

Hannover

12th European Conference on Tourette Syndrome and Tic Disorders

ABSTRACTS

Hannover | May 15-17 2019

**12th European Conference on Tourette Syndrome and
Tic Disorders**

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



Hannover, Germany | May 15 - 17, 2019

European Society for the Study of Tourette Syndrome



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.



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ABIDE
THERAPEUTICS

EMALEX
biosciences

THERAPIX
BIOSCIENCES

WAYLAND

PROGRAMME

NOTE:

All sessions and lectures will take place in the **main conference room**.

(for the 3 parallel meetings, May 15th 13:00-16:00, this room will be divided into 3 smaller rooms).

The 3 following sessions on May 15th will take place in another room called **"Studio"**:

- 1) 8:00-10:00, fMRI TIC Genetics
- 2) 10:00-15:30, EMTICS session
- 3) 16:00-17:00, ESSTS guidelines meeting



May 15

10:00-15:30	EMTICS session (open to all interested parties) Organizers: -Pieter Hoekstra -Davide Martino
10:00-10:20	Update of database, explanation of codebook, explanation of shared folder, overview of paper proposals, how to submit a paper, explanation of co authorships Andrea Dietrich & Pieter Hoekstra
10:20-10:40	Common data analytic strategies and considerations Andrea Dietrich & Pieter Hoekstra
10:40-11:00	Progress of papers of Martina Haas & colleagues (initial findings, progress, difficulties, common issues)
11:00-11:30	Progress of genetic papers (initial findings, progress, difficulties, common issues) Fotis Tsetsos
11:30-11:50	Progress of papers of Jaana Schnell & colleagues (initial findings, progress, difficulties, common issues)
11:50-12:10	Progress of papers of Zsanett Tarnok & colleagues (initial findings, progress, difficulties, common issues)
12:10-13:00	Lunch break




13:00-13:20	Progress of papers of Tami Steinberg & Noa Benaroya & colleagues (initial findings, progress, difficulties, common issues)
13:20-13:40	Progress of papers of Matan Nahon & colleagues (initial findings, progress, difficulties, common issues)
13:40-14:00	Progress of papers of Roberta Creti & colleagues (initial findings, progress, difficulties, common issues)
14:00-14:20	Progress of papers of Thaira Openneer and Andrea Dietrich & colleagues (initial findings, progress, difficulties, common issues)
14:20-14:40	Progress of papers of Ute-Christiane Meier & colleagues (initial findings, progress, difficulties, common issues)
14:40-15:00	Progress of papers of Davide Martino & Anette Schrag & colleagues (initial findings, progress, difficulties, common issues)
15:00-15:20	Progress of papers of Francesco Cardona & colleagues (initial findings, progress, difficulties, common issues)
15:20-15:30	Wrap-up and plans for follow-up

13:00-16:00	Behavioural therapy for tics: Work in progress (English)	HRT workshop (German language)	Patient Advocacy session
	<p>13:00-13:20 Psycho-education -Necessary elements in psycho-education, Zsanett Tárnok</p> <p>13:20-14:20 Improving tic treatment and quality of life -Inhibitory learning and how to apply intensive ERP-20 mins, Cara Verdellen -Tackle your Tics -20 mins, Annet Heijerman -ACT-based behavioral therapy for tics-20 mins, Sharon Zimmerman</p> <p>14:20-14:40 Coffee break</p> <p>14:40-15:40 Additional and online interventions-Function based interventions - back to basics -20 mins, Jolande van de Griendt</p>	<p>Speakers: -Katrin Woitecki -Ewgeni Jakubovski</p>	<p>Organizer: Laura Beljaars</p>




	<p>-Online coaching-20 mins, Paula Viefhaus iCBiT-20 mins, Katja Kunert</p> <p>15:40-16:00 Case discussion and questions</p>		
16:00-17:00	<p>ESSTS guidelines session (open to all interested parties)</p> <ul style="list-style-type: none"> - Assessment: Danielle Cath - Behavioural therapy: Cara Verdellen - Pharmacotherapy: Veit Roessner - DBS: Kirsten Müller-Vahl 		
17:00-19:00	<p>Opening ceremony and keynote lectures</p> <p>-A few words from the organizers & ESSTS chair</p> <p>-Guitar solo by Michael Seubert</p> <p>-Lectures: Nature and control of explosive outbursts - an update Julie Leclerc (Chair: Andreas Hartmann)</p>		

	<p>Interoception, social stimulation and inhibition: Interacting brain mechanisms influencing the expression of tics</p> <p><u>Hugo Critchley</u> (Chair: Kirsten Müller-Vahl)</p>
<p>19:00</p> 	<p>Welcome reception at the Crowne Plaza Hotel</p>




May 16

Time	Session	Topics	Speaker
Pack your running shoes! 7:00 Morning run at Eilenriede forest. (600m from Crowne Plaza Hotel)			
9:00-9:45	Lecture	Genetics of TS for non-geneticists	Christel Depienne (Chair: Andreas Hartmann)
9:45-10:30	Lecture	Pathophysiology of TS for non-pathophysiologists	Yulia Worbe (Chair: Christos Ganos)
10:30-11:15	Lecture	Refractory TS	Davide Martino (Chair: Renata Rizzo)
11:15-11:35	Coffee break		
11:35-12:30	EMTICS lecture	Is exposure to streptococci related to onset or exacerbations of tics? Results from the EMTICS study	Pieter Hoekstra

		<p>Clinical precursors of tic onset. An EMTICS study</p>	<p>Andrea Dietrich</p>
		<p>The Premonitory Urge for Tics Scale in a large sample of children and adolescents: Psychometric properties in a developmental context. An EMTICS study</p>	<p>Thaira Openneer</p>
		<p>YGTSS: a critical look at the psychometric quality of the gold standard based on EMTICS data</p>	<p>Martina Haas</p>
		<p>Association between hypovitaminosis D and comorbid attention-deficit hyperactivity-disorder in patients with chronic tic-disorders: A large pan-European cross-sectional study</p>	<p>Ute Meier</p>
		<p>Developmental milestones in children with tics</p>	<p>Tamar Steinberg</p>
		<p>Discussion</p>	

