Larsson, PhD^{3,5}, and David Mataix-Cols, PhD^{1,2}

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⁴ Department of Psychological and Brain Sciences, Indiana University, Bloomington, Indiana; ⁵ School of Medical Sciences, Örebro University, Örebro, Sweden

Background:

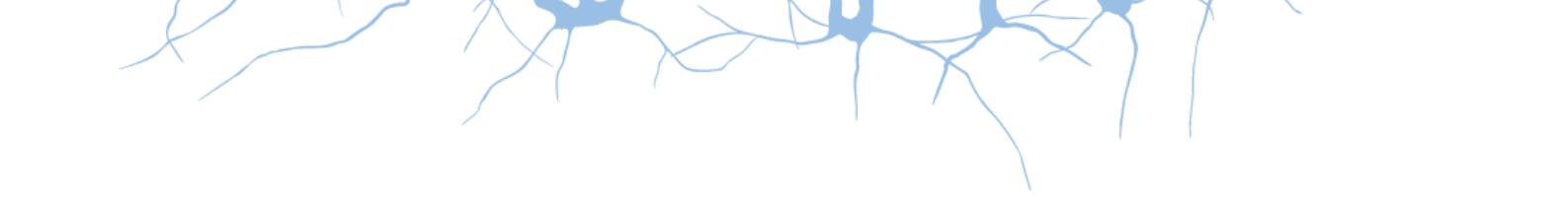
Tourette's and chronic tic disorders (TD/CTD) clearly affect the person's functioning and quality of life. However, the impact of TD/CTD on academic performance has not been objectively quantified. Our aim was to investigate the impact of TD/CTD on objectively measured educational outcomes in a nationwide cohort, adjusting for measured covariates and unmeasured factors shared between siblings, and for common psychiatric comorbidities.

Materials & Methods:

A population-based birth cohort, consisting of all individuals born in Sweden in 1976-1998, was followed until December 2013. A total of 2,115,554 individuals were identified, 3,590 of which had a validated diagnosis of TD/CTD according to the International Classification of Diseases in the Swedish National Patient Register. We further identified 726,198 families with at least two singleton full siblings; of those, 2,697 families included siblings that were discordant for TD/CTD. We examined the association between TD/CTD and the following educational milestones: eligibility to access upper secondary school after compulsory education, finishing upper secondary school, starting a university degree, and finishing a university degree.

Results and Conclusions:

Of the 2,115,554 individuals in the cohort, 3,590 had a registered TD/CTD diagnosis in specialist care (78.6% male; median age at first diagnosis 14.0 years). Of 726,198 families with at least two singleton full siblings, 2,697 families included siblings discordant for TD/CTD. Compared to the unexposed individuals, TD/CTD cases were significantly less likely to pass all core and additional subjects at the end of compulsory school (odds ratios [ORs] ranging from 0.23 to 0.36) and to access a vocational (adjusted OR=0.31, 95% CI [confidence interval] 0.28–0.34) or academic program (adjusted OR=0.43, 95% CI 0.39–0.47) in upper secondary education. Individuals with TD/CTD were also less likely to finish upper secondary education (adjusted OR=0.34, 95% CI 0.32–0.37), start a university degree (adjusted OR=0.41, 95% CI 0.37–0.46), and finish a university degree (adjusted OR=0.39, 95% CI 0.32–0.48). The results were only marginally attenuated in the fully adjusted sibling comparison models. Exclusion of patients with comorbid neuropsychiatric disorders, particularly attention-deficit/hyperactivity disorder and pervasive developmental disorders, resulted in attenuated estimates, but TD/CTD patients were still significantly impaired across all outcomes. Help-seeking individuals with TD/CTD seen in specialist settings experience substantial academic underachievement across all educational levels, spanning from compulsory



school to university, even after accounting for multiple confounding factors and psychiatric comorbidities.

O22. Exposure and Response prevention in a large Danish clinical cohort of children and adolescents with Tourette syndrome

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¹Affiliation: Tourette syndrome Clinic, Department of Pediatrics, Herlev University Hospital, Denmark

Background:

Historically, Tourette syndrome (TS) has been managed with pharmacological therapies but recent years' behavioural therapy (BT), such as exposure response prevention (ERP) and habit reversal therapy (HRT), has shown to be effective in reducing tic severity. HRT is currently the most researched and widely applied BT for TS, but both ERP and HRT are currently equally recommended as first-line BTs in existing guidelines.

To meet the growing demand for BT-treatment, we introduced ERP and HRT in our tertiary Tourette clinic in autumn 2013. Treatment has been provided as classic treatment with physical meetings, via telemedicine or in groups.

Methods:

The authors retrospectively reviewed medical charts of 95 children and adolescents with TS treated with ERP. The cohort was divided into three groups: one group that completed ERP as planned; one group that stopped earlier than planned because of reduction in tics; and one group that dropped out due to lack of motivation. Efficacy of the three different modes of BT (i.e., classic, telemedicine, groups) was compared. Patients who completed ERP as planned were followed for one year. YGTSS was used to monitor severity of tics and PedsQL was used as screening for quality of life (QoL).

Results and conclusion:

Mean age at start ERP 13.6 years, 68.4 % were boys and the mean duration of tics was 7.0 years. 53.7% have completed ERP, 18.9% stopped because of reduction of tics, and 27.4% dropped out. In all three groups, both tics and QoL improved with no statistically significant differences between groups. 63.2% received classic ERP, 32.6% via telemedicine, and 4.2 % as group therapy. Results showed a significant reduction in total tic severity score and total tics with no statistically significant differences between groups. We have long-term follow-up data on 32 patients. Of these, 40.6% received classic ERP, 46.9% via telemedicine and 12.5% group therapy. Results showed a significant decrease in YGTSS scores. There were no statistically significant differences in efficacy between classic ERP and telemedicine. The effect of ERP was statistically significant better after classic ERP compared with the group sessions. The results are consistent with the growing body of literature supporting ERP as an effective treatment for TS also regarding the long term effect. Results indicate that telemedical approaches could be an opportunity to facilitate wider accessibility. Further experience with offering BT in groups is needed.



Selected poster presentations from submitted abstracts

P1. Development of a Screening Instrument to Identify Tics in Children

Adam B. Lewin, Ph.D., ABPP¹, Erin M. Brennan¹, and Tanya K. Murphy, MD, MS¹

¹ University of South Florida, Department of Pediatrics, Rothman Center for Neuropsychiatry

Background:

Current prevalence estimates for Tourette Syndrome (TS) and other tic disorders (TD) (~1% of youth) may be underestimated due to under-diagnosis. Tics, let alone TD, may go undetected by parents and clinicians. Intuitively, a first step in improving the identification of TD is accurately identifying tics. Although a number of instruments for assessing tic characteristics and severity exist, lacking is a validated tool for screening and/or diagnosis of tics/TD. Intuitively, a screening instrument for tic disorders must reliably identify the presence of tics. A validated screening instrument for tics has potential utility not only for improving the accuracy of prevalence estimates, but for early identification for clinical evaluation and relevant treatment referrals. Consequently, objective of this work was to produce a validated screening instrument to identify at least 85% of children with tics, in order to improve the identification of tic disorders, and potentially related neurodevelopmental and mental disorders.

Materials & Methods:

Following expert review of potential items, an initial 26 items were piloted and qualitative feedback was gathered. The scale was shortened to 20 items, which (completed by 37) youth/parent dyads recruited from a tic/OCD specialty clinic. The scale was reduced to 14-items (MOVE-IT-14) which was completed by 41 dyads recruited from an academic tic/OCD clinic and a general pediatric clinic. Reliability was examined using internal consistency, item-to-total correlations, and parent-child agreement. Signal detection was used to examine performance.

Results and Conclusions:

A threshold of 10 was considered to be optimal for parent reports (sensitivity = 0.90, specificity = 0.82, PPV = .84, NPV = 0.89, Efficiency = 0.86), and 8 for child reports (sensitivity = 0.86, specificity = 0.63, PPV = 0.72, NPV = 0.80, efficiency = 0.75) on the MOVE-IT-14. The MOVEIT-14, initially validated in a limited clinical population, had high sensitivity in addition to good specificity. Additional validation is needed in a large independent sample in non-specialty settings such as pediatric clinics) in comparison to gold-standard assessment.

P2. I wish I could accept my child, flaws and all: Exploring Relationship Obsessive-Compulsive Disorder (ROCD) symptomatology among children presenting with Tic-related disorders and their parents

Amit Ben-Zvi¹, Sharon Zimmerman-Brenner^{1, 2}, Michael Rotstein^{3, 4}, Tammy Pilowsky^{5, 6}, Aviva Fatal-Valevski⁴ & Guy Doron¹

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Background:

Obsessive-compulsive disorder (OCD) clinical presentation may vary among individuals. One OCD presentation that has recently gained significant research attention has been Relationship Obsessive-compulsive Disorder (ROCD). This presentation involves obsessive-compulsive symptoms centering on interpersonal relationships. Research mostly focused on two main presentations in the romantic context: relationship-centered obsessions, and partner-focused obsessions (i.e., partner's perceived flaws). Recently, an extension to partner-focused presentation has been explored—ROCD in the parent-child context. This line of research suggests parents' preoccupation with their child's perceived flaws may impact on parental mood, OCD symptoms and the experience of parenting.

Although tics are the hallmark of Tic disorders, research suggests high prevalence of psychiatric and psychosocial difficulties. We propose that tic-related difficulties may repeatedly provoke pre-existing parental fears and preoccupations, and, in turn, increase children's likelihood of developing preoccupation with his/her own social and emotional "flaws" due to the associated increase in parental attention and reactivity. In the current study we examined the associations between parent-child ROCD symptoms and children's self-obsessions in both clinical group (children with Tic disorders) and community cohort.

Materials & Methods:

We investigated the link between parent-child ROCD symptoms and their children's obsessions regarding their own perceived flaws, among 65 Israeli parents-child dyads (aged 9 to 15). We also compared levels of ROCD symptoms between dyads from the clinical cohort to the community controls. The experimental group consisted of 35 children presenting with Tic disorders (Tourette's syndrome or Chronic Tic disorder), and their parents, from a baseline sample of a clinical trial examining the efficacy of CBIT group intervention, at Ichilov-Dana-Dwek Children's Hospital. The control group consisted 30 dyads from a community sample. All dyads completed self-report questionnaires regarding ROCD symptomology and affective symptoms.

Results and Conclusions:

Parents' obsessions regarding their child's perceived flaws were associated with their child's self-obsessions among both groups, as well as specific links regarding two specific equivalent domains: morality and appearance. Parent-child ROCD symptoms were associated with negative parental mood. Children self-obsessions were not related with their affective symptoms. Surprisingly, when comparing the clinical and community groups, parental-child ROCD symptoms and children's self-obsessions were lower in the clinical group than in our community sample.

Our findings are consistent with previous theoretical framework suggesting the similarity between the OC cycle of parent-child ROCD presentation to other OCD presentations. The findings suggest that parent's preoccupations with their children flaws may lead to elevated levels of parental reactivity to children's characteristics and behaviors that, in turn, may accentuate children's preoccupation with their own perceived flaws. Moreover, the current research suggests that child psychopathology may offset one own parent preoccupation in the child perceived flaws. The child having clearly recognized symptoms (i.e., reoccurring motor and/or vocal tics) and diagnosis may have offset such symptoms in two ways; either the day-to-day burden associated with tic related psychosocial difficulties may have distracted parents from their own vulnerabilities, or by the interpretation of the child's difficulties as being tic-related. Thus, clinical attention is needed to the mutual effects among child's difficulties, parental preoccupation and reactivity, and the child's self-perceptions.





P3. Guided imaginary Music therapy (GIM) given to 14 Tourette Clients

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Background:

It has been proved that music beyond stimulating the primary acoustic centres, also stimulates many other areas in the brain. Especially the prefrontal cortex, basal ganglia, hypothalamus, the limbic system, especially hippocampus and amygdala, the brain stem and cerebellum.

Music is also a strong activator for several neurotransmitters, especially dopamine, oxytocine, serotonin, endorphine, endocannabinoids, immunoglobuline A, opioid receptors, melatonine and are reducing the threshold of cortisol. It is also proved that music can stimulate arousal and hereby improve concentration and social adaptation. There is now evidence for effect of music therapy in 10 diseases (reg. Cochrane). E.g. Stress, anxiety, depression etc.

Until now there is no scientific material which confirms that music therapy reduces tics. But there are a lot of case stories referring to suppressing tics by playing an instrument or by singing, dancing or listening to music. In my clinic we have previously performed a pilot study with GIM-therapy in 9 children with Tourettes Syndrome. All patients but one suppressed tics in relation to the music therapy session. 5 of 9 demonstrated reduction of the tics by 50% in the course.

Goal:

- 1: If a group of children and adolescents (+ 1 adult) with Tourettes Syndrome could benefit from listening to music by participating in a receptive music therapy course and
- 2: Furthermore to investigate if the client experience tic reduction only by thinking of the music used in the project.

Materials & Methods:

14 patients, 7 boys aged 12-18 + 1 adult 26 years old, 6 girls aged 12 – 19, participated in the project in the period February 2014 to May 2015.

Part 1: All clients received GIM therapy in Anne G. Korsgaard's neurologic clinic.

Part 2: All clients did also do self training at home between the music sessions.

All were offered 6 music sessions in the clinic followed by instructions in home training 20 - 30 minutes 5-7 days per week for 3 months. The duration of self training was individualized to avoid creating stress.

YGTSS scale was performed on all clients before first and after the last music session.

Results and Conclusions:

The present project describes results of modified GIM therapy (Guided Imaginary Music Therapy) plus self training at home by 14 clients finished in the autumn 2015. It was the plan to present this poster at the congress in Warsaw in 2016, but due to acute illness I was unable to participate why I present this at ESSTS in Copenhagen together with a follow up on ten of 14 clients. The project disclosed that GIM therapy combined with self training has by 12/14 a positive effect on tics reduction and furthermore considerable reduction of stress and an improved self confidence, thereby improved quality of life. This result is still confirmed by the 10 clients followed up in April. 6 clients experienced effect just by thinking of the music.