12:30-13:15	Guided e-poster tours (parallel)	Poster tours 1 - 5	For Authors: see abstracts
13:15-14:00	Lunch break		
14:00-15:00	Keynote lecture	New AAN guidelines for the treatment of TS	Tamara Pringsheim (Chair: Davide Martino)
15:00-16:00	Lecture	How to dismantle the circle of tension and tics?	Julie Leclerc (Chair: Yulia Worbe)
16:00-16:30	Coffee break	+ discussion with poster (screens) authors	
16:30-18:00	Oral presentations from submitted abstracts	<p>Impulsivity in Tourette disorder: neuronal correlates and medications effects</p> <p>Characteristics of different clinical trajectories of tics during adolescence: a prospective follow-up study</p>	Cyril Atkinson-Clement Camilla Groth

		<p>Executive functioning in children with Tourette syndrome and attention-deficit/hyperactivity disorder: cross-disorder or unique impairments?</p> <p>Resting state functional connectivity differences in pediatric patients with Tourette Syndrome and Obsessive-Compulsive Disorder</p> <p>Genome-wide association study of Tourette investigates the genetic determinants of Tourette and implicates neuronal and synaptic processes</p> <p>Alexithymia and interoception in children with Tourette syndrome: A clinical audit</p>	<p>Andrea Dietrich</p> <p>Sankalp Tikoo</p> <p>Fotis Tsetsos</p> <p>Maria Hadji-Michael</p> <p>(Chairs: D. Cath, K. Müller-Vahl)</p>
18:00-19:00	GENERAL ASSEMBLY MEETING		
From 20:00	Congress DINNER at Hugo's		



May 17

Time	Session	Topics	Speaker
<p>Pack your running shoes!</p> <p>7:00</p> <p>Morning run at Eilenriede forest. (600m from Crowne Plaza Hotel)</p> 			
9:00-9:45	Keynote lecture	Functional movement disorders	<u>Selma Aybeck</u> (Chair: A. Hartmann)
9:45-11:00	Podium discussion including discussion with the audience	How to differentiate tics and functional tic-like movements Introduction with patient videos	Moderator: Kirsten Müller-Vahl Discussants: D. Cath Ch. Ganos T. Hedderly S. Aybeck J. Stern R. Rizzo
	Oral presentation from submitted abstracts	Tic-like attacks and functional neurological movements: CBT with external attention focusing	<u>Sally Robinson</u>

11:00-11:30	Coffee break	+ discussion with poster (screens) authors	
11:30-12:30	Controversy: Pro/con Discussion with the audience followed by a poll	<p>Is it time to rename Tourette's?</p> <div data-bbox="476 371 759 660">  </div> <div data-bbox="476 660 764 810"> <p>We are interested in your opinion, please vote here!</p> </div>	<p>Moderator: Andrea Cavanna Pro: Kirsten Müller-Vahl Con: Andreas Hartmann Discussants: Sven Rüger Laura Beljaars</p>
	Oral presentation from submitted abstracts	Tic Disorders revisited: Introduction of the term "Tic Spectrum Disorders"	<p><u>Ewgeni Jakubovski</u></p>
12:30-13:30	Lunch break		
13:30-14:30	Lecture	Best papers of last year! -> Where is the field headed?	<u>Kevin Black</u>

<p>14:30-16:00</p>	<p>Oral presentations from submitted abstracts</p>	<p>Cognitive tics in Gilles de la Tourette syndrome - phenomenology and clinical associations</p> <p>The impact of a cognitive-physiological therapy on motor planning and execution in Tourette syndrome patients</p> <p>Tackle your Tics: feasibility of a brief, intensive group-based exposure therapy programme for children with tic disorders</p> <p>Randomized double-blind controlled trial of thalamic versus GPi stimulation in patients with Gilles de la Tourette Syndrome</p>	<p>Anna Dunalska</p> <p>Simon Morand-Beaulieu</p> <p>A.P. Heijerman</p> <p>Kirsten Müller-Vahl Natalia Szejko</p>
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		<p>Pain and tics: a daily experience – is there more opportunity in the multi-disciplinary team for physiotherapy?</p> <p>Missed diagnosis of ADHD in children referred to a Tic Disorder Clinic</p>	<p>Seonaid Anderson</p> <p>Idura N.Hisham</p> <p>(Chairs: Danielle Cath, Kirsten Müller-Vahl)</p>
16:00-16:30	Coffee break		
16:30-17:30	CLINICAL ROUNDS		<p>Co-Chairs: Tammy Hedderly, Jeremy Stern</p>
17:30	PRIZES & AWARDS - CLOSING CEREMONY		



Survey time!

-Is it time to rename Tourette's?

We are interested in your opinion; please vote here right after the debate! (11:30 on May 17)



-What about Best poster presentation & Best oral presentation from submitted abstracts?
Please vote here!



Note: Online voting opens at 9:00 on May 16 and closes at 16:30 on May 17.

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INVITED SPEAKER

Interoception, social stimulation and inhibition: Interacting brain mechanisms influencing the expression of tics

Hugo D Critchley^{1,2,4} and Charlotte L Rae(s)^{2,3}

Brighton and Sussex Medical School, 2 Sackler Centre for Consciousness Science

³School of Psychology, University of Sussex

⁴Sussex Partnership NHS Foundation Trust Sussex, UK

Background: Interoception describes how the brain and mind sense the internal state of the body. Through interoceptive signaling, changes in bodily arousal underpin emotional and motivational feelings, including social anxiety, compulsions, and the premonitory sensations that occur before tics. Within the brain, interoceptive signals are translated into feelings within a cortical region called the insula. We undertook a research programme involving people with and without Tourette Syndrome, to examine the impact of interoception on the control of actions, and to identify brain mechanisms by which emotional and social simulation can trigger or intensify the experience of tics.

Methods: We related objective (task performance) and subjective measures of interoceptive sensitivity to individual differences in the capacity to inhibit actions, quantified using both experimental tasks and questionnaires. Next, using functional neuroimaging, we measured differences between people with and without Tourette Syndrome in brain responses to social (face) stimuli, and tested how these differences related to the symptoms of Tourette Syndrome.

Results and Conclusions: We observed that low-level interoceptive signals of bodily arousal help inhibit motor responses in people without tics. Moreover, people who are objectively more sensitive to internal bodily signals report lower impulsivity. We also observed that people with Tourette Syndrome show a noisier representation of inner bodily state, indicated by a mismatch between objective and subjective measures of interoception compared to people without tics. Here, heightened subjective sensitivity to internal bodily signals predicts the severity of tics and premonitory sensations. In brain imaging studies, we showed that insula cortex is hyperreactive to social stimuli in people with Tourette Syndrome, such that the neural cross-talk with motor regions increases the severity of premonitory sensations and tic symptoms. Together, these studies highlight how the representation of the inner state of the body, and its modulation by the social environment, is integral to the expression and control of tics. These findings fit with a novel “Bayesian” framework for understanding Tourette Syndrome, which may ultimately guide effective treatment strategies.

Pathophysiology of TS for non-pathophysiologists

Yulia Wrobe

Department of Physiology, Sorbonne University, Paris, France

The concepts on pathophysiology of Tourette syndrome have been constantly evolving from clinical description by George Gilles de la Tourette. This syndrome has been described as disorder of neurodevelopmental origin, resulting from the imbalance of excitatory and inhibitory mechanisms within neuronal networks or to excess of dopamine within basal ganglia structures, as well as related to more widespread cognitive abnormalities and default of social interactions. In this lecture I would review core concepts and new theoretical frameworks on pathophysiology of TS.



Is exposure to streptococci related to onset or exacerbations of tics?

Results from the EMTICS study.

Pieter J. Hoekstra¹ & EMTICS collaborative group

¹University of Groningen, University Medical Center Groningen, Department of Child and Adolescent Psychiatry, Groningen, Netherlands

Background: A specific interest in a role for exposure to group A streptococcus (GAS) has been drawn by the description in 1998 of Paediatric Autoimmune Neuropsychiatric Disorders Associated with Streptococcal Infections (PANDAS), a putatively autoimmune syndrome manifesting with obsessive–compulsive symptoms, tics, emotional lability, anxiety and regressive behaviour triggered by this pathogen. However, the existing evidence for this relies primarily on small prospective or larger retrospective population-based studies, and is therefore still inconclusive.

Methods: The EMTICS study, a longitudinal observational European multicentre study involving 16 clinical centres investigated the association of GAS exposure with the onset and course of tics and/or obsessive-compulsive symptoms through the prospective observation of at-risk individuals (ONSET cohort: 260 children aged 3-10 years who are tic-free at study entry and have a first-degree relative with a chronic tic disorder) and affected individuals (COURSE cohort: 715 youth aged 3-16 years with a tic disorder)

Results and Conclusions: There is no indication that new GAS exposures are temporally associated with the onset of tics. While new GAS exposures were present in 18.8% of visits in which onset of tics had been documented, this was the case in 24.9% of ONSET study visits in which no tic onsets were notified. There was also no indication that new GAS exposures are temporally associated with tic exacerbations: 14.1% of tic exacerbations were preceded by a recent new GAS exposure (i.e. a new GAS exposure occurring within the past 4 months), a percentage which was not significantly higher than the 13.0% of visits without a tic exacerbation that were preceded by a recent new GAS exposure.

Thus, the EMTICS study indicates that the co-occurrence of tic exacerbations and recent new GAS exposures is most likely due to chance. Our findings have important clinical implications: our findings suggest that assessing recent GAS exposure in children with tic disorders is not clinically meaningful.

New AAN guidelines on the treatment of tics in people with Tourette syndrome and chronic tic disorders

Tamara Pringsheim¹

¹ Department of Clinical Neuroscience, University of Calgary, Canada

Background: The purpose of the AAN guidelines was to systematically evaluate the efficacy of treatments for tics and the risks associated with their use, and to make recommendations on when clinicians and patients should treat tics and how clinicians and patients should choose between evidence-based treatment options.

Methods: In May 2016, a multidisciplinary panel consisting of 9 physicians, 2 psychologists, and 2 patient representatives was recruited to develop this guideline. This guideline follows the methodologies outlined in the 2011 edition of the AAN's guideline development process manual. We included systematic reviews and randomized controlled trials on the treatment of tics that included at least 20 participants (10 participants if a crossover trial), except for neurostimulation trials, for which no minimum sample size was required. To obtain additional information on drug safety, we included cohort studies or case series that specifically evaluated adverse drug effects in individuals with tics. The multidisciplinary panel developed practice recommendations, integrating findings from the systematic review and following an Institute of Medicine-compliant process to ensure transparency and patient engagement. Recommendations were supported by structured rationales, integrating evidence from the systematic review, related evidence, principles of care, and inferences from evidence.

Results and Conclusions: The AAN Tourette guideline is under embargo until May 6th 2019, therefore no further information can be given at this point.

Clinical precursors of tic onset. An EMTICS study

Andrea Dietrich¹, **Thäira J.C. Openneer¹**, **Chaim Huyser^{2,3}**, **Davide Martino⁴**, **Anette Schrag⁵**, **Pieter J. Hoekstra¹** and the EMTICS collaborative group

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Background: Children with Tourette Syndrome (TS) show a high level of comorbidity, particularly with attention deficit/hyperactivity disorder (ADHD) and obsessive-compulsive disorder (OCD). While the occurrence of subtle premorbid symptoms has been suggested in various neuropsychiatric disorders, the presence of clinical precursors that may exist before the marked onset of TS is unknown. This prospective study aimed to find clinical precursors of tic onset by comparing a range of clinical characteristics assessed at baseline of children and adolescents with a tic onset to those without a tic onset.

Methods: A sample of 260 3-10-year-old children, who are first-degree relatives (siblings) of patients with TS, participated in the longitudinal European Multicenter Tics in Children Study (EMTICS) study, of whom 61 developed tic onset over the course of three years. In this study, we compared 105 children aged 8 years and older without a tic onset on a range of clinical measures assessed at baseline to the children with a tic onset. We used the least absolute shrinkage and selection operator (LASSO) method, a penalized logistic regression approach. We conducted sensitivity analyses in an age- and sex-matched subsample.

Results: We observed several baseline precursors related to tic onset. Participants with a tic onset more frequently were male, had higher baseline severity of compulsions, hyperactivity-impulsivity, externalizing symptoms, and autism spectrum disorder symptoms, and also a lower quality of life total score than those without a tic onset. Severity of compulsions was a female-specific predictor related to tic onset, whereas severity of autism spectrum disorder symptoms was a male-specific predictor. The sensitivity analyses largely confirmed the results.

Conclusions: This study supports the presence of clinical precursors related to tic onset.