P4. Tackle your Tics: feasibility of a brief, intensive group-based exposure therapy programme for children with tic disorders

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Background:

Behavioural treatment for tics is considered a first-line intervention for tic disorders. However, despite its demonstrated efficacy, there is room for improvement; patients reach an average tic reduction of only 30% and the lack of specialized therapists is a barrier for local treatment. Patient associations claim with an urgent need for more easy-to-undergo and personalized treatments, which also support children to cope with their symptoms. This pilot study aims to enhance tic reduction and to overcome treatment barriers, by studying the feasibility of a brief, intensive group-based programme.

Materials & Methods:

Tackle your Tics is a four-day group-based programme for children (9-17 years) with tic disorders, consisting of evidence-based exposure and response prevention (ERP) treatment, psycho-education, the training app *BT-Coach*, coping strategies, relaxation activities, group support and parent meetings. Feasibility will be assessed by semi-structured interviews with parents, children and professionals. Assessments (e.g. YGTSS) will be performed pre- and posttreatment and at 2 months follow-up, to give the first indications of effectiveness. The results of this feasibility study will provide guidelines for further development of the programme.

Results and Conclusions:

This pilot study was recently awarded with a research grant by Tourettes Action (April 2018). Two therapy weeks are planned in June and September 2018. Results are expected at the end of 2018. In 2019, we aim to start a 5-year RCT on the efficacy of the *Tackle your Tics* programme.

P5. Executive control development in Tourette syndrome and its role in tic Reduction

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Background:

Tourette syndrome (TS) is a childhood-onset disorder characterized by motor and vocal tics. While the involvement of cognitive performance in TS is unclear, recent findings point to a possible role of executive functions system development in the tic reduction observed with age. The goal of the present work was to track the development of executive functions system measured by well-



established cognitive tasks and its correlation with diminished tic severity over time in order to understand the role of executive functions in the remission process observed in most adults.

Materials & Methods:

The first study followed 25 young TS patients, measuring their executive functions and clinical condition at three time- points. In the second study we compared executive functions performance of 19 adult TS patients with 19 healthy controls and 12 remitted TS patients

Results and Conclusions:

The first study showed that tic reduction is related to the development of the executive functions components associated with response inhibition. The second study similarly showed impaired inhibition ability in TS patients but not in controls or the remitted TS patients. The remitted group performed at normal or even higher levels on certain measures. We conclude that inhibition, an important executive function, is impaired in subjects suffering from TS and that intact executive function development is related to remission processes.

P6. Delay Discounting in Patients with Tourette syndrome

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Background:

Tourette syndrome (TS) is associated with a hyperdopaminergic state that leads to increased sensitivity to positive reinforcement. The current study addresses the question whether this extends to impaired decision-making in the Delay Discounting (DD) task. The DD task is employed to operationalize impulsive decision-making - the preference to choose smaller sooner over larger later rewards. To our knowledge DD has not been tested in patients with TS. We hypothesize altered decision-making in the DD task in patients with TS compared to healthy controls. Furthermore, we want to explore if our findings relate to comorbid symptomatology.

Materials & Methods:

18 adult patients with TS and 18 healthy controls matched for age, sex and education performed the well-established DD task. Behavioral results were modeled by calculating the subjective value according to the hyperbolic model and softmax action selection. The estimated parameters k (larger values correspond to steeper discounting) and *temperature* (larger values correspond to more stochastic behavior). These parameters and psychometric scores (BDI, OCI-R, WURS-K) were compared between groups using two-sided independent t-test. In addition, for patients with TS two-tailed Pearson's correlation coefficients were determined for k and *temperature* with regard to psychometric scores.

Results and Conclusions:

We found no significant differences regarding the discounting function (k) between adult patients with TS and healthy controls. We did, however find significantly increased stochasticity (*temperature*) in the behavior of patients with TS. Importantly, neither parameter correlated



significantly with comorbid symptomatology. This indicates a general impairment in decision-making while choices are not more or less impulsive than in healthy controls.

P7. Treatment of patients with Tourette syndrome with cannabis and cannabis-based medicine

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Background:

Based on anecdotal reports and results from 2 controlled trials using tetrahydrocannabinol (THC), in our Tourette outpatient clinic, several patients have been treated with cannabis-based medicine (CBM) including THC, nabiximols (Sativex®), and medicinal cannabis (alone or in combination) or used cannabis illegally. However, until today, the database is limited and it is unknown, whether CBM are indeed effective in the treatment of Tourette syndrome (TS) and which CBM should be preferred. This study was designed to further investigate the efficacy of CBM in TS and to explore patients' preferences regarding type (THC vs. nabiximols vs. cannabis) and route of intake.

Materials and Methods:

This study consisted of 2 parts: First, we retrospectively analyzed medical records of TS patients, who have been treated with CBM between 1996 and 2017. Thereafter, all these patients were asked to participate in a prospective online survey to further evaluate patients' use of CBM including kind, dose, and route of intake of CBM; influence on tics and comorbidities, side effects, and quality of life.

Results and Conclusions:

From medical records, we identified 98 patients with TS (84 m, 14 f, mean age = 28.2, SD = 13.7, range = 18-77), who have been treated with the following CBM: medicinal cannabis from the pharmacy (66%), THC (18%), and nabiximols (11%), or used illegal cannabis (5%). All patients (21/21), who used medicinal cannabis, reported about a tic reduction compared to 90% (60/67) after use of illegal cannabis, 77% (27/35) when using THC, and 76% (25/33) when using nabiximols. 40/98 (41%) patients agreed to take part in the prospective online survey. 23 (57%) of these still used CBM: medicinal cannabis (39%), illegal cannabis (35%), nabiximols (26%) and THC (17%). Altogether, 22/23 (96%) patients reported about a clinically relevant tic reduction, an improvement in quality of life, and experienced an improvement in comorbidities. Most patients felt that cannabis (from pharmacy and illegal) caused less side effects compared to THC and nabiximols. From this preliminary data it is suggested that (medicinal) cannabis is more effective and better tolerated than THC and nabiximols. Patients with TS prefer the use of legal treatment with CBM supervised by a medical doctor instead of using "street cannabis" illegally.





P8. Motor tics reduction during sleep and its neural correlates in a novel chronic animal model of tic disorders

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Background:

Motor tics, the hallmark symptom of Tourette syndrome (TS), typically wax-and-wane over multiple timescales and are modulated by behavioral and environmental factors. Experimental findings and theoretical models have associated TS with abnormal striatal inhibition. The expression of tics has been transiently induced in non-human primates and rodents by the injection of GABA_A antagonists into the striatum, leading to temporary disinhibition.

Materials & Methods:

The novel chronic model of tic expression utilizes a mini-osmotic pump implanted subcutaneously in the rat's back for prolonged infusion of bicuculline into the motor parts of the striatum. Using a wireless recording system we monitored both neural activity, in the striatum and M1, and the rat's tic and non-tic movements during the wake-sleep cycle.

Results and Conclusions:

Tics were expressed over a period of multiple days while the rat presented different behavioral states. In the wake state, tic expression was stable and maintained similar properties.

Electrophysiological recordings revealed the existence of tic-related local field potential spikes (LFP spikes) and individual neuron activity changes that remained stable throughout the infusion period. During sleep, tics were reduced in both amplitude and frequency and eventually vanished. The LFP spikes initially continued to appear despite tic reduction and after a short period they ceased too. These occurred simultaneously to changes in the activity of individual neurons.

During wakefulness, the chronic tic expressing model provides similar behavioral and neuronal correlates of tics to the acute striatal disinhibition model but over prolonged periods of time. The chronic model also enables the examination of different factors affecting tic expression over time. For example, here we present the neural basis of motor tics dynamics during the wake-sleep cycle which may explain the reduction of tic expression in Tourette syndrome patients during sleep and potentially during other behavioral states.

P9. Blinking and Blink Suppression Discomfort in Tourette Syndrome

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Background:

Functional neuroimaging studies have attempted to explore tic-related brain activity in Tourette syndrome (TS), but have been limited by the difficulty of disambiguating brain activity required to perform a tic, or activity caused by the tic, from brain activity that generates a tic. Inhibiting the



urge to tic is important to patients' experience of tics. We hypothesize that inhibiting a compelling motor response to a natural urge—such as the urge to blink, which shares many similarities to premonitory urges to tic—will differ in TS subjects compared to controls. Previous neuroimaging studies with the same hypothesis have used a one-size-fits-all approach to extract brain signal putatively linked to the urge to blink. Our objective was to create a subject-specific and blink-timing-specific pathophysiological model, derived from out-of-scanner blink suppression trials, in order to better interpret blink suppression fMRI data.

Materials & Methods:

Eye closure and continuously self-reported discomfort were recorded during 5 blink suppression trials in 30 adult volunteers, 15 with a chronic tic disorder. For each subject, data from four of the trials were used with an empiric mathematical model to predict discomfort from observed eye closure in the remaining trial. Accuracy measured by comparing this prediction to the actual reported discomfort in the excluded trial was calculated for each of the 5 trials and averaged within subject.

Results and Conclusions:

The novel model of discomfort during blink suppression, which accounts for blink timing and each subject's individual response characteristics, much better reflected each subject's urge to blink compared to 2 previously proposed models. Combining this approach with observed eye closure during fMRI blink suppression trials should therefore extract brain signal more tightly linked to the urge to blink.

Furthermore, the TS group blinked almost 3 times more often during the blink suppression block, and reported higher baseline discomfort, smaller excursion from baseline to peak discomfort during the suppression block, and slower return of discomfort to baseline during the recovery block. We conclude that discomfort and blinking during a blink suppression task differ in TS and controls, and discuss how this result fits with prior data.

P10. Stimulation-dependent functional connectivity of effective deep brain stimulation for Tourette Syndrome

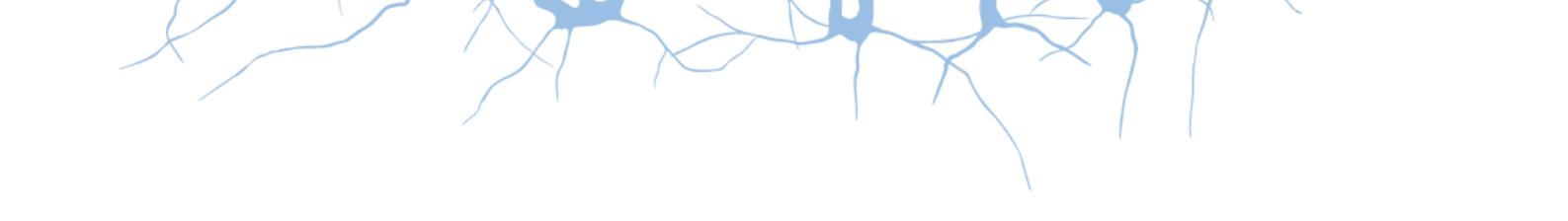
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Background:

Neuromodulative therapies are gaining increasing interest in the treatment of Tourette Syndrome. So far, deep brain stimulation has provided promising results in treatment-refractory patients but the underlying mechanisms remain elusive. Comparable effects of different brain targets have yielded towards the hypothesis that a common network might carry out beneficial effects. Which regions functionally connected to stimulation sites carry out beneficial effects and whether connectivity is able to predict individual outcomes was the aim of this study.

Materials & Methods:



We included 14 patients undergoing thalamic deep brain stimulation. Response to the intervention was determined as percentage change of the Yale Global Tic Severity Scale after one year. Optimal functional connectivity patterns seeding from individual volumes of activated tissue were calculated based on publicly available normative connectome data. This connectivity pattern was then used to predict individual outcomes in a leave-one-out design.

Results and Conclusions:

Optimal normative connectivity profiles of effective stimulation encompass connectivity to (pre-) motor areas as well as insular cortices. Regions-of-interest analysis revealed significant positive correlations for outcome after year of DBS and connectivity to the supplementary motor area (left: $r=0.541$ ($p=0.025$); right: $r=0.680$ ($p=0.006$)) and bilateral insula (left: $r=0.590$ ($p=0.021$); right: $r=0.598$ ($p=0.012$)). With this model, we were able to significantly predict individual outcomes of DBS ($r=0.485$; $p=0.040$; one-tailed).

Our results demonstrate that individual functional connectivity profiles of stimulation sites are able to predict clinical outcome in Tourette Syndrome. The resulting optimal connectivity profiles may further serve to improve target selection for both invasive and non-invasive neuromodulation for Tourette Syndrome.

P11. Evaluation of deficits in theory of mind in Gilles de la Tourette Syndrome.

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Background:

Neuroanatomical characteristics of Gilles de la Tourette Syndrome (GTS) as well as clinical observations suggest the possibility of empathy and social deficits in patients with GTS which may stem from difficulties in emotion recognition and formulation of mental representations. To date, limited number of research investigating aspects of social cognition in GTS is available. The main goal of the study was to assess the presence of possible theory of mind (ToM) deficits in children and adolescents with GTS as well as identification of possible relationships between ToM deficits and the connection between type and severity of the tics (vocal or/and motor).

Materials & Methods:

Participants: 25 children and adolescents with GTS, 25 healthy control, and 25 participants diagnosed with ASD. The study group mainly consists of children and adolescents aged 9 to 14 with the diagnosis of GTS psychiatric in- or/and outpatients (patients treated in psychiatric units in hospitals or under the care of mental health clinics). Materials: ToM test was developed based on Theory of Mind Task Battery, Strange Stories Test, and Faux Pas Recognition Test, and additionally Yale Global Tic Severity Scale, polish version of Autism Spectrum Rating Scale, and Stanford - Binet Intelligence Scale (SB-5).