The Premonitory Urge for Tics Scale in a large sample of children and adolescents: Psychometric properties in a developmental context. An EMTICS study

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Background: Premonitory urges are uncomfortable physical sensations preceding tics that occur in most individuals with a chronic tic disorder. The Premonitory Urge for Tics Scale (PUTS) is the most frequently used self-report measure to assess the severity of premonitory urges. We aimed to evaluate the psychometric properties of the PUTS in the largest sample size to date ($n=656$), in children aged 3-16 years, from the baseline measurement of the longitudinal European Multicenter Tics in Children Study (EMTICS).

Methods: Our psychometric evaluation was done in three age-groups: children aged 3-7 years ($n=103$), children between 8-10 years ($n=253$), and children aged 11-16 years ($n=300$).

Results and Conclusions: The PUTS exhibited good internal reliability in children and adolescents, also under the age of 10, which is younger than previously thought. We observed significant but small correlations between severity of urges and severity of tics and obsessive-compulsive symptoms, and between severity of urges and ratings of attention-deficit/hyperactivity disorder and internalizing and externalizing behaviors, however, only in children of 8-10 years. Consistent with previous results, the 10th item of the PUTS correlated less with the rest of the scale compared to the other items and therefore should not be used as part of the questionnaire. We found a two-factor structure of the PUTS in children of 11 years and older, distinguishing between sensory phenomena related to tics, and mental phenomena as often found in obsessive-compulsive disorder. The age-related differences observed in this study may indicate the need for the development of an age-specific questionnaire to assess premonitory urges.

YGTS: A critical look at the psychometric quality of the gold standard based on EMTICS data

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Background: The Yale Global Tic Severity Scale (YGTS) is a clinician-rated instrument considered as the gold standard for assessing tics. Previous psychometric investigations of the YGTS are limited by methods used or small sample sizes resulting in contradictory conclusions. The aim of this study was to use a large sample and appropriate methods to investigate: (1) internal consistency, (2) factorial structure, and (3) convergent and discriminant validity of the YGTS.

Methods: We used the baseline data of the European Multicentre Tics in Children Study (EMTICS) consisting of children and adolescents (N=715) with the established diagnosis of a chronic tic disorder. As an indicator for internal consistency, McDonald's omega (Ω) was calculated. Factorial structure of the previously assumed factor model was investigated using Confirmatory Factor Analysis (CFA). To investigate convergent and discriminant validity we calculated Spearman rank correlations (ρ) between each of the YGTS sum scores (YGTS total tic score (TTS), YGTS motor and phonic tic score) and other assessments of tic severity (Clinical Global Impression Scale - Severity for tics, CGI-S (tics)) as well as assessments for attention deficit hyperactivity disorder (Swanson, Nolan, and Pelham, version IV, SNAP-IV) and obsessive-compulsive disorder (Children's Yale-Brown Obsessive Compulsive Scale, CY-BOCS).

Results: Acceptable internal consistency was identified for the YGTS-TTS ($\Omega=.57$), YGTS motor tic score ($\Omega=.73$), and YGTS phonic tic score ($\Omega=.67$). CFA yielded fit indices of root mean square error of approximation (RMSEA)=0.09 [0.08; 1.00], comparative fit index (CFI)=0.90, and Tucker-Lewis Index (TLI)=0.87 demonstrating a marginal model fit. In addition, we identified correlated errors. Correlations between YGTS sum scores (YGTS-TTS, YGTS motor and phonic tic scores) and CGI-S (tics) ranged from $p=.50$ to $p=.64$, while correlations between YGTS sum scores (YGTS-TTS, YGTS motor and phonic tic score) and SNAP-IV and CY-BOCS, respectively, were between $p=.21$ and $p=.26$.

Conclusions: Our results confirm sufficiently good convergent and discriminant validity of the YGTS. However, based on our findings, internal consistency is merely acceptable, but not excellent as previously assumed. The factor model yielded results just above the threshold for acceptable fit and only when applying very liberal guidelines for fit indices. Our finding of correlated errors indicates the need to further improve the YGTS for example by reducing the complexity of the scale.

Developmental milestones in children with tics

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Background: Tics are common neuropsychiatric phenomena in children and youth, and may appear around the age of 4-6 years. In many cases developmental disorders are apparent before tics start, specifically attention problems speech and language delays and developmental motor coordination disorders.

Comorbidities such as are attention deficit hyperactivity disorder, obsessive-compulsive behaviors, autistic spectrum disorders, specific learning disorder, are very common in children with tics. It was speculated the genes involved in brain development are responsible both for the development of tics and comorbidities and of the developmental delays.

In this study we would like to further investigate the early developmental milestones of patients with tics and their effect on later tics and comorbidities.

Methods: Our study sample consisted of 715 3-to-16 year old children and adolescents presenting with a chronic tic disorder. All were participants in the baseline measurement of the longitudinal European Multicenter Tics in Children Study (EMTICS). Children and adolescents were asked to complete questionnaires on premonitory urges, tic history and severity, and on symptoms of ADHD, ODD, ASD, and internalizing and externalizing disorders. In the baseline visit medical history of each participant was obtained including family history and developmental milestones. A clinical diagnosis of a chronic tic disorder, OCD, and/or ADHD was made according to DSM-IV-TR criteria.

Results: The study population included 549 males and 166 females, between the ages of 3 y and 16 y. 5.7 % of them were attending a special education school, and 19.5 % reported any cognitive impairment or learning difficulty. 52.8% of the patients had delayed speech with either delayed first words or delayed composition of sentences as defined by the Denver II developmental screen test. Mean ages for Motor milestones were not delayed on average. Pearson correlations were used to look at correlations between developmental milestones and tic measures; delayed walking was correlated with total tic severity and impairment as measured by the Yale Global Tic Severity Scale (YGTSS). Delayed speech was significantly correlated vocal tics and with premonitory urges. Both motor and speech delays were significantly correlated with OCD as measured by CY BOCS and with behavioral problems and ADHD according to the SDQ.

Conclusions: On average the study cohort showed prominent delays in language milestones, known to be correlated with cognitive and mental disorders. In addition, the prevalence of learning disorders in TD patients of this cohort was high. Tic disorders and their common comorbidities appear to be related to developmental delays in accordance with the view that they are prototypical examples of developmental psychopathology.



Impulsivity in Tourette disorder: neuronal correlates and medications effects

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Background: Little is known about the different types of impulsivity in Tourette disorder (TD). The present study aimed to assess action and choice impulsivity as well as implicated neuronal networks.

Methods: We recruited 62 adults patients with TD (37 unmedicated and 25 medicated) and 33 controls. Action impulsivity was assessed using the 4-choice task (4CSRTT), where participants responded on a cue as fast as possible; proportion of premature responses were considered as main outcome. Choice impulsivity was assessed using the delay discounting task (DDT), where participants choose between a small immediate reward and a higher delayed reward. Preference of immediate reward was an indicator of impulsive choice. We performed whole brain voxel-based and resting state functional connectivity (rs-fMRI) analyses on main tasks outcomes.

Results: In the 4CSRTT, patients with TD had a higher proportion of premature responses and this difference was driven by unmedicated patients with TD. In this group of patients, a higher proportion of premature responses was associated with a higher grey matter signal in the accumbens nucleus, the anterior cingulate gyrus and the orbitofrontal cortex. Rs-fMRI connectivity analysis showed increased connectivity between orbito-frontal cortex and caudate, as well as higher connectivity among associative cortical regions. In the DDT all patients, independently of medication status, preferred immediate small rewards. These were no correlation with structural cerebral changes. However, decreased connectivity between the orbito-frontal cortex and subthalamic nucleus correlated with preference for immediate reward, as well as hypoconnectivity within the sensori-motor, mostly supplementary motor area, and inferior frontal gyrus.

Conclusions: (i) TD patients showed a propensity to a cognitive impulsivity; (ii) the different types of cognitive impulsivity were underpinned by distinct but partially overlapping structural and / or functional networks.



Characteristics of different clinical trajectories of tics during adolescence: a prospective follow-up study

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Background: Tourette syndrome (TS) is a childhood onset neurodevelopmental disorder characterized by frequent comorbidities and by improvement of both tics and comorbidities during adolescence. However, the clinical presentation is heterogeneous and varies significantly from few tics without comorbidities to severe tics and disabling comorbidities and coexisting psychopathologies.

Prognostic prediction for the clinical development of tics and comorbidities is difficult. In a prospective follow-up study we have explored clinical childhood predictors for the clinical course of tics and we concluded that the strongest predictors of high tic scores, present OCD or ADHD diagnoses in early adulthood were the corresponding tic, OCD and ADHD severity in childhood. However, in a clinical perspective the subgroups continuing have a high tic score, the increasers and the decreasers of tics into early adulthood are not well characterized. Here we elucidate the characteristics of different clinical trajectories of TS through adolescence to improve prognostic prediction.

Methods: The clinical cohort was recruited at the Danish National Tourette Clinic at Herlev University Hospital. Data was collected by uniform clinical examinations at baseline (T1, 2005-07) (n=314, age range 5-19 years) and 6 years later at follow-up (T2, 2011-13) (n=227, age range 11-26) to examine development in tics-expression and comorbidities. Tics were assessed with the Yale Global Tic Severity Scale Score (YGTSS). According to the change in YGTSS score the participants were divided in High Persisters (HP) (minimum 30 points at baseline and follow-up, equivalent to moderate severity), Increasers (In) (increased ≥ 15 points), Decreasers (De) (decreased ≤ 15 points) and Low Persisters (LP) (≤ 10 points at baseline and follow-up equivalent to minimal severity). These sub-groups were assessed for comorbidities and examined for possible associations between the tic symptomatology and related clinical factors.

Results: High Persisters (n=23) were characterized by higher frequency of comorbidities at both baseline and at follow up (ADHD T1: 48%, T2: 61%; OCD T1: 65%, T2: 44%) than the other subgroups as well as an increase in ADHD frequency. Increasers (n=21) differed from Decreasers (n=54) by having more frequent comorbidities at follow up (ADHD T1; In: 29%, De: 54%, T2; In: 48%, De: 29%; OCD T1; In: 33%, De: 41%, T2; In: 48%, De: 13%). Low Persisters

(n=22) had low comorbidity both at baseline and at follow-up (ADHD T1: 29%, T2: 14%; OCD T1: 36%, T2: 18%).

Conclusions: We have elucidated characteristics of different clinical trajectories of TS through adolescence in a large clinical cohort. The High Persisters are characterized with frequent and persistent comorbidities. The Increasers not only increase in Global Tic Score but also in frequency of comorbidities.

These findings are directly applicable to other clinical TS populations and along with the clinical predictors they may assist in providing guidance as to the expected clinical course, to early interventions strategies and implementing preventive measures for the children at highest risk. As pharmacological and behavioural treatment effects were not included this study is indicative of the clinical course and not necessarily the natural course.



Executive functioning in children with Tourette syndrome and attention-deficit/hyperactivity disorder: cross-disorder or unique impairments?

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Background: Findings of executive functioning deficits in Tourette syndrome (TS) have been largely inconsistent, possibly due to small sample sizes and comorbid attention-deficit/ hyperactivity disorder (ADHD) not having been taken into account.

Methods: We aimed to examine several areas of executive functioning (response inhibition, attentional flexibility, cognitive control, and working memory) and psychomotor speed in 174 8-to-12-year-old children with TS (n=34 without [TS-ADHD] and n=26 with comorbid ADHD [TS+ADHD]), ADHD without tics (n=54), and healthy controls (n=60). We compared executive functioning measures between these groups and related these to tic and ADHD severity across the whole sample.

Results: Children with TS+ADHD, but not TS-ADHD made more errors on the cognitive control task than healthy children, while TS-ADHD had a slower psychomotor speed compared to healthy controls. The ADHD group showed impairment in cognitive control and working memory versus healthy controls. Moreover, higher ADHD severity was associated with poorer cognitive control and working memory across all groups. However, there was no relation between any of the executive functioning measures and tic severity.

Conclusions: We found little evidence for executive function impairments inherent to TS. Executive function problems appear to manifest predominantly in relation to ADHD symptomatology, with both cross-disorder and unique features of neuropsychological functioning when cross-comparing children with TS and ADHD.

Resting state functional connectivity differences in pediatric patients with Tourette Syndrome and Obsessive-Compulsive Disorder

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Background: TS is a neurodevelopmental disorder that is frequently associated with psychiatric comorbidities and specifically with OCD. Several clinical features seem to distinguish classic OCD from the “tic-related” one. Although functional connectivity (FC) has been investigated in both disorders separately, no study evaluated to date the neural pathway differences in pediatric patients with either TS or OCD.