Results and Conclusions:

The groups differ with a test of statistical significance of the trend on understanding non-literal language and patients with GTS reason differently on the fauxpas task. Understanding of false belief (first, second and third order), understanding of hints, white lie and joke appeared to be intact. GTS may be associated with changes in reasoning on tasks involving social, emotional, and non-literal language aspects. These findings are similar to structure of social cognition impairments reported by previous studies. Additionally, we found strong negative relationship between type and

severity of the vocal tics and level of ToM deficits. There are numerous limitations associated with our study, especially methodological issues related to the sample selection and size.

P12. Rage Attack Questionnaire (RAQ): Investigation of rage attacks in Patients with Chronic Tic Disorders

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Background:

Rage attacks are short-lasting, intense, impulsive and unproportional reactions to harmless situations that cannot be controlled willingly. Rage attacks occur in 25-70% of patients with chronic tic disorders (CTD). Since there is no standardized measurement available, we developed the Rage Attack Questionnaire (RAQ), the first self-assessment to measure rage attacks. This study aimed to validate the RAQ on the one hand and to investigate the frequency and intensity of rage attacks in adult patients with CTD as compared to healthy controls (HC) on the other hand using an online survey.

Materials & Methods:

The RAQ consists of 22 items given on a 4-point Likert scale. For convergent and divergent validation the following self-assessments were used: Adult Tic Questionnaire (ATQ) for tic severity, Obsessive-Compulsive Inventory-Revised (OCI-R) for obsessive compulsive disorder (OCD), ADHS-Selbstbeurteilungsbogen (ADHS-SB) for attention deficit/hyperactivity disorder (ADHD), ICD-10-Symptom-Rating (ISR) for general psychological symptoms, for impulsivity both the Barratt Impulsiveness Scale-short version (BIS-15) and the Scale of Impulsive Behavior (I-8) and the Gilles de la Tourette Syndrome–Quality of Life Scale (GTS-QoL).

Results and Conclusions:

One hundred twenty-seven (89m, 38f) patients with CTD and 645 age- and sex-matched HC were included. Compared to HC, patients with CTD demonstrated significantly more rage attacks using the RAQ (CTD: 25 ± 16 , HC: 10 ± 9 , $p < 0.001$). There was only a low correlation between rage attacks and impulsivity (according to I-8 (r between $+0.310$ and -0.193) and BIS-15 ($r=0.128$)) indicating that rage attacks and impulsivity represent different clinical phenomena. While rage attacks did not correlate with tic severity ($r=0.194$), there was a moderate correlation between RAQ and comorbidities including OCD ($r=0.348$), ADHD ($r=0.353$), and general psychological symptoms ($r=0.432$) as well as quality of life ($r=0.478$).

Our data demonstrates that a) the RAQ is a simple to use self-assessment to measure rage attacks, b) rage attacks are more common in patients with CTD compared to HC, c) rage attacks as assessed by RAQ represent a clinical phenomenon that is not covered by measurements for ADHD and impulsivity, and d) rage attacks impair patients' quality of life.

P13. Schizotypal personality traits in Tourette syndrome: Increase in traits co-varies with tics and OCD symptoms.

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Background:

Tourette syndrome is a neurodevelopmental disorder with tics as the hallmark symptom. Tourette syndrome is associated with a high co-occurrence of especially Attention-Deficit Hyperactivity Disorder and Obsessive-Compulsive Disorder in addition to depression, rage, anxiety, and autism spectrum disorders. A handful of studies have also indicated increased prevalence of schizotypal personality traits (1-5). However, these results have been largely neglected both in research and in the clinic.

Materials & Methods:

In the current study, 166 adolescents with Tourette syndrome (mean age 18.6 years) and 48 healthy, matched controls were screened with the brief version of the Schizotypal Personality Questionnaire (SPQ-B) consisting of 22 questions relating to schizotypal personality traits, along with a clinical examination of their tic severity and comorbid disorders of ADHD, OCD and ASD.

Results and Conclusions:

We found a significantly higher occurrence of schizotypal personality traits in the Tourette syndrome group compared to controls ($t(212) = 4.510, p < .0001, d = 0.681$). This increase was highly associated with tic severity ($r(164) = .510, p < .0001$) and comorbid symptoms of Obsessive-Compulsive Disorder ($r(164) = .522, p < .0001$), but not with “pure” Tourette syndrome per se ($p = .89$). Further, when applying a cut-off score on the top 10% in the control group, 34.3% of the Tourette participants score above this cut-off again indicating increased prevalence of schizotypal personality traits. Thus, our results corroborate and extend previous studies, supporting the importance of further research of schizotypal personality traits and their impact in Tourette syndrome. We also advocate for screening for these traits in the clinic, as the SPQ-B only takes 2 minutes to fill out, but with possibly valuable information to the assessment and treatment of the patients.

P14. Nurse-led Behavior training for tics in adults

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Background:

Tics are physically and socially stressful. We offer tics-training for selected patients over the age of 18, who suffer from tics. The aim is to help patients gain better control over their tics, as well as reduce the tics.

Materials & Methods:



Tics-training is based on the method “Behavior therapy for tics in children and adults” as well as material from the Dutch Psychologists Verdellen, Van de Griendt and others.

Consultant Neurologist, Heidi Biernat, selects the patients for the training. They must be motivated and willing to learn. Other psychopathology or other sub-diagnoses in relation to the tics/Tourettes diagnosis must not hinder the ability to be able to concentrate on or participate in the training.

We contact the patients by telephone to inform them of the process and our expectations of them. The process consists of 10 sessions with the same nurse.

The patient will during the process be made aware of their premonitory urge to tic and will be trained in enduring and suppressing the tics.

The patient will be counting tics and will be practicing suppressing the tics at home every day following individual instruction. The process can be terminated before time, if the patient is happy with the result or shows non-compliance. At the final session we advise the patient on the future handling of the tics. The effect of the training will be evaluated in the material by calculating the percentage of improvement in the tics-scoring from start to finish.

Results and Conclusions:

Of the 18 patients who have started tics-training sessions since March 2016, 3 have dropped out. Our patients have shown an improvement in the tics-scoring between 8-100% and the median is 68%. The majority of the patients have, during the process, expressed that they have gained better control over their tics and an improved ability to endure the urge to tic. Most have felt that the training with the nurse has been rewarding, as they have gained workable solution-proposals from a nurse with experience in tics and Tourettes. One patient felt that the training was too time-consuming and not adequately effective.

We conclude, that tics-training meets its purpose in relation to control and reduction of tics.

P15. Prevalence of sensory and emotional features in children with tic disorders.

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Background:

Tic disorders negatively interrupt a child’s daily functioning. The premonitory urge (PU) is described as localised discomfort immediately before a tic and may play a role in tic generation. Broader somatic hypersensitivity has also been described in this population. Therefore, tics may involve sensorimotor phenomena, rather than a ‘pure’ movement disorder.

Families reported their child’s tics were absent or reduced when physically active such as playing sport. Children reported implementing self-selected and self-initiated sensorimotor strategies, such as chewing gum, stretching and wearing tight clothing to manage their tics prior to consulting with health professionals for treatment.

We have also observed a possible relationship between psychological stress and tic expression, with tics increasing in intensity and frequency in stressful situations. A case study completed in 2016 with 10 participants showed promising results that a sensorimotor approach may be helpful in treating children with tic disorders.



Objective:

This prevalence study aimed to explore the relationship between sensory and emotional control features in children with tic disorders. This study aimed to probe the prevalence of sensory symptoms in children with tic disorders. No studies have assessed both the sensory and emotional control features concurrently.

From clinical observations, we hypothesised that:

- Prevalence of sensory features in children with tic disorders are greater than healthy controls.
- Children with a tic disorder have increased emotional control difficulties compared with controls.

Materials & Methods:

A total of 163 children, (with tic disorders (n=103) and healthy controls (n=60)) were recruited into this prevalence study through the Tic Clinic at the Children's Hospital at Westmead in Sydney, Australia. Parents completed 5 questionnaires: Sensory Processing Measure (SPM), Sensory Profile 2 (SP2), Pediatric Quality of Life Inventory™ (PedsQL), Strengths and Difficulties Questionnaire (SDQ) and Behaviour Rating Inventory of Executive Function 2 (BRIEF2) Parent Form. Scores from the SP2 were converted to a total raw score using the Short Sensory Profile 2 (SSP2). A clinician (staff specialist) completed the Yale Global Tic Severity Scale and the Premonitory Urge to Tic Scale.

Results and Conclusions:

As hypothesised, compared with healthy controls, participants with tic disorders reported experiencing:

- Significantly more sensory sensitivities as measured on the SPM and SSP2 ($T=9.256$; Mean=15.360; $p<0.001$; $T=9.398$; Mean=15.360; $p<0.001$).
- Significantly greater emotional control difficulties as measured using the BRIEF2 (Emotional Regulation Index (ERI)), SDQ (Emotional problems scale) and PedsQL (Emotional Function Score) ($T=11.786$; Mean=13.204; $p<0.001$; $T=11.297$; Mean=3.779; $p<0.001$; $T=-11.698$; Mean=-34.881; $p<0.001$).

There was a strong relationship between sensory sensitivities (SSP2) and emotional control difficulties (ERI) in children with tic disorders ($r=0.718$). This study provides useful information for clinicians relating to the sensory profile and specific sensory sensitivities of children with tic disorders.

A clear understanding of the impact of emotional control and sensory sensitivities on tic severity may improve the treatment paradigm of tic disorders. Therefore, further research into the inclusion of sensorimotor and emotional control strategies to complement existing first-line treatment for tic disorders is required.

P16. The use of guanfacine in the treatment of tics – a review

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Background:

Tourette syndrome and chronic tic disorder are disorders, in which patients experience vocal and/or motor tics during more than a year. Patients with Tourette syndrome often experience comorbidities



such as ADHD, anxiety, OCD or autism. Different pharmacological treatments for tics exist, but due to a lack of controlled clinical studies, strong evidence does not yet exist. Antipsychotic agents and clonidine (an α 2A-agonist) are recommended in the European guidelines for treatment of tics, while in other countries, guanfacine is recommended. Guanfacine is a selective α 2A-agonist and is therefore supposed to have fewer side effects than clonidine. In Denmark, guanfacine is approved for the treatment of ADHD. We have reviewed the existing clinical studies examining the effect of guanfacine.

Materials & Methods:

Review over the existing literature. We included four controlled clinical trials and randomized controlled trials concerning the use of guanfacine as treatment for tics.

Results and Conclusions:

Results from the studies are contradictory. Some studies have found a positive effect of guanfacine on tic severity measured with Yale Global Tic Severity Scale (YGTSS) or with Tic Symptom Self-Report (TSSR), while others could not find any positive effect on tic severity. The studies are difficult to compare due to differences in among others design, included subjects, dosage of guanfacine, and presence of comorbidity. Compared with clonidine, guanfacine seems to have fewer side effects and more positive cognitive effects. Future studies, including large randomized, double-blind, placebo-controlled trials, are needed.

P17. A Study of Sensory Dysregulation in Children with Tic Disorders

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Introduction:

Disrupted somatosensory processing characterized by over- or under- responsiveness to environmental stimuli, plays an important, yet often overlooked, role in typical development and is aberrant in various neurodevelopmental disorders. These dysfunctional somatosensory processes have been conceptualized as an entity termed somatosensory dysregulation (SMD). Since Tourette syndrome (TS) is a prototypical example of developmental psychopathological disorder we hypothesised that SMD would be a feature found in children suffering from the disorder.

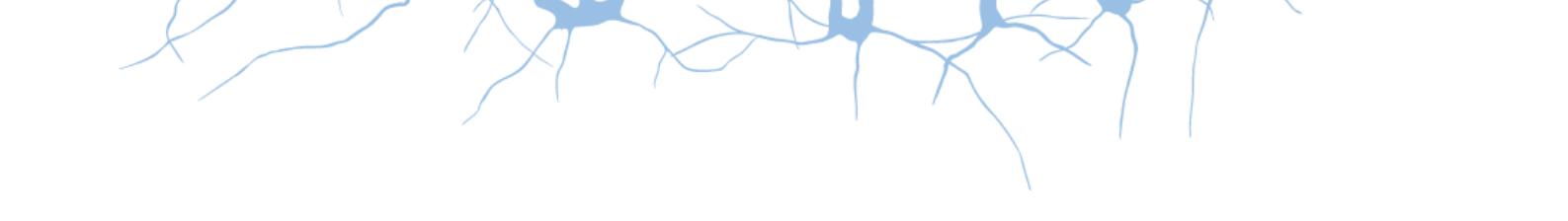
Objectives:

To evaluate subjective and objective measures of SMD in tic disorders pediatric patients

Materials & Methods:

Ninety two subjects representing consecutive admissions to a tertiary paediatric Tourette syndrome clinic were admitted to the study. Comorbid conditions included ADHD; depression; anxiety disorder and OCD. For purposes of the study, patients completed a battery of self-, caregiver- and clinician-rated psychological instruments measuring TS core symptoms and comorbidities and quality of life. Sensory modulation was measured by self-report and by objective measures such as stimulation with Von Frey filaments.

Results:



Almost 50% of the cohort had no SMD. Of the remainder, 14 (15%) had suspected SMD and 32 (34.8%) had SMD. SMD was significantly more common and severe when there were comorbidities. The presence of SMD was associated with more severe impairments in quality of life and less participation in daily activities.

Conclusions:

The SMD, as measured by subjective measures but not by objective, is probably more associated with central processing rather than peripheral perception.

P18. Aggressive Symptoms in Children with Tic disorders

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Introduction:

Sudden and explosive episodes of anger or aggression are postulated to be a significant source of psychosocial morbidity in children and adolescents with tic disorders. However, scientifically, this issue remained a controversy.

Objectives:

To study the relationship between tic disorders, their associated comorbidities, and aggressive behavior.

Materials & Methods:

Fifty six children and adolescents (ages 7-17) suffering from Tourette syndrome or other chronic tic disorders were assessed. Thirty two healthy children served as a control group. The participants in the study group were assessed by: Yale Global Tic Severity Scale; Yale Brown Obsessive Compulsive Scale; ADHD Rating Scale IV; Screen for Child Anxiety Related Emotional Disorders; Child Depression Inventory; Overt Aggression Scale.