Methods: 30 TS, 10 OCD, and 11 Healthy controls (HC), aged 8-14 years, underwent 3T resting-state fMRI. Yale Global Tic Severity Scale (YTGSS) and Children Yale-Brown Obsessive-Compulsive Scale (CYBOCS) assessed tic severity and OCD symptoms, respectively. fMRI data were processed by using FSL. After image pre-processing, independent component analysis decomposed the data into 30 spatial components. Seven networks of interest were selected, i.e. Basal Ganglia (BG), Cerebellum (CB), Frontoparietal (FP), Default-Mode (DMN), Orbitofrontal (OBF), Salience (SN), Sensorimotor Network (SMN), to investigate between-group differences in FC and clinical correlations ($p < 0.05$, FDR corrected). Customized children T1 template was used for analysis.

Results: Patients with TS showed higher FC in the BG, CB, DMN and SMN and lower FC in FP and SN if compared with HS. Patients with OCD showed higher FC in the CB, FP, SN and SMN than HS and higher FC in CB and FP than TS subjects. Differences between OCD and TS whole group persisted even when splitting the TS sample into pure-TS (CYBOCS score ≤ 7 , $n=16$) and TS plus OCD (CYBOCS score ≥ 8 , $n=14$). In TS patients, YTGSS scores positively correlated with FC in BG and SMN and negatively with CB and FP. In OCD patients, CYBOCS scores positively correlated with FC in FP and SMN, and negatively with CB.

Conclusions: Our results confirm the role of sensorimotor networks in TS pathophysiology and their relationship with tic severity. Furthermore, TS and OCD are likely characterized by different neural underpinnings since they exhibit different FC abnormalities. In particular, OCD displays an increased connectivity in the CB and FP networks that distinguishes it from TS. This finding persisted also when comparing OCD with TS plus OCD, suggesting that TS with or without OCD could rather constitute a different entity from classic OCD.

Genome-wide association study of Tourette investigates the genetic determinants of Tourette and implicates neuronal and synaptic processes

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Background: Tourette Syndrome is polygenic and highly heritable, thus making GWAS approaches and geneset analyses useful for interrogating its genetic architecture and determinants.

Methods: GWAS meta-analysis, gene-based association, and genetic enrichment analyses were conducted in 4,819 Tourette syndrome cases and 9,488 controls. Replication of top loci was conducted in an independent, population-based sample (706 cases; 6,068 controls). Relationships between Tourette polygenic risk scores (PRS), other tic disorders, ascertainment, and tic severity were examined. We employ literature-mined curated genesets that target genes found expressed in particular cell types and operating in specific neuronal functions, using set-based association and MAGMA.

Results and Conclusions: GWAS and gene-based analyses identified one genome-wide significant locus within FLT3 on chromosome 13, rs2504235 (SNP $p=2.1e-8$; Gene $p=8.9e-7$). Genetic variants spanning evolutionarily-conserved regions explained 92.4% of Tourette syndrome heritability (Bonferroni corrected $p\text{-value}=0.005$). Tourette-associated genes were preferentially expressed in human dorsolateral prefrontal cortex ($p=1.2e-4$). Tourette PRS predicted both Tourette syndrome ($p=5.3e-9$) and tic spectrum disorders ($p=4.2e-4$) status in the population-based sample. Tourette PRS also correlated with worst-ever tic severity ($p=0.026$) and was higher in cases with a family history of tics than in simplex cases. The SBA analysis identified three significant hits, with the top being the Ligand-gated Ion Channel Signaling ($p\text{-value}: 2.67e-4$), followed by the Lymphocytic ($p\text{-value}: 3.5e-4$), and the Cell Adhesion and Transsynaptic Signaling ($p\text{-value}: 1.07e-3$). MAGMA analysis identified a single geneset, the Cell Adhesion and Trans-synaptic Signaling

geneset, achieving a p-value of $6.17\text{e-}5$. Tourette PRS derived from sufficiently large samples may be useful in the future for predicting conversion of transient tics to chronic tic disorders, tic persistence and lifetime tic severity. The Lymphocytic geneset, driven by variants in the FLT3 gene, raises a compelling argument for the involvement of a neuroinflammatory element in TS pathogenesis. The LICs set reinforces the role of GABA in TS, while the CATS set, associated in both methods, supports the role of adhesion molecules in neuropsychiatric phenotypes.



Alexithymia and interoception in children with Tourette syndrome:

A clinical audit

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Background: Patients with Tourette syndrome (TS) report higher sensitivity to internal bodily signals (interoception)¹. Atypical interoception, both atypically high or low sensitivity, is routinely associated with difficulties identifying and describing one's own emotions (alexithymia³). Previous research investigating alexithymia children with TS⁴ is limited to children with mild/moderate tics, no comorbidities and has relied solely on self-report. This audit is of children with mild-severe TS with multiple comorbidities. Parent and child report of alexithymia and interoceptive attention are explored, and results will be compared to another clinical control group.

Methods: Parents and children (8-18 years) completed questionnaires assessing rates of alexithymia, (CAM⁵, EQI-YV⁶) and interoceptive attention (CSI-24)⁷. Participants also completed a measure assessing severity and impairment of tics (YGTSS⁸). Rates of neuropsychiatric and neurodevelopmental difficulties were also recorded.

Results and Conclusions: Of 27 children with TS, 74% were male (N=20) and 26% were female (N=7). Ages ranged from 8-17 years (m=11.6). Of these, 37% had no comorbidities, 37% had 1, 22% had 2 and 4% had 3 or more. Comorbidities included ADHD (22%), ASD (11%) and LD (7%), anxiety (37%) and somatic symptom disorders (19%).

Positive correlations were found between severity of tics and child's attention to bodily sensations ($rs=0.489$, $p=0.013$). Parent reported alexithymia, age and anxiety/depression accounted for 72% of the variance for noticing internal bodily sensations. Children's self-rated anxiety ($p=0.010$) and depression ($p=0.011$) were the largest predictors of interoceptive attention. Parents reported that children who have greater interoceptive attention have greater difficulties interpreting their emotions (i.e. are more alexithymic; $rs=0.411$, $p=0.033$).