Results:

No significance difference in aggression score was found between tics group and control group. Verbal aggression was found in 70% of the subjects with tic disorders, which was also the most prevalent type of aggression. The level of aggression was not correlated to tic severity. ADHD and OCD enhanced the probability of explosive outbursts in the group with tic disorder. Aggression score was significantly associated with compulsive behavior. Regression analysis showed that the only significant predictor of aggression was ADHD severity score in the study group.

Conclusions:

Our study suggests that there is no difference in aggressive behavior between children with tics and a control group. It is possible that aggressive behavior in tic disorders is associated with the co-morbidities ADHD and compulsive behavior.



P19. Behavioral intervention for tics (CBIT): Does it achieve more than its' focus? The effect of focused intervention for tics regulation on cognitive inhibition and emotion regulation

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Background:

Tourette Syndrome (TS) is a neurodevelopmental disorder characterized by sudden appearance of motor/vocal tics. Since inhibitory control is a significant concern in TS, Comprehensive Behavioral Intervention for Tics (CBIT) focuses on training individuals with TS to inhibit and control tics to reduce tics' severity, with evidence based support for its effectiveness. However, little is known regarding the effect of CBIT treatment on general inhibition ability. We performed a randomized controlled trial of two behavioral interventions to examine the effect of CBIT on cognitive and emotional-behavioral inhibition.

Materials & Methods:

Forty-five children and adolescents with TS or chronic motor tics, aged 8-15 years, were randomly assigned to one of two group treatments: group-CBIT and group-Psycho-Educational-Support (PES), not focusing on inhibition. Group treatment protocol was followed for both groups, including children and parents' group meeting. Inhibition abilities were evaluated in both neuropsychological assessment cognitive inhibition as well as emotion regulation strategies (cognitive reappraisal and expressive suppression), and emotion regulation of depression and anxiety related symptoms. Inhibition abilities were assessed pre-treatment, post-treatment (after 8 sessions), and 1-month after intervention (after one booster session).

Results and Conclusions:

Regarding neuropsychological functioning, cognitive inhibition abilities were not affected by either treatment. However, regarding emotional functioning, following both treatments participants reported a decrease in anxiety symptoms. Furthermore, following CBIT only, participants reported an increased use of cognitive reappraisal, which is considered as more adaptive emotion regulation strategy, and a decrease in depression related symptoms. Thus, current results support the idea that CBIT contributes to inhibition, as apparent in emotional-behavioral change, and may suggest the benefits of CBIT exceed tics' reduction and include improvement in general emotional functioning.

P20. Psychoeducation groups for parents of children with tic disorders

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Background:

Emotional, behavioural and learning difficulties are commonly reported in children and young people with tic disorders (TD), with co-morbidities often contributing to lower self-esteem, reduced quality of life and parenting stress. As part of a stepped care approach, we developed a psychoeducation group intervention to 1) provide families with information and practical strategies for managing tics and other commonly reported issues, 2) create a forum for parents to support one another by sharing their own experiences and advice. A clinical audit was conducted to evaluate whether the intervention was successful at meeting families' needs and expectations.

Materials & Methods:

Parents of children with TD who were seen in the TANDEM clinic were invited to attend a psychoeducation group intervention, which was delivered five times between 2015 and 2018. The intervention comprised four sessions, each lasting two hours, delivered once a month for four consecutive months. Each session covered a specific topic, 1) Introduction to tics and Tourette syndrome, 2) Anxiety and self-esteem, 3) Coping better at school, 4) Managing anger and emotional outbursts. Sessions included educational information, group discussion and provision of resources. Before and after each session, parents completed questionnaires about their perceived understanding and competence in managing the issues covered. Ratings regarding the quality and ease of understanding sessions were also collected.

Results and Conclusions:

A total of 39 families attended the psychoeducation group intervention, with children of a mean age of 10 years. There was a statistically significant improvement in parents' scores regarding their perceived understanding and confidence in managing the issues discussed, with the content of sessions rated very positively. Qualitative feedback indicated that parents found the sessions informative, helpful and valued meeting other parents. These findings highlight that educational support groups for parents of children with TD can be a useful intervention to help improve parental understanding and management of tics and co-morbid concerns, such as anxiety, learning difficulties and emotional outbursts. As such, psychoeducation groups represent a time- and cost-effective intervention to support parents in managing the challenges associated with TD during development.

P21. Behavioural therapy training by Tourettes Action and ESSTS: Barriers to improving access to treatment in the UK

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Background:

The European clinical guidelines for Tourette Syndrome (TS) suggest that behavioural therapies (BT) are 'first line treatments for tics for both children and adults'. However, a barrier to delivering this treatment in the UK is a lack of access to specialised clinicians. To relieve this problem there has been successful research on BT delivered by telemedicine, group interventions, remote access and online treatments.

Tourettes Action (TA) is a national charity in the UK which offers subsidised training in BT. The European Society for the Study of Tourette Syndrome (ESSTS) also runs training at the annual conference. TA anticipates the training it runs in the UK will increase patient access to BT. We



estimated the number of therapists trained in BT both at ESSTS and by TA in the UK. We examined the numbers attending the BT training in the UK and whether this resulted in more clinicians on the TA list of trained therapists.

Materials & Methods:

Estimates of numbers of therapists trained in BT by TA and by ESSTS were gathered from the ESST leadership and from TA. The question on the feedback form at the end of the TA UK training was: *'Are you happy to have your details added to the TA therapists lists of people offering CBITS in the UK? Yes/No. If no, why not?'*

Results and Conclusions:

Estimates of trained professionals throughout Europe in general and in the UK were collected. An approximation of 415-455 English-speaking clinicians were trained at ESSTS from 2010-2017. 195 were trained in the UK by TA from 2013-2017. TA organised BT training in Glasgow, Liverpool, Belfast, Newcastle and London (2x) during 2016 and 2017. Of the 2017 Glasgow trainees responded to the feedback question 17 (N=26) said they would join the list (65%), 9 individuals said no. Of the 2017 Liverpool trainees 16 (N=19) said they would join (84%), 3 said no. 100% (N=20) of the 2017 London trainees said they would join. 76 people in total were trained in 2017 through the TA's BT training, but this only translated to 19 people joining the list (25%). In total, of 141 trainees, 53 wanted to join the list (36%). Reasons for not being included on the list were: having no patients with tics on caseload; issues relating to NHS services, having no capacity to see additional patients and unable to take on more referrals; a lack of positivity from employers, often related to service commissioning or lack of awareness of TS. Some trainees were willing to consider private work (in conjunction with their NHS work) and to join the TA therapist list. Importantly the lack of access to supervision expertise & subsequent lack of confidence seems to be an issue.

To conclude it is very difficult to measure the impact training has had and whether it has increased the numbers of clinicians/therapists offering BT in the UK. Clinicians might work with many patients with tics but are not on the TA list. The inverse may also be true with a clinician who may be on the TA list but seldom treats patients with tics.

P22. Group-Based Exposure with Response Prevention for children with Tourette Syndrome (TS): A pilot study

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Background:

Both Habit Reversal Therapy (HRT) and Exposure with Response Prevention (ERP) have a growing evidence base for the management of tics in children with chronic tic disorders (CTD) via individual sessions. Little is understood about how effective these treatments are when delivered in a group format, with the exception of one promising study outlining the positive impact of group-delivered HRT. In this pilot study we sought to develop and evaluate the delivery of ERP group program for children with TS/CTD and their parents.

Materials & Methods:

Families attending the TANDEM clinic were invited to take part in the group-based ERP programme for children and a parallel parent psychoeducation group. The intervention consisted of eight, weekly, 1 hour sessions which included learning and increasing awareness of the children's tics and tic urges and learning to tolerate the tic urge and 'hold tics' for gradually extended periods of time. The children's parents attended four weekly meetings to introduce the strategies that the children were learning and techniques to support their child's engagement with tic practice at home. Ten children with CTD enrolled in the groups (8 boys, 2 girls; mean age=9 years, range=8-13years). Children and parents completed The Motor tic, Obsessions and compulsions, Vocal tic Evaluation Survey (MOVES) and the clinician-rated, Yale Global Tic Severity Scale (YGTSS) to assess tic impairment and severity pre- and post-treatment. A qualitative measure was also administered to gather information on the acceptability of, and satisfaction with, the group.

Results and Conclusions:

Post intervention a reduction in tics was reported in seven of the children with an average decrease of 29.13 in YGTSS scores. Five parents reported a reduction in tics as rated on the MOVES, with an average decrease in total score of 12.4. Half the children reported a reduction in tics, as rated on the MOVES, with an average reduction in total score of 5.25. Qualitative feedback gathered post-group suggested overall satisfaction from both children and their parents. The current findings provide preliminary support that group-based ERP intervention may have a positive effect on tic reduction for children with TS/CTD. Larger controlled trials exploring the efficacy of group-based interventions for children and adults with tic disorders are required.

P23. Task Switching in Tourette syndrome

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Background:

Tourette syndrome is linked to alterations in cognitive control and enhancement of cognitive control has been associated with reduced symptom severity. The cued task-switching paradigm is a well-established method to study preparatory and reactive cognitive control processes. Specifically, a cue indicates the relevant stimulus dimension/task set of the following target, while a switch of task set elicits prolonged reaction times (i.e. switch costs). Extended cue-target intervals allow for preparatory processes that reduce those switch costs. We hypothesized generally increased switch costs in adult patients with Tourette syndrome.

Materials & Methods:

We included 18 adult patients with Tourette syndrome and 18 healthy controls matched for sex, age and education. Participants performed a computerized task-switching paradigm where the relevant dimension (number, color, shape) of a multivalent target was indexed by a cue presented either 100 ms or 800 ms before target onset. We employed a mixed-measures ANOVA with the factors group (patients, controls), trial type (switch, repeat) and preparation interval (short, long) for the dependent variable reaction time.



Results and Conclusions:

We found a significant main effect of trial type, a significant main effect of preparation interval and a significant trial type x preparation interval interaction. These findings illustrate successful induction of switch costs that were augmented for short preparation intervals. Crucially, we also found a significant trial type x preparation interval x group interaction indicating a larger reduction of switch costs for the long preparation interval in healthy controls compared to patients with Tourette syndrome. This indicates impaired preparatory processes in patients with Tourette syndrome.

P24. Altered perception-action binding modulates inhibitory control in Gilles de la Tourette syndrome

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Background:

Gilles de la Tourette Syndrome is a multi-faceted neuropsychiatric developmental disorder with onset in childhood or adolescence and frequent remissions in early adulthood. A rather new emerging concept of this syndrome suggests that it is a disorder of purposeful actions, in which sensory processes and their relation to motor responses (actions) play a particularly important role. Thus, this syndrome might be conceived as a condition of altered 'perception-action binding'. In the current study, we test this novel concept in the context of inhibitory control.

Materials & Methods:

We examined N=35 adolescent Gilles de la Tourette patients and N=39 healthy controls in a Go/Nogo-task manipulating the complexity of sensory information triggering identical actions; i.e. to inhibit a motor response. This was combined with event-related potential recordings, EEG data decomposition and source localization.

Results and Conclusions:

Gilles de la Tourette patients showed worse performance compared to controls and larger performance differences when inhibitory control had to be exerted using uni-modal visual compared to bi-modal auditory-visual stimuli. This suggests increased binding between bi-modal stimuli and responses leading to increased costs of switching between responses instructed by bi-modal and those instructed by uni-modal stimuli. The neurophysiological data showed that this was related to mechanisms mediating between stimulus evaluation and response selection; i.e. perception-action binding processes in the right inferior parietal cortex (BA40). Stimulus-action inhibition binding is stronger in GTS patients than healthy controls and affects inhibitory control corroborating the concept suggesting that GTS might be a condition of altered perception-action integration (binding); i.e. a disorder of purposeful actions.



P25. Enhanced procedural learning in Tourette syndrome and its relation to premonitory urges

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Procedural learning enables us to extract probabilistic regularities embedded in the environment and contributes to the acquisition of automatic behaviors. Tourette syndrome (TS) is associated with frontal/basal-ganglia abnormalities, which often lead to impairments in procedural learning. However, in TS, the results are contradictory as some studies reported intact or even enhanced procedural learning in TS, while others found impairments. In the present study, we further investigated procedural learning in TS to explore the previously proposed cognitive advantages. Furthermore, an enhanced sensitivity to probabilistic regularities in the environment could be related to the detection of tics and premonitory urges preceding tics. To unravel this question, we also examined premonitory urges and their relation to procedural learning.

To investigate procedural learning, we used the Alternating Serial Reaction Time (ASRT) task, which is a visuomotor probabilistic sequence learning task. Furthermore, we used the Yale Global Tic Severity Scale to measure tic severity and the Premonitory Urge for Tics Scale to measure the subjective premonitory urges.

According to our results, children with TS showed a higher sensitivity to the probabilistic regularities of the task, hence enhanced procedural learning. Furthermore, we found a positive correlation between procedural learning and the presence of premonitory urges, indicating that children who showed higher sensitivity to probabilistic regularities also show a higher detection of premonitory urges. In conclusion, our results showed enhanced procedural learning which was not related to tic severity in TS but was associated with premonitory urges.

P26. Exposure with Response Prevention for Tourette's syndrome: a case study of a 6 year-old

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Background:

Write about the background here Exposure with Response Prevention (ERP) is an effective treatment for reducing tic frequency and has been recommended as first line treatment for adults and children with Tourette's syndrome (TS) and other tic disorders (Verdellen, Van De Griendt, Hartmann, et al., 2011). However, the application of ERP in children under the age of 7 hasn't been systematically studied and both case studies and RCTs have only included children over 7 years old. The aim of this case study is to evaluate ERP to treat tics in a 6 year old child.