Results demonstrate that children with TS report increased levels of interoceptive attention. Children with increased attention to bodily sensations are rated as having more difficulties identifying their emotional states. Interoceptive attention was also associated with greater severity of tics and higher levels of mental health difficulties. Further studies should explore the impact of interoception and alexithymia in the TS population using multiple measures of interoception.

Tic-like attacks and functional neurological movements: CBT with external attention focusing**Dr Sally Robinson^{1,2}, Dr Tamsin Owen¹, Dr Kate Golding² and Dr Tammy Hedderly¹**¹Tic and Neurodevelopmental Movement Service, Children's Neurosciences, Evelina London Children's Hospital, Guys and St Thomas' NHS Foundation Trust, London²Paediatric Neuropsychology Service, St Georges University Hospital, London

Background: Tic-like attacks typically occur in individuals who have been diagnosed with Tourette Syndrome (TS) and include both tics and movements that may look like tics but are not. These tic-like movements are best described as Functional Neurological Movements (FNM), i.e. movements that appear to be of neurological origin but do not have an identifiable neurological or medical basis. In adults, cognitive behavioural therapy (CBT) has been shown to be more effective than standard medical care (Goldstein, et al., 2010; Sharpe, et al., 2011). To date, there are no studies reported in the literature that provide detailed information on the psychological management of children with FNM, with only one study reported in the literature that documents the management of tic-like attacks in TS (Robinson, & Hedderly, 2016).

Methods: 18 children (9 female; 9 male) with a mean age 13 years (range 10-18 years) and FNM, which included functional tics and tic-like attacks (N=8), loss of functional movement in legs and hands (N=7), tremors (N=3), clawed hands/feet (N=2) and non-epileptic seizures (N=1). Following a multidisciplinary assessment, children underwent 1:1 psychological intervention for management of the FNM (mean number of sessions 11, range 1-17 sessions). The sessions involved psychoeducation about FNM, followed by CBT with external attention focusing strategies. Four cases underwent neuropsychological evaluation. Treatment effectiveness was assessed using the Children's Global Assessment Scale (CGAS) and clinical evaluation of FNS.

Results and Conclusions: Psychological intervention resulted in significant improvement in FNM for all children, with complete resolution of functional symptoms for 14 cases. Pre-treatment mean CGAS score = 38, Serious Problems (range 31-62); post-treatment mean CGAS score = 72, Doing All Right (range 60-88). Four children reported persistent symptoms at follow-up, which included functional tics and a functional tremor; though all reported symptoms only occurring when highly anxious. Four cases had undiagnosed cognitive and/or specific academic difficulties that required additional school support. These cases provide promising preliminary evidence for CBT with attention training components for the treatment of tic-like attacks and FNM in children.



Tic Disorders revisited: Introduction of the term “Tic Spectrum Disorders”

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Background: Although, in the DSM-5 chronic motor tic disorder (CMTD) and Tourette syndrome (TS) are distinct diagnostic categories, there is no genetic or phenotypic evidence that supports this diagnostic categorization. The aim of this study was to compare patients with both diagnoses along a number of clinical characteristics to provide further diagnostic clarity.

Methods: Our sample consisted of 1018 of both adult and child patients suffering from chronic tic disorders. Tic severity was assessed via Shapiro Tourette-Syndrome Severity Scale (STSS). Lifetime prevalence of other comorbid conditions was assessed in a semi-structured clinical interview.

Results: Both groups did not differ significantly on any of the clinical or demographic variables. Patients only differed in tic severity with CMTD patients (n=40) having lower mean tic severity (STSS=2.0 vs. 2.8;p<.001), prevalence of complex motor tics (27.5% vs.55.9%;p<.01), copropraxia (0% vs. 16.2%;p<.01) and echopraxia (10.0% vs. 23.8%;p<.05), and a markedly lower comorbidity score (1.9 vs. 2.7;p<.001) as compared to TS patients (n=978).

Conclusions: Our results suggest that both disorders exist along a symptom severity continuum of which TS constitutes a more severe and CMTD a less severe form. We therefore suggest the introduction of the term “tic spectrum disorders”, instead of using different diagnostic categories.



Cognitive tics in Gilles de la Tourette syndrome - phenomenology and clinical associations

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Background: Gilles de la Tourette syndrome (GTS) is characterized by motor and vocal tics, usually preceded by premonitory urges. One third of patients will develop Obsessive-Compulsive Disorder (OCD) and in up to 80% of them Obsessive-Compulsive Symptoms (OCS) will appear. Cognitive tics (CTs) are phrases or words that intrude into consciousness, similarly to obsessions. The aim of the study was to establish if CTs belong to tic spectrum or OCD spectrum and to assess their incidence and associations.

Methods: We performed a prospective, one-registration study in a cohort of 203 consecutive patients with GTS (males: n=158, 77.8%). Mean age of children was 10.4±3.1 years; mean age of adults 27.2±7.4 years. Duration of GTS was 4.9±3.0 years (range: 1–13) in children and 18.3±7.3 years (range: 6–39) in adults. The patients were evaluated for the clinical diagnosis of GTS and co-morbid mental disorders according to DSM-IV-TR. Mental coprolalia, echolalia, palilalia, counting and repeating of words/phrases in thought were recognized as CTs during the interview and analysed in this study.

Results: CTs were found during active inquiry, none of the patients reported them spontaneously. They occurred at some point in the lifetime of 19.6% (n=38) of patients, more often in adults than children (29.3% (22/75) and 13.4% (16/119), respectively, p=0.03). In 9 patients CTs were not possible to evaluate. Gender did not differ between CTs+ and CTs- groups (males, 81.6% vs. 76.9%; p=0.667). CTs were continuing in 26 patients (68.4%) at the time of evaluation. Age at onset of CTs was known in 28 patients (mean: 13.9±5.2 years; range: 3–26). CTs started 7.4±5.0 years after the onset of first tics. The patients with CTs were older at evaluation (p=0.013), had more severe tics (p=0.0005), more frequently experienced preceded premonitory urges (p=0.003), suffered more often from OCD/OCS (p=0.018), anxiety disorders (p=0.025) and depression (p=0.028). Multivariate logistic regression analysis showed significant associations of CTs with tic severity (p=0.034) and premonitory urges (p=0.013), but not with any co-morbid psychiatric disorders including OCD/OCS (p=0.634).