Materials & Methods:

One child diagnosed with TS was treated at a specialist outpatient clinic during 12 1-hour sessions of ERP. Sessions were attended by the child and both parents. Daily 20-min practice at home was recommended. Treatment follow a standard-protocol specifically designed for children (Verdellen, Van De Griendt, Kriens, & van Oostrum, 2011). Primary outcome was tic severity assessed with the Yale Global Tic Severity Scale (YGTSS) (Leckman et al., 1989). Secondary outcomes included CGAS, Peds-QL, parent SDQ and goal-based outcome measures (GBO).

Results and Conclusions:

After 12 sessions, frequency of tics was reduced and quality of life improved. There was a 35-point reduction in the YGTSS (from moderate-severe range to mild range), an improvement in all parent and child-rated PEDS-QL dimensions, and in parents and child GBOs. There was a 10-point improvement in clinician rated CGAS score and a reduction in parent-rated SDQ. Improvement was maintained at 2 months follow-up. It is feasible and potentially effective to use ERP for tics in children as young as 6 years old. Parents support may play an important role in treatment success.

P27. Stimulus sensitization in patients with Gilles de la Tourette syndrome

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Background:

Stimulus sensitization, defined as heightened sensitivity to tactile, auditory, and visual stimuli that resulted in uncomfortable sensation, tension, or non-tic movement is often seen in patients with autistic spectrum disease (ASD). ASD may co-exist with tics in subjects with Gilles de la Tourette syndrome (GTS). The aim of the study was to assess the prevalence and associations of stimulus sensitization in GTS.

Materials & Methods:

Our study sample included 165 patients with GTS, 125 male (75.8%) and 100 children (60.6%). The average age was 17.0 +/- 9.7 years (range 5-50 years), average disease duration 10.0 +/- 8.3 years (range 0-39 years) with average age of tic onset at 6.4 +/- 2.7 years.

Results and Conclusions:

Stimulus sensitization was found in 74 patients (44.8%). The most often reported preceding stimulus was touch (n=53, 71.6%), smell (n=24, 32.4%), sound (n=22, 29.7%), sight (n=15, 20.3%), restricted food intake (n=5, 6.8%), pain (n=5, 6.8%), cold (n=2, 2.7%). All patients had oversensitization to stimuli and half GTS subjects experienced more than one stimulus followed by sensitization. In our cohort correlates of stimulus sensitization were anxiety disorder (p=0.003), pervasive developmental disorder (p=0.030, present in 7/165 patients, 4.2%) and significant social skills problems (p=0.005, present in 27/165 patients, 16.4%). We can therefore conclude, that stimulus sensitization indicates presence of autistic traits and should prompt to look for ASD in GTS patients.

P28. Cannabis-based medicine as treatment of tics and comorbidities in children with Tourette syndrome

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Background:

For the treatment of tics, behavioral therapy, antipsychotics, and α -adrenoceptor agonists (in case of comorbid attention deficit/hyperactivity disorder (ADHD)) are first line treatments. In those patients with Tourette syndrome (TS), who do not respond to these treatments, only very limited alternatives can be offered such as topiramate, tetrabenazine, botulinum toxin, and in rare exceptional cases deep brain stimulation. Due to insufficient benefit and intolerable side effects, a substantial number of patients seeks for alternative treatments. While there is already evidence that cannabis-based medicines (CBM) might be effective in adults with TS, in children only one case report in a 15 year old boy is available suggesting beneficial effects of delta-9-tetrahydrocannabinol (THC).

Case presentation:

We present two cases of successful treatment with CBM in children with TS. The first patient is a 7-year-old boy with severe TS and comorbid ADHD. He presented during an episode with increased tics resulting in depression, suicidal ideation, separation anxiety and finally social isolation. As treatment with various antipsychotics (risperidone, aripiprazole, tiapride) and Habit Reversal Training turned out to be unsuccessful, we implemented therapy with oral THC as oil-based drops. Starting dose was as low as 0.7 mg THC/day once a day and was gradually increased up to a maximum dose of 29.4 mg THC/day, resulting in a significant improvement of both tics and behavioral symptoms. Follow-up visits over a period of 12 months demonstrated a sustained treatment effect without any adverse events.

The second case is a 12-year-old boy with TS. He presented with severe motor tics resulting in insomnia. Previously, the parents – both of whom were medical doctors - decided to initiate treatment with 0.02 g vaporized medicinal cannabis (Bedrocan containing 22%THC and 1% cannabidiol (CBD); equivalent to 4.4 mg THC). This resulted - according to the parents' report - in an immediate and nearly complete remission of tics. Due to a further increase of tics, the parents decided – in consultation with us - to implement a regular treatment with a combination of vaporized cannabis (up to 0.1 g cannabis/day, varieties Bedrocan and Amnesia Haze, corresponding to 22 mg THC/day) plus orally administered oil-based THC drops (maximum daily dose = 12.5 mg THC) resulting in a marked tic reduction. During follow-up visits over 8 months we were able to observe the reported beneficial effects of cannabis: tics, premonitory urges, behavioral symptoms and overall impairment significantly improved according to both examiner assessments as well as parent and clinician questionnaires. Importantly, no adverse events were reported.

Conclusions:

From these case studies it is suggested that CBM such as oral THC and vaporized medicinal cannabis (alone or in combination) might be effective and safe in the treatment of severe tics even in minors with TS, who do not respond to well-established treatment strategies.



P29. The ORBIT study (Online Remote Behavioural Intervention for Tics): adapting the therapist-guided Swedish BIP-TIC intervention for patients and clinicians in England

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Background:

Tourette syndrome (TS) affects ~70,000 children in England, and is frequently distressing for the child and their families. Service provision and treatment availability for tics varies across the country: many children with tics receive medication as first-line treatment, but these do have many side effects. Behavioural therapies, such as Exposure and Response Prevention (ERP), have been shown to be as effective as medication in helping young people manage their tics, and young people have expressed preferences for behavioural therapies. However, there are a limited number of trained therapists in the UK; families may face long waiting times and large travel distances to access these. Remotely-delivered treatments are an alternative option. BIP TIC, an online intervention based on ERP, has been developed and evaluated in Sweden, showing promising findings in reducing tic severity. This online intervention offers therapy for children and their parent(s), with a therapist providing remote online support. Here, we present how BIP TIC was adapted for the NHS England healthcare system in preparation for a RCT, comparing online ERP to online psychoeducation, for children (9-17 yrs) with TS or persistent tic disorder.

Materials & Methods:

The online ERP intervention required partial translation from Swedish to English, and modification to be suitable for implementation into NHS England. We explored how ERP works in clinical practice and adapting this for delivery in an online NHS delivered intervention with remote therapist support, though collaboration with specialist clinicians and Swedish colleagues who developed and delivered BIP TIC. We also established a Patient and Public Involvement (PPI) panel consisting of children with TS and their parents who have experience with behavioural therapies. This panel were involved in the design of the study and the interventions, including reviewing online ERP and psychoeducation child and parent interventions. The intervention has been refined through feedback from academics, researchers and clinicians in the UK and Sweden involved in ORBIT.

Results and Conclusions:

Two online interventions, each with a child program and a parent program, have been developed and refined through clinical expertise and PPI review. The approach taken in this study was critical to ensure that the interventions are relevant and acceptable to children and their families and present a feasible way of delivering treatment for managing tics, and also to make sure that it able to be integrated into NHS clinical care.



P30. Emotion Regulation in Children with Tourette Syndrome

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Background:

Difficulties in emotion regulation (ER) are frequently part of the symptomatology in children with Tourette syndrome (TS) with explosive outbursts and aggression being reported clinically and in research. Although previous studies have examined emotional aspects of behavior, the majority of studies has relied on self- or parent-report measures or has been carried out with adults. In this study we examined ER abilities in children with TS with a novel, validated, observational measure to contribute to the understanding of these difficulties.

Materials & Methods:

A total of 150 children participated in the study: 49 with TS, 23 with attention-deficit/hyperactivity disorder (ADHD), 16 with TS and ADHD, and 62 controls. Participants completed the Tangram Construction Task; a five-minute, complex puzzle solved in the presence of a parent. The performance was filmed and coded on items covering parent and child behavior, respectively, with the Tangram Emotion Coding Manual that reliably generates quantitative measures such as overall ER ability, emotion communication, and parent-child interaction. We assessed differences in group scores with the chi-square test of homogeneity. For significant results, we used the Holm-Bonferroni method for pairwise comparisons to establish the nature of group differences.

Results and Conclusions:

The TS group and the control group did not differ on the primary outcome measure of overall ER ability; however, the ADHD group scored significantly lower than the control group ($p = 0.01$) and the TS group ($p = 0.03$) and similarly the TS + ADHD group differed from the control group ($p = 0.02$) and the TS group ($p = 0.02$). The groups differed on one additional item for children, namely one of three resulting factors representing emotional control. Again, both groups including children with ADHD scored lower than the control group and the TS group ($p = 0.02$ for all comparisons), and there was no difference between the control group and the TS group. These results suggest that children with TS may have ER abilities that are similar or close to those of typically developing children and are in line with previous literature suggesting a central role for ADHD in the presence of dysregulated emotions.

P31. A survey summary on Tic Disorder in children in China

Mingyan Shao, Yunqing Zhao

Independent researchers





Background:

It has been estimated that there are about 2.7 million children in China with Tic Disorder (TD). However, there is no large-scale database of these children to support doctors and families for the treatment and management of TD. The survey was launched on a social media support group for families of children with TD that has almost 20,000 members. The aim of this study is to provide baseline data foundation for doctors and researchers of the current situation of TD in China, and to study the effectiveness of the social media support group to the children and families.

Method and Analysis:

We designed a survey questionnaire and collected 1,177 completed forms in a week. The survey is completed by the parents or other caregivers of a child younger than 21 year old. The questions are designed to cover the following categories:

- Relationship between the child and the adult who is completing the form
- Basic information about the child: gender, DOB, ethnic group of China, province
- Basic information about the adult: age, occupation, marriage status, highest education level
- Family information: other children, family income
- School information
- Diagnosis information on TD/TS, OCD, ADHD, Anxiety, alcohol/drugs, violent behaviours, eating disorders
- Category of TD/TS, any CBIT treatment
- Frequency and scales of motor and vocal tics, Parent Tic Questionnaire
- Simplified Child Tourette's Syndrome Impairment Scale (CTIM-P)
- Support from the society

Discussion:

The collected data provides valuable information for further research from a range of perspectives including diagnosis of TD, treatment, management and support. Social media support groups have been shown to offer an encouraging environment for psychoeducational support to families of children with TD. In the future, it would be a constructive and positive platform for doctors to deliver, supervise and monitor treatments of TD.

P32. Sleep and cognitive learning in young people with tic disorders

Dr Charlotte Hibberd (Clinical Psychologist)¹, Professor Tony Charman (Chair in Clinical Child Psychology)¹, Professor Paul Gringras (Consultant Paediatrician)², Dr Tammy Hedderly (Consultant Paediatric Neurologist)², and Dr Sally Robinson (Paediatric Clinical Neuropsychologist)^{2*}

¹ Department of Psychology, Institute of Psychiatry Psychology & Neuroscience (IoPPN), King's College London; ² Children's Neurosciences Centre, Evelina London Children's Hospital, Guy's and St Thomas' NHS Foundation Trust, London

Background:

Sleep difficulties are assumed to be common in young people with tic disorders, such as Tourette syndrome; however, this assumption is based on a limited and heterogeneous evidence base. This project adopted a naturalistic approach to study relationships between sleep and functional



outcomes in children with/without tic disorders. It aimed to explore the process of overnight consolidation alongside measures of sleep, cognitive and emotional functioning.

Materials & Methods:

Sleep was assessed in 32 adolescent males, with adolescents with tic disorders (n=16) matched to typically developing controls (n=16) on the basis of age, gender and IQ. Sleep was assessed using actigraphy over a two week period. Overnight learning was assessed using 'Sleepsuite' games; a set of iPad-based tasks designed to assess verbal learning (*Animals* task), continuous performance (*Balloons* task) and spatial learning (*Mazes* task). Participants completed the tasks before and after a single night of sleep. A comprehensive neuropsychological battery and a range of child/parent clinical questionnaires to assess psychopathology were also administered.

Results and Conclusions:

Sleep was highly variable in the clinical group, but with no significant differences in movements and sleep between groups. However, longer onset latency was associated with poorer performance on the verbal memory task and significantly more symptoms of depression and panic for young people with tic disorders. Neuropsychological test performance did not differ between groups, but trends in the data suggest distinct overnight learning profiles and consolidation processes. This study suggests that sleep in young people with tic disorders may differ from normal, with greater difficulties falling asleep associated with psychopathology and changes in patterns of learning. This highlights the importance of the systematic screening of sleep difficulties in clinical practice, with consideration of the potential relationship between sleep problems, mental health and education so that appropriate therapeutic interventions and support can be provided.

P33. Why does no-one in Uganda have tics? A mixed-methods study of knowledge, attitudes and experience of health professionals in Uganda

Tara Murphy,^{1, 2} Kirstie Fleetwood,² and James Nwsereko²

1 Great Ormond Street Hospital NHS Foundation Trust, London ,UK; 2 Butabika Hospital, Kampala, Uganda

Background:

Previous work has suggested that tic disorder is rare and possibly absent in sub Saharan Africa (Robertson, 2008). Data from a specialist clinic in North America (Thomas et al, 2015) regarding the ethnicity of their patients identified a relative under-representation of children from African heritage compared with children of other background. Feedback from health professionals in Uganda is that tic disorders are very rare and many report not having seen patients with tics in decades of clinical practice. However, within two months of being involved in child and adolescent mental health service (CAMHS) clinics, two patients have presented seeking help for tics. European studies have shown that lack of knowledge about tics in professionals can lead to a delay in diagnosis for patients (Mol Debes and Skov, 2008) although other factors may also apply (Shilon, Pollak, Benarroch and Gross-Tsur, 2008). It could be that lack of awareness about tics is the driving factor for why so little focus has been placed on tic disorders to date.

We describe a mixed-methods study of Ugandan health professionals regarding their knowledge of and attitude towards identification and diagnosis of tic disorder in children and adults in Uganda.



The second aspect is an opportunistic clinic based survey of children and teenagers with tic disorder who present to a specialist outpatient CAMHS at Butabika Hospital Kampala, Uganda. Data will be collected months between May and November 2018. an anticipated 150-250 patients will be included during the observation period. Demographics and diagnostic clinical assessment will be collected on all outpatients.

Materials & Methods:

The study has two parts. The first part of the study involves a wide network of mental health professionals in Uganda (approximately N= 120-140) who will be invited to complete a survey regarding their knowledge, attitude and experience of diagnosing tic disorders in children and adults. In addition, semi-structured interviews will be carried out with 5-8 professionals in urban and rural Uganda to understand more about knowledge and experience of tic disorders. The data will be analysed using thematic analyses.

The second aspect is an opportunistic clinic based survey of children and teenagers with tic disorder who present to a specialist CAMHS at Butabika Hospital Kampala. Data will be collected for six months between May and November 2018. Typically, 20-40 patients present for assessment per week, therefore an anticipated 150-250 patients will be included during the observation period. Demographics and diagnostic clinical assessment will be collected on all outpatients.

Results and Conclusions:

We can now conclude that people in Uganda do have tics but have little information about how the symptoms present, are understood or treated.

This study will explore the reasons why there is so little research on individuals with tics in Uganda and poor detection and diagnosis of tic disorders by professionals.

Once there is better awareness of tic disorders by professionals and the general population, it will be interesting to see if clinical practice and research focus changes in sub-saharan Africa. To date, much the focus has been on life limiting disease such as human immunodeficiency virus, perhaps this may change as treatment for such communicable diseases is more effective and education for professionals becomes more diverse.



Mary Robertson Award

Efficacy of a Resource Activation Treatment in Children with Chronic Tic Disorders – A Within-Subject Analysis

Paula Viefhaus², Marion Feldhausen², Anja Götz-Dorten^{1,2}, Helene Volk², Manfred Döpfner^{1,2} & Katrin Woitecki²

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Background:

Pharmacological and problem-focused behavioral interventions for children and adolescents with tic disorders have limited effects on symptoms and impairment. Therefore, there is a need to develop and evaluate alternative psychological interventions. The aim of this pilot study is to evaluate the efficacy of a resource activation program as an alternative intervention for children and adolescents with tic disorders.

Materials & Methods:

A within-subject design with two phases (8 weeks diagnostic; 16 sessions treatment) was analyzed using multilevel modeling ($n = 24$). Multiple outcome measures were used to assess the effects on the course of the tic symptoms (clinical rating, video observation, parent and self- ratings). Additionally, self-esteem, comorbid disorders, impairment and subjective burden ratings were assessed.

Results and Conclusions:

During the treatment phase, significant reductions of tics were found in clinical rating (YGTSS), parent rating and video observation (motor tics). Moreover, an improvement was shown on most tic-related impairment and subjective burden ratings. No significant improvement was found regarding comorbid problems and self-esteem. Compared to the preceding diagnostic phase, a significant incremental treatment effect emerged in clinical rating of tic symptoms (YGTSS) and video observation (motor tics). This pilot study provides first hints that resource activation may represent an effective treatment for reducing tic symptoms, impairment and subjective burden. However, further research is needed in order to establish resource activation as an effective treatment for tic disorders.





Invited speakers

In the borderland of normality - Tics as models of increased perception action binding

Alexander Münchau

Department of Pediatric and Adult Movement Disorders and Neuropsychiatry, Institute of Neurogenetics, Center for Brain, Behavior and Metabolism, University of Lübeck, Germany

Gilles de la Tourette syndrome (GTS) is a common multifaceted neuropsychiatric disorder with motor and phonic tics as cardinal and defining clinical features. Other characteristic signs are urges preceding tics, echo- and coprophenomena. Despite an abundance of neuroscientific studies in children and adults with GTS and good evidence that abnormalities predominantly in the basal ganglia and fronto-striatal loops play a prominent role in the pathophysiology, no generally accepted concept of tics or GTS has emerged. The nature of tics is still unclear. One of the main problems appears to be a lack of a coherent theoretical framework for tics and other associated phenomena in GTS. Several characteristics set tics apart from other 'classical' movement disorders, so that tics might be conceptualized as a surplus of physiological movements and actions. The intricate and unique relation between tics and preceding urges, suggesting abnormal internal monitoring, i.e., perceptual, attentional and response selection processes during tic generation, calls for a concept encompassing both action and perception. To shed light on the biology of tics and echoes in GTS and to further a better understanding of behavioral treatment approaches a shift in the view of tics and GTS based on a cognitive approach to action control might be helpful. In this respect, the 'Theory of Event Coding' (TEC) is an attractive framework for tics and GTS, which will be outlined in this presentation.

Updates on large scale collaborative studies for Tourette Syndrome

Peristera Paschou

Department of Biological Sciences, Purdue University, West Lafayette, IN, USA

As we are starting to reach an inflection point at which results are starting to become reproducible, Dr Paschou will provide an update on most recent findings from multiple large-scale efforts aiming to identify the genetic basis of TS. She will present results from two of the largest collaborative efforts for TS: EMTICS (European Multicentre Tics in Children Study) and TS-EUROTRAIN (a Marie Curie Initial Training Network). Besides a genomewide association study on 1500 patients with TS, we also present results from the largest family-based exome-sequencing analysis to date as well as plans for integration with neuroimaging as part of ENIGMA-TS. Meta-analysis of TS GWAS with GWAS for ADHD and ASD sheds light into the shared etiology identifying genes that play a role across the spectrum of neurodevelopmental disease. Leveraging power from large-scale collaborative efforts and participation from a multitude of clinical sites and researchers from around the world we move towards a better understanding of the cause and phenomenology of TS.



Structural variants and protein networks in Tourette syndrome

Zeynep Tümer

Kennedy Center, Department of Clinical Genetics, Copenhagen, University Hospital, Denmark

Structural variants, including copy number variations (CNV) such as microdeletions and duplications, have been instrumental in understanding the disease aetiology in several neurodevelopmental disorders, including autism. Similarly, several genome wide CNV studies have been carried out for Tourette syndrome, and candidate susceptibility genes were suggested as rare contributing factors. In a smaller Danish cohort of clinically well described Tourette syndrome patients, we have carried out chromosome microarray studies and identified several genes of interest. In this study, some of these genes will be presented and their involvement in disease pathogenesis will be discussed.

Genome-wide methylomic analysis of neonatal blood from Danish twins discordant for mental illness

Shantel Weinsheimer^{1,2}, Anna Starnawska^{1,3,4}, Christine S. Hansen^{1,5}, Alfonso Buil^{1,2}, Jonas Bybjerg-Grauholt^{1,5}, Marie Bækvad-Hansen^{1,5}, David M. Hougaard^{1,5}, Thomas Sparsø^{1,2}, Marcelo Bertalan^{1,2}, Preben B. Mortensen^{1,6,7}, Carsten B. Pedersen^{1,6,7}, and Thomas M. Werge^{1,2,8}

1iPSYCH – The Lundbeck Foundation’s Initiative for Integrative Psychiatric Research, Denmark; 2Institute of Biological Psychiatry, Mental Health Center, Sct. Hans, Mental Health Services, Copenhagen, Denmark; 3Aarhus University, Aarhus, Denmark; 4iSEQ, Centre for Integrative Sequencing, Aarhus, Denmark; 5Statens Serum Institute, Copenhagen, Denmark; 6National Centre for Register-Based Research, Aarhus University, Aarhus, Denmark; 7Centre for Integrated Register-Based Research, Aarhus University, Aarhus, Denmark; 8Institute of Clinical Sciences, Faculty of Medicine and Health Sciences, University of Copenhagen, Copenhagen, Denmark.

Purpose:

Emerging evidence implicates altered DNA methylation in mental illness including autism, ADHD, bipolar disorder, major depressive disorder, anorexia and schizophrenia. However, it is unclear whether the DNA methylation changes observed to date are causative or reflect disease progression or treatment. The neonatal period is a time of rapid neurodevelopment during which alterations in DNA methylation may contribute to the risk of mental illness later in life. Hence, we explored whether differences in DNA methylation in neonatal blood taken at birth were associated with twin discordance for mental illnesses including autism, ADHD, affective disorder, anorexia, schizophrenia or bipolar disorder.

Methods:

A total of 597 pairs of twins (220 monozygotic) discordant for mental illness born between 1981 and 2005 were identified for methylomic comparison. Blood samples obtained from neonatal Guthrie cards were used for DNA extraction and genome-wide profiling of DNA methylation with the use of Infinium HumanMethylation450 BeadChip or EPIC array from Illumina. Quality control, data pre-processing and statistical analysis was performed using the minfi package in R. Data were normalized using the ssNoob method and adjusted for batch effects using the Combat tool. Blood cell composition was estimated using FlowSorted.CordBlood.450k. Using linear regression models and including potential confounders such as sex, blood cell composition and zygosity, we observed differentially methylated positions (DMPs) associated with mental illness. We used VarElect to identify which genes are known to directly associate with mental illness. The GeneMania tool was used to visualize gene interactions in a network.



Results:

We observed significant DMPs ($P<10^{-6}$) for ADHD (mapping to TET2, HNRNPH2, HMGN5), autism (mapping to ATP1B4), and anorexia (ITGB4, GJA3, NXN). Interestingly, there is an enrichment of DMPs mapping to genes in the dopaminergic and serotonergic synapse KEGG pathways including KCNJ5, PRKCA, CACNA1D, CREB5, and ALOX12 ($P<0.05$). In addition, we identified 67 DMPs ($P<10^{-5}$) mapping to genes which have known direct association with at least one mental illness and are connected in a complex genetic network. Our data indicate that DNA methylation differences are quantifiable in neonatal blood from twins discordant for mental illness later in life and suggest that susceptibility to mental illness is conferred by dysregulated neurodevelopmental genes.

Update on PANS and PANDAS

Tanya Murphy

University of South Florida, St Petersburg, FL, US

Background

Research that began in the late 1980's has provided support that a subset of rapid childhood onset obsessive-compulsive disorder (OCD) and/or tic disorders begin following an infection, including Pediatric Acute-onset Neuropsychiatric Syndrome (PANS), along with the specific subgroup, Pediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcus (PANDAS). OCD and tic symptoms in PANDAS/PANS are similar to those in the classic forms of childhood OCD and tic disorders, but have differences in the quality of onset symptoms, co-occurring symptoms and course. PANS/PANDAS symptoms are thought to be precipitated and exacerbated by infections, most notably Group A Streptococcus (GAS), Mycoplasma pneumonia, Influenza, or Lyme disease. Swedo et al. found that patients with PANDAS are more likely to have comorbid ADHD (40%), Oppositional Defiant Disorder (40%), and Major Depression/Dysthymia (48%). More recently, researchers noted that many children suffered from symptoms of PANDAS without documented streptococcal infection, thus the criteria for Pediatric Acute-Onset Neuropsychiatric Syndrome (PANS) was proposed. The PANS criteria include acute onset of OCD or food restriction, and at least two of the following associated symptoms: frequent urination, worsening handwriting/cognition, inattention, anorexia, separation anxiety, oppositionality, irritability/rage outbursts, and emotional lability. Thus, PANS potentially include other pathogens/substances as triggers, and PANDAS is a strep-specific subset of PANS.

Many children with the PANS phenotype exhibit extremely impairing and disruptive associated neuropsychiatric symptoms, including rage outbursts, behavioral regression, compulsions, motor and vocal tics, and school dysfunction (due to ADHD symptoms, cognitive regression). Although large placebo-controlled studies are lacking in this population, most children receive antibiotics and failing response to antibiotics, IVIG. Other treatment considerations have included steroids, nonsteroidal anti-inflammatory medications and plasma exchange. However, confusion exists among clinicians and parents as to which children best fit the PANS definition and how best to proceed with treatment.

Materials





This presentation will briefly discuss research updates related to the diagnosis, identification of biomarkers, treatment, and etiopathogenesis of PANDAS and PANS.

Conclusions

As increasing research and expert consensus has decreased the controversy regarding PANDAS/PANS, additional empirical evidence guiding treatment is needed. Furthermore, it is becoming clear that a large portion of children with PANDAS/PANS symptoms who do not present with an infectious trigger are being missed. This seminar will identify clinical characteristics that are unique to patients with PANS/PANDAS, and help inform upon a proper diagnoses and treatment approach for these individuals.

What are we learning about Tourette's from population-based studies? The example of autoimmune diseases.

David Mataix-Cols

Karolinska Institutet, Stockholm, Sweden

The large nationwide administrative registers available in the Nordic countries potentially offer great opportunities to study important questions about the risk factors and consequences of Tourette's Syndrome (TS). However, for this potential to be fulfilled, several prerequisites need to be met. First, the diagnostic codes need to be valid and reliable. Second, the patients in these registers should be similar to other patients seen in specialist clinics around the World (reasonable representativeness). Third, we should be able to replicate known facts about TS, before we can explore additional questions. Fourth, cohort sizes should be sufficiently large (statistical power). Fifth, for outcomes with long latency (e.g. suicide, cardiovascular diseases), long follow-up periods (often several decades) are needed. In this talk, I will argue that all these prerequisites are met, at least in part. I will then present examples of our ongoing register-based research in Sweden, focusing specifically on a family study of autoimmune diseases in OCD and TS.