Conclusions: CTs are part of the tic spectrum not obsessions. They appear most often in adolescence and are mostly associated with tic severity and premonitory urges.



The impact of a cognitive-psychophysiological therapy on motor planning and execution in Tourette syndrome patients

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Background: In recent years, cognitive-behavioral therapies have made important progress among available treatment options for Tourette syndrome (TS). One of these treatment, the cognitive-psychophysiological (CoPs) therapy, aims at regulating the chronically heightened sensorimotor activation and elevated muscle tension in TS patients. It has been proved to effectively decrease tics, but can also improve motor skills. However, the neurobiological mechanisms underlying such changes are not fully understood. Therefore, the current project aims at studying the impact of the CoPs therapy on electrocortical brain activity related to motor planning and execution in TS patients. We hypothesized a delay in motor planning and larger electrocortical activity related to motor execution. We also hypothesized that these electrocortical would allow a good prediction of treatment outcome.

Methods: The electroencephalogram (EEG) was recorded in 21 TS patients and 21 healthy controls paired on age, sex and handedness, during a Stimulus-Response Compatibility task. EEG data were processed into lateralized readiness potentials (LRP). The LRP are obtained through a double event-related potentials subtraction, to eliminate any activity unrelated to motor processes. Both the stimulus-locked (sLRP) and response-locked (rLRP) were assessed. Measures of LRP onset and maximum peak were taken before and after the therapy for the TS group. The control group was also tested twice with a similar interval between assessments.

Results: Results showed that prior to therapy, sLRP onset was delayed in TS patients, compared to healthy controls. The CoPs therapy allowed an acceleration of the sLRP onset in TS patients, comparable to the controls. In healthy controls, the sLRP onset did not change over the 4-months interval, suggesting that the acceleration seen in TS patients is attributable to the therapy and not to repetition. The LRP measured before CBT also predicted the symptom outcome (motor tic) following CBT.

Conclusions: CoPs therapy appear to induce a normalization of cerebral motor processes. It also appear that cortical processes related to motor planning are able to predict successful treatment outcome in TS patients.

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 is a first-line intervention for tic disorders. Despite its demonstrated efficacy, there is room for improvement and a need to optimise treatment with respect to tic reduction. In addition, the lack of behavioural therapists specialised in tic treatment is a barrier for local treatment. Patient associations emphasise the need for easy-to-undergo treatments which additionally support children to cope with their symptoms. This pilot study, funded by Tourettes Action UK, aimed to enhance treatment outcome and to overcome treatment barriers, by studying the feasibility of a brief, intensive group-based programme, Tackle your Tics.

Methods: Tackle your Tics is a four-day intensive group-based programme for children and adolescents (9-17 years) with tic disorders, consisting of evidence-based exposure and response prevention treatment, psycho-education, the training app BT-Coach, coping strategies, relaxation activities, group support and parent meetings. Assessments were performed pre- and posttreatment and at 2 months follow-up, to explore effects on tic severity (as measured with the Yale Global Tic Severity Scale), premonitory urges, quality of life, emotional and behavioral functioning and treatment satisfaction.

Results and conclusions: Two therapy weeks were held in September 2018 and February 2019 (N=14). Experiences with the Tackle your Tics programme seem promising. Parents and children were unanimously positive about this form of treatment. Preliminary data of the first pilot week show improvement on tic severity and on quality of life, especially in girls. Conclusions: intensive CBT holds promise for a feasible treatment programme to improve both tic severity as well as quality of life.

Randomized double-blind controlled trial of thalamic versus GPI stimulation in patients with Gilles de la Tourette Syndrome

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Background: While the vast majority of patients with Gilles de la Tourette syndrome (GTS) exhibits only mild to moderate tics and benefits from behavioral and pharmacotherapy, a small number of patients suffers from extreme and seriously impairing tics resistant to standard treatments. In these patients, deep brain stimulation (DBS) has been suggested as an alternative treatment option. However, until today the number of controlled trials is very limited, available results obtained from open and controlled studies are partly inconsistent, long-term effects have been rarely investigated, and the optimal target is still unclear. This study, therefore, was designed to compare efficacy and safety of bilateral DBS of thalamus (CM-Voi) and posteroventral lateral globus pallidus internus (pvl GPi) in a randomized double-blind sham stimulation controlled trial (RCT) followed by an open uncontrolled long-term follow-up study.

Methods: We included 10 patients (3 female, mean age=29.4±10.2 SD, range, 18-47) who underwent three 3-months blinded periods including (i) sham, (ii) GPi (on-GPi), and (iii) thalamic stimulation (on-thal) followed by an open uncontrolled study with individually determined target and stimulation settings. We used a large number of self- and examiner assessments to measure severity of tics and comorbidities, quality of life and adverse events (AEs).

Results and Conclusion: Nine patients completed the RCT, which demonstrated a significant tic reduction compared to baseline after on-GPi according to both the Yale Global Tic Severity Scale-Total Tic Score and a video tic assessment. All other assessments and direct comparison of effects of different stimulation settings resulted in inconsistent or negative findings. During open follow-up, only single patients still benefited from DBS, while there was no improvement of tics, comorbidities, and quality of life at group level. At last follow-up (89.9 months (mean) after surgery), 50% of patients had decided to discontinue DBS. Hardware infections occurred in 3 patients. From our data it is suggested that pvl GPi DBS is superior to thalamic (CM-Voi) DBS. While GPi DBS resulted in a significant tic reduction after 3 months during the blinded study phase, in the long-term after several years we found no significant effect on tics, but half of the patients experienced an overall improvement.

Pain and tics: a daily experience – is there more opportunity in the multi-disciplinary team for physiotherapy?

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Background: The charity, Tourettes Action (TA) often hears reports from patients that their tics cause chronic pain and tissue damage. Although the literature suggests that 'tics can, in rare cases, cause injuries'¹ this may not be the full story or it may be that it has not been systematically explored. The European Guidelines suggest that during clinical interviews the clinician also ask about the 'physical consequences of tic (including pain/injury of muscles and joints)' ². Pain may be from the recurrent or forceful tics causing discomfort by sudden or repeated extreme movements¹. There is a possibility that pain could be managed within the multi-disciplinary team, including using physiotherapy. There is a lack of high quality research evidence supporting physiotherapy interventions for Tourette Syndrome (TS) and little is known about how people with TS manage their pain day-to-day or whether they seek