The Role of Dopamine in Tourette Syndrome: A Computational Account

Tiago Maia

Instituto de Medicina Molecular, Faculdade de Medicina, Universidade de Lisboa, Portugal

Tourette syndrome (TS) has long been associated with dopaminergic disturbances, but the precise nature of those disturbances and how, mechanistically, they give rise to tics has remained controversial. This talk aims to provide a comprehensive, integrative account of the role of dopamine in TS. To achieve this aim, the talk is divided into four interrelated parts. The first part of the talk shows that a comprehensive review of the evidence from molecular-imaging studies of the dopaminergic system in TS suggests that the most parsimonious explanation for those studies is that TS involves dopaminergic hyperinnervation. This dopaminergic hyperinnervation likely causes a hyperdopaminergic state. Consistent with this hypothesis, the second part of the talk shows that all medications that are typically used to treat TS reduce dopaminergic signaling. Dopaminergic hyperinnervation likely increases both phasic and tonic dopamine. The third part of the talk shows computationally how increased phasic and tonic dopamine increase the propensity for tic learning



and expression, respectively. Finally, TS is strongly associated with premonitory urges, whose termination has been hypothesized to cause tic learning via negative reinforcement. The fourth part of the talk shows computationally how the termination of premonitory urges induces positive prediction errors that likely are signaled by phasic dopamine, thereby causing tic learning. Overall, then, a simple pathogenic hypothesis (dopaminergic hyperinnervation), elaborated by detailed consideration of its mechanistic consequences, provides a parsimonious explanation for a wide range of molecular-imaging, pharmacological, and behavioral findings in TS.

Insights from animal models on the pathophysiology of tics and comorbid symptoms

Izhar Bar-Gad

The Leslie and Susan Gonda Brain Research Center, Bar-Ilan University, Ramat-Gan, Israel

Background:

The cortico-basal ganglia pathway is involved in the processing of motor, associative and limbic information and implicated in multiple movement and behavioral disorders. Abnormal inhibition within multiple basal ganglia nuclei has been associated with Tourette syndrome.

Materials & Methods:

We used microinjections of the GABA_A antagonist bicuculline in experimental animals to generate focal disinhibition within the input nucleus of the basal ganglia, the striatum. The procedure was used to generate tics and comorbid symptoms in rodents and non-human primates both transiently (one hour) and for prolonged periods (multiple weeks). During the symptom expressing period we used microelectrodes to record the neurophysiological activity along the pathway and kinematic sensors to evaluate the properties of the symptoms. In addition, we utilized electrical and optical microstimulation to manipulate the information flow within the pathway. Finally we tested the effect of both normal changes in the animal's behavioral state and of pharmacological agents on the expression of symptoms.

Results and Conclusions:

Microinjection of bicuculline into the motor part of the striatum led to the expression of motor tics in a body part which was dependent on the somatotopic location of the microinjection. Similar injections into the limbic part of the striatum led to a state of hyperactivity and enhanced rate of behavioral-switches. Stimulation of the motor cortex determined the timing but not the form of individual tics. Finally, both normal behavioral states (such as sleep) and a pharmacological agent (Aripiprazole) reduced the rate of tic expression. The behavioral symptoms expressed following striatal disinhibition in experimental animals highly resemble the ones apparent in Tourette syndrome patients and provides a promising tool for the development and evaluation of pharmacological and behavioral treatments of the disorder.

Comorbidities in clinical versus non-clinical populations of children and adolescents with TS

Elena Cravedi

Department of Child and Adolescent Psychiatry, Pitié-Salpêtrière Hospital, France & Pediatric Neurology Unit, University of Firenze, Florence, Italy



Comorbidities and coexistent pathologies occur in the majority of patients with Tourette syndrome and, more than the severity of tics, contribute to the psychological and psychosocial impairment observed in Tourette syndrome. In this sense, TS comorbidities provide a better understanding of the syndrome not only in terms of classification and aetiopathogenesis but also in terms of outcome and led to a patient-tailored therapeutic approach. Comorbidities of TS have been described in clinical and non-clinical populations through different methods and instruments but leading to results mostly similar and overlapping. In particular, the available evidence suggests that neurodevelopmental comorbidities in TS are common and tend to aggregate, evidencing a possible common etiological background and leading to a complex multidisciplinary therapeutic approach.

Course of Tourette Syndrome and Comorbidities in a Large Prospective Clinical Study

Camilla Groth¹, Nanette Mol Debes¹, Liselotte Skov¹

1: Paediatric Department, Herlev University Hospital, Herlev, Denmark

Background:

Tourette syndrome (TS) is a childhood onset neurodevelopmental disorder characterized by frequent comorbidities and improvement of tics during adolescence. The clinical presentation is heterogeneous and can vary significantly from few tics without comorbidities to severe tics and disabling comorbidities and coexisting psychopathologies. This large prospective study describes the clinical course of tics and comorbidities in a large prospective longitudinal study, the development of phenotypes and the prevalence of comorbidities and coexisting psychopathologies in a cross-sectional view.

Materials & Methods:

The clinical cohort was recruited at the Danish National Tourette Clinic. Data was collected with uniform clinical examinations at baseline (n=314, age range 5-19 years) and at follow-up (n=227, age range 11-26) 6 years later to examine the development in expression of tics and comorbidities and of phenotypes. Additionally, a cross-sectional screening for coexisting psychopathologies with The Development and Well-Being Assessment (DAWBA) was performed at follow up reporting the presence of DSM IV diagnoses (n=146).

Results and Conclusions:

Tics, OCD and ADHD severity scores are significantly age-related and all decline during adolescence though with different rates. Although ADHD severity declined based on DSM IV criteria, analyses based on the Danish national norm scores showed that adolescents aged 11-18 (n=83) had a significantly raised norm score in inattention, hyperactive- impulsivity and conduct. The development in phenotypes changed towards less comorbidity with 40% presenting with TS-only at baseline and 55% at follow-up which can help guide patients and can be used for genetic, etiological and clinical research purposes.

At baseline only 10.2% were regarded as TS pure. At follow up, prevalence of comorbidities and coexistent psychopathologies was 61.2% whereas 38.2% presented pure TS. Cross-sectionally at follow up, we found a broader spectrum of TS-associated comorbidities and coexistent psychopathologies in the emotional, behavioral and neurodevelopmental spectrum.



In spite of general improvement and partial remission, considerable comorbidities and coexisting psychopathologies persist in adolescence and threshold symptoms and difficulties still have to be considered in clinics.

Efficacy and safety of the endocannabinoid modulator ABX-1431 in Tourette Syndrome: results from a phase 1b study

Kirsten Müller-Vahl

Department of Psychiatry, Socialpsychiatry and Psychotherapy, Hannover Medical School, Hannover, Germany

Background:

Many patients with Tourette Syndrome (TS) are unsatisfied with available treatment strategies and therefore seek alternative treatment options. Anecdotal reports and small controlled trials provide preliminary evidence that exocannabinoids including cannabis, nabiximols, and tetrahydrocannabinol (THC) are effective in the treatment of tics and psychiatric comorbidities. However, not only exocannabinoids, but also inhibitors of endocannabinoid degradative enzymes can be used to enhance the activity of the endocannabinoid system. ABX-1431 is a first-in-class, oral, highly selective inhibitor of the enzyme monoacylglycerol lipase (MGLL), which catalyzes the hydrolysis of the endocannabinoid 2-arachidonoylglycerol (2-AG), an endogenous agonist of the cannabinoid receptors CB1 and CB2. MGLL inhibition elevates 2-AG concentrations and potentiates 2-AG signaling. In the nervous system, 2-AG signaling through CB1 is triggered by postsynaptic activity and reduces the probability of subsequent neurotransmitter release, thus serving as a natural brake for excessive neurotransmission in active circuits. MGLL is co-localized with CB1 in presynaptic neurons and in neighboring glia, positioning the enzyme to exert tight control of 2-AG signaling. MGLL is abundant in the basal ganglia, which is implicated in the physiology of tics in TS. Thus, it can be speculated that ABX-1431 might be an effective treatment for tics and comorbidities in patients with TS.

Materials & Methods:

20 adult patients (16 men, 4 women, age 18-54) with moderate-severe TS were treated in a single-dose crossover study with 40 mg ABX-1431 or placebo. Endpoints were tic severity according to the Yale Global Tic Severity Scale Total Tic Score (YGTSS-TTS), the Modified Rush Video-Based Tic Rating Scale (MRVS), and the self-assessment Adult Tic Questionnaire (ATQ), as well as premonitory urges according to the Premonitory Urge for Tics Scale (PUTS).

Results & Conclusions:

Patients displayed a placebo-adjusted ABX-1431-related tic improvement in the YGTSS-TTS at 8 hours ($p=0.0384$), with improvement in motor tics at 4 hours ($p=0.0016$) and 8 hours ($p=0.0049$), and a reduction in self-reported tic intensity (ATQ) at 4 hours ($p=0.0005$) and 8 hours ($p=0.0008$). A placebo-adjusted ABX-1431-related improvement in premonitory urges was observed at 4 hours (PUTS, $p=0.0369$), while no significant difference was observed with the MRVS. The most common adverse events were headache, somnolence, and fatigue, which resolved in all cases. From our data, therefore, it is suggested that modulation of the endocannabinoid system by selective inhibition of MGLL using ABX-1431 is effective and safe in the treatment of tics in adult patients with TS. To corroborate preliminary data, a longer-term trial including a larger number of patients is in preparation.





An update on deep brain stimulation on Tourette Syndrome.

Tom Foltynie

Sobell Department of Motor Neuroscience, UCL Institute of Neurology, National Hospital for Neurology and Neurosurgery, London, UK

The aim of my talk will be to provide an update on the current knowledge of the efficacy of Deep Brain stimulation for Tourette syndrome.

I will include discussion of the recently published randomised trials, and the potential issue of trial design in the attempt to demonstrate efficacy using double blind methodology.

I will also discuss the development and latest publications from the Global registry of outcomes of DBS for Tourette syndrome, focussing on the different targets used to date.

Finally I will discuss the latest situation regarding availability/ commissioning of DBS for Tourette syndrome in the UK, as an example of the ongoing challenges that persist in accessing treatments despite publication of encouraging data.

Evidenced-Based and Emerging Treatments for Tourette Syndrome

Michael Bloch

Yale Child Study Center, Department of Psychiatry, Yale University, New Haven, CT, United States

Objective:

To review the current evidence-base for commonly utilized pharmacological treatments for tic disorders and discuss emerging pharmacological agents that are additionally being studied to treat tic disorders.

Methods:

We will summarize the results of several published systematic reviews and meta-analyses that examined the efficacy of pharmacological agents for the treatment of tic disorders including antipsychotic medications and alpha-2 agonists. We will discuss systematic reviews examining the treatment of common comorbidities including ADHD and OCD and the moderating effects of tics on treatment selection. We will also discuss emerging treatments for Tourette syndrome currently under study.

Results:

Meta-analysis demonstrated a significant benefit of antipsychotics compared to placebo (standardized mean difference (SMD)=0.58 (95% confidence interval (CI): 0.36-0.80). Stratified subgroup analysis found no significant difference in the efficacy of the 4 antipsychotic agents tested (risperidone, pimozide, haloperidol and ziprasidone). Meta-analysis also demonstrated a benefit of alpha-2 agonists compared to placebo (SMD=0.31 (95% confidence interval CI: 0.15-0.48)). Stratified subgroup analysis and meta-regression demonstrated a significant moderating effect of co-occurring ADHD. Trials which enrolled subjects with tics and ADHD demonstrated a medium-to-large effect (SMD=0.68 (95%CI: 0.36-1.01) whereas trials that excluded subjects with ADHD demonstrated a small, non-significant benefit (SMD=0.15 (95%CI: -0.06 to 0.36)).

Conclusion:



Pharmacological treatments that are currently utilized in the treatment of tic disorders either have significant side-effects or only marginal efficacy. Available behavioral treatments are sufficient to control symptoms in a large proportion of children with TS. However, novel pharmacological treatments are needed, especially for children with tic disorders who either lack access or do not respond to behavioral treatments. Emerging pharmacological agents that have a mechanism of action on the cannabinoid system (cannabis-derivatives, FAAH-inhibitors, MAG-Lipase Inhibitors) and the dopamine system (VMAT2 inhibitors, D1/D5 antagonists) are currently being studied for Tourette syndrome.

Biosketches

Alexander Münchau

Prof. Alexander Münchau studied medicine in Hamburg and Berlin, Germany. After a formative final year clinical attachment with Dr. John Patten in Guildford, UK, he was trained in Clinical Neurology and Clinical Neurophysiology in the Neurology Department of St. Georg Hospital in Hamburg. With support from the Jung Stiftung für Wissenschaft und Forschung (Hamburg) and the Tourette Syndrome Association (USA) he spent 3 years at the National Hospital for Neurology and Neurosurgery, Queen Square, London, under the supervision of David Marsden, Niall Quinn, Kailash Bhatia, Mary Robertson and Michael Trimble sub-specialising in Movement Disorders and Neuropsychiatry. During that period, he carried out experimental neurophysiology research at the Institute of Neurology, predominantly in the Human Movement and Balance Unit, in the groups of John Rothwell, Adolfo Bronstein and Michael Gresty. From 2001 to 2013 Alexander Münchau was working in the Neurology Department of Hamburg University Hospital where he became Consultant in 2003 and Deputy Head of Department in 2005. Supported by the Volkswagenstiftung, the Deutsche Forschungsgemeinschaft (DFG; German Research Council) and European research support he set up a Movement Disorders and Motor Systems Neuroscience group with a special focus on paediatric movement disorders and the pathophysiology of paediatric and adult movement disorders. In 2013, he became head of the newly founded interdisciplinary Department of Paediatric and Adult Movement Disorders and Neuropsychiatry in the Institute of Neurogenetics at Lübeck University. A. Münchau is speaker of the Lübeck Center for Rare Diseases, founding member of the German Academy of Rare Neurological Disease, head of the Habilitation Committee of the University of Lübeck and chairman of N.E.MO., a charity for the support of clinical care and research of paediatric movement disorders. He is also founding member of the “Agentur für Überschüsse” (Agency for Surplus), a Neuroscience / Theatre science / Philosophy group addressing the implications and repercussions of movements deviating from set rules.

Peristera Paschou

Dr Paschou is an Associate Professor at the Dept of Biological Sciences at Purdue University. has established and played a leading role in several large-scale efforts aiming to understand the etiology of TS, including the “Tourette Syndrome Genetics – Southern and Eastern European Initiative” (TSGeneSEE), the Cost Action the “European Network for the Study of GTS” (a multinational initiative with 23 participating countries), and the Marie Curie Initial Training Network TS-EUROTRAIN. She also leads the genetics Work Package in the EU FP7-HEALTH project EMTICS, coordinating a large genomewide association and genomewide gene-expression study for Tourette Syndrome and she is the Chair of the ENIGMA-TS Working Group, aiming to bring together TS neuroimaging and genetic datasets from around the world towards large scale studies on brain structure, neurophysiology and the molecular underpinnings of the disorder. She has served as Chair of the European Society for the Study of Tourette Syndrome and from that position she helped establish the European Awareness Day for Tourette Syndrome and the International Meeting for Tourette Syndrome Support and Advocacy Groups.



Zeynep Tümer

Professor in applied molecular genetics

Kennedy Center, Department of Clinical Genetics, Copenhagen University Hospital, Rigshospitalet

Main research areas: Molecular disease mechanisms in monogene and complex hereditary disorders; epigenetics and imprinting.

Main research interest is to understand the underlying molecular disease mechanisms involved in various human genetic disorders, including neurodevelopmental disorders and rare congenital disorders, through investigation of cytogenetic abnormalities (using high-throughput mapping of translocations), copy number variations (using high resolution chip technologies), and sequence variations (using NGS based technologies) followed by functional studies (quantitative methodologies, tissue *in situ* hybridization techniques, stem cell studies).

Main aim of research is to apply the research results to clinical practice (applied molecular genetics).

The current projects include, but not limited to: 1) Investigation of the role of epigenetic and genetic mechanisms in Tourette syndrome and co-morbidities (ADHD, OCD, Autism); 2) underlying (epi)genetic changes in intellectual disabilities including Rett syndrome; 3 imprinting disorders; 4) copy number variation related genomic disorders; 5) congenital developmental defects including the cohesin deficiency disorder Cornelia de Lange syndrome.

Shantel Weinsheimer

Shantel Weinsheimer is a Senior Post-doc at the Institute of Biological Psychiatry, Mental Health Services, Copenhagen, Denmark. She has a PhD in Molecular Biology and Genetics from Wayne State University, Michigan, USA. She has expertise in epigenetic studies of psychiatric disorders including methylation profiling in neonatal blood spots from twins and individuals with neuropsychiatric CNVs. She has a special interest in the application of OMICS methods (epigenomics, transcriptomics, metabolomics & genomics) in psychiatric disease to discover multiple disease-causing genes and disease mechanisms.

Tanya Murphy

Dr. Tanya Murphy is the Director of the Rothman Center for Pediatric Neuropsychiatry. She is a professor at the University of South Florida with appointments in the departments of pediatrics and psychiatry and is the Vice Chair of Academic Affairs in the USF Department of Pediatrics. She holds the Maurice A. and Thelma P. Rothman Endowed Chair of Developmental Pediatrics. She actively participates in numerous professional organizations including the American Academy of Child and Adolescent Psychiatry, the National Tourette Association of America Scientific Advisory Board, the International Obsessive Compulsive Foundation Scientific/Clinical Advisory Board, and as a distinguished fellow in the American Psychiatric Association. With regard to research, Dr. Murphy has received numerous grants as a PI and Co-PI, and has extensive experience in designing and coordinating studies for pediatric clinical trials, including pediatric autoimmune neuropsychiatric disorders associated with streptococcus (PANDAS), childhood obsessive-compulsive disorder (OCD), tic disorders, anxiety disorders, autism-spectrum disorders, and adult





clinical trials of OCD and stuttering. As part of her focus on immunological factors in pediatric OCD and tics, she has participated as a PI in an NIMH-funded R01 prospective study of PANDAS and in both NARSAD and Massachusetts General Hospital funded double-blind, placebo-controlled trials of antibiotic treatment for PANDAS/Pediatric Acute Neuropsychiatric Syndrome (PANS). Furthermore, she has authored over 280 peer-reviewed papers and 30 book chapters. Dr. Murphy has been an active voice for PANDAS/PANS within the psychiatric community by presenting up to date research on the identification and pharmacological interventions which have proven effective in treating this disorder.

David Mataix-Cols

Professor Mataix-Cols is a clinical psychologist specialised in the study and care of patients with obsessive-compulsive and related disorders. He completed his PhD in 1999 (University of Barcelona). In 2000 he was awarded a Marie Curie Fellowship to conduct post-doctoral research at Imperial College London. From 2002, he was appointed lecturer at King's College London, where he eventually became a full professor in 2012. In parallel, he developed his clinical activity at the Maudsley Hospital. He is now professor of child and adolescent psychiatric science at the Karolinska Institutet, Stockholm, where he runs a program of research aimed at understanding the causes of obsessive-compulsive and related disorders across the lifespan and the development of cost-effective treatments for these conditions. From 2006-2013, he was advisor to the DSM-5 Obsessive-Compulsive and Related Disorders Workgroup. He is author of over 200 peer-reviewed publications and recipient of multiple grants and awards from the UK, US, EU, Sweden and Spain. His H-Index is 53 (ISI Web of Science) and he has appeared in the Clarivate most cited researcher list for 3 years in a row (2015-2017). He is currently associate editor of the Journal of Obsessive Compulsive and Related Disorders.

Tiago Maia

Tiago V. Maia is Associate Professor at the Faculty of Medicine of the University of Lisbon (Portugal). Before moving to Portugal, he was Assistant Professor of Clinical Neurobiology (in Psychiatry) at the Department of Psychiatry of Columbia University (USA). Research in his laboratory uses computational modeling, functional magnetic resonance imaging, and behavioral experiments to investigate Tourette syndrome, obsessive-compulsive disorder, and attention-deficit/hyperactivity disorder. This clinical and translational research is complemented by research in healthy humans on the cognitive processes and brain structures that are disrupted in these disorders.

Izhar Bar-Gad

Biosketch not available.

Elena Cravedi

I trained as child neuropsychiatric at the Pediatric Neurology and Psychiatry Unit, Children's Hospital A. Meyer-University of Florence, attending the general neuropsychiatric ward and



acquiring a good experience in the neuropsychological evaluation of children affected by neurodevelopment disorders. I integrated this experience with a stage as researcher and clinical observer at Department of Child and Adolescent Psychiatry in Pitié-Salpêtrière Hospital.

Camilla Groth

MD. PhD Camilla Groth has performed a large follow-up study of children and adolescent with Tourette syndrome. She defended her PhD thesis in 2017 from the University of Copenhagen and Herlev University Hospital. Her main interest is the clinically development of tics and comorbidity. Furthermore, she did a cross sectional study on coexisting psychopathologies, executive function, education, quality of life and use of addictive agents.

She is part of two Cochrane reviews of the benefits and harms of methylphenidate in children with ADHD.

She has published 24 peer-reviewed publications, 6 as first author. She became cand. Med in 2007 and started specialist training in child and adolescent psychiatry, continued with the PhD study and is currently during specialist training as pediatrician at Herlev University Hospital.

Kirsten Müller-Vahl

Dr. Kirsten Müller-Vahl, M.D., is a Professor of Psychiatry at the Department of Psychiatry, Socialpsychiatry and Psychotherapy at the Hannover Medical School (MHH), Germany. She is a specialist in both neurology and adult psychiatry. Since 1995, she is the head of the Tourette Syndrome outpatient department at the MHH. From 1997 to 2003 she was a grant holder of the German government (Dorothea-Erxleben-Stipendium) for scientific research related to Tourette syndrome. From 2012-2016, she was the vice president of the European Society of the study of Tourette syndrome (ESSTS). Since 1998 she is a member and 2. Chairwoman of the national German Association for Cannabinoid Medicines (ACM). She is a founding member (2000) of the International Association for Cannabinoid Medicines (IACM), has been the 1. Chairwoman of the IACM (2007-2009) and is presently the Vice President of the IACM (since 2015). Since 2016 she is a member of the committee of experts for narcotic drugs at the federal opium bureau of the Federal Institute for Drugs and Medical Devices (BfArM) in Germany.

Her scientific work related to Tourette syndrome included several clinical studies as well as controlled trials on the effects of different types of treatment on tics including cannabis-based medicines. In 2015, the German Research Foundation (DFG) approved a large multicentre randomized controlled trial for funding investigating the efficacy and safety of nabiximols (Sativex®) in the treatment of adult patients with TS (CANNA-TICS).

At the 9th IACM Conference on Cannabinoids in Medicine 2017 she received the IACM Award 2017 for Clinical Research for her special achievements regarding the re-introduction of cannabis and cannabinoids as medicine.

Dr. Müller-Vahl has published over 100 scientific articles, is the author of several book chapters and the leading German textbook on Tourette syndrome.



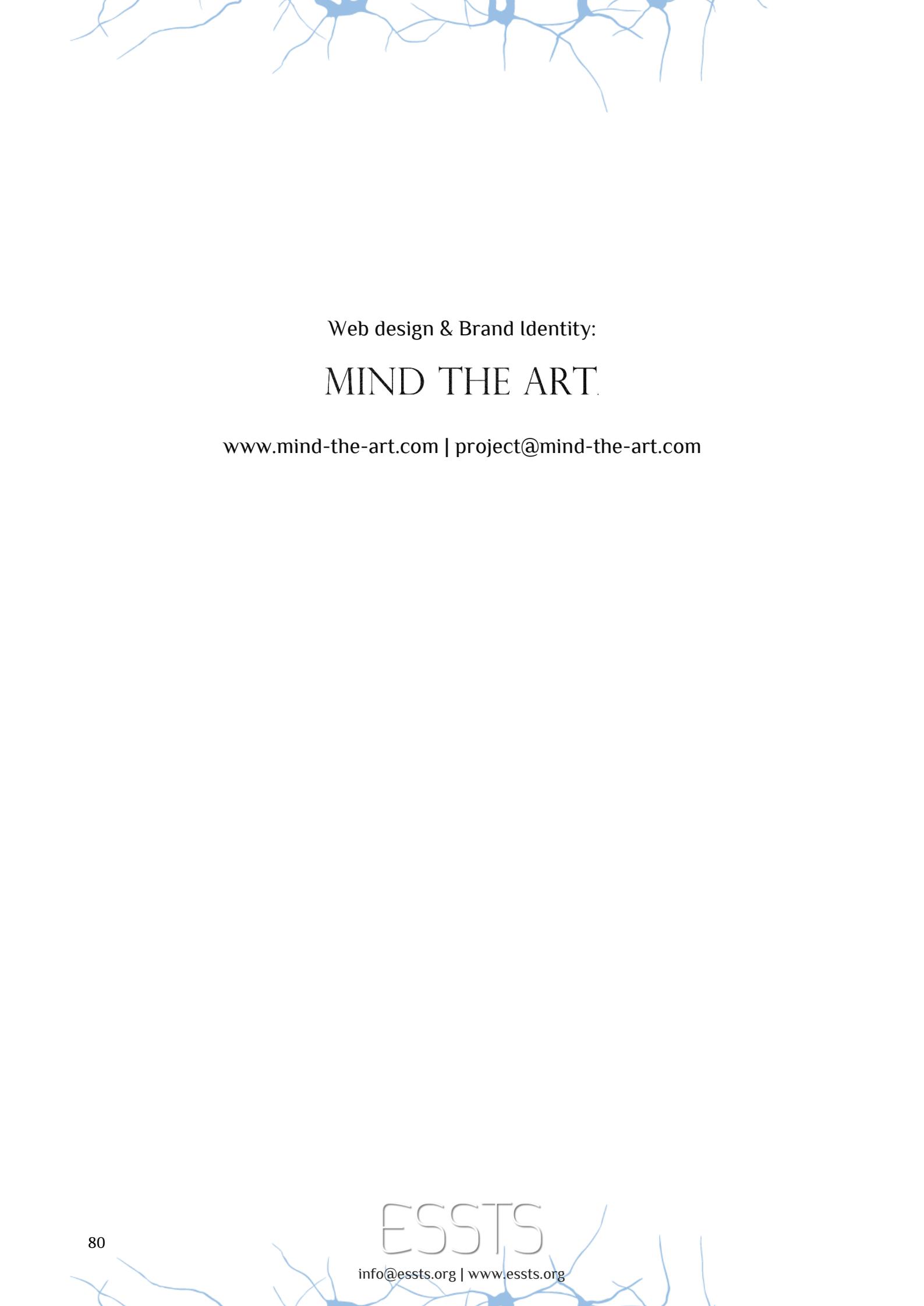
Tom Foltynie

Professor Tom Foltynie is Consultant Neurologist at the Sobell Department of Motor Neuroscience at the UCL Institute of Neurology and National Hospital for Neurology and Neurosurgery, Queen Square, London. He completed Neurology training in Cambridge, UK. He is responsible for Movement disorder patients, particularly PD patients undergoing advanced treatments such as Deep Brain Stimulation. He is chief investigator for a series of trials of potential neurorestorative treatments for PD, as well as trials of Deep Brain stimulation as a treatment for the cognitive problems associated with advanced PD. Prof Foltynie is also the lead for trials of Deep Brain Stimulation for the treatment of patients with severe Tourette syndrome.

Michael Bloch

My research has focused on improving the evidence base for child psychiatric conditions and developing better treatments and prognostic information for children and families dealing with mental illness. My research approach has focused primarily on utilizing meta-analysis, clinical trials and neuroimaging to improve our understanding and treatment of a variety of conditions. In recent years, that research has begun to focus on utilizing ketamine as a potential treatment for mood and anxiety disorders and using meta-analysis to improve treatment and prognosis in Major Depression. I have previously successfully conducted ketamine studies in OCD and social anxiety disorder. Reducing morbidity and mortality associated with Major Depression is an increasing focus of my current research. I have successfully mentored several promising emerging young scientists like Dr. Dwyer, including publishing papers first-authored by 22 different mentees.





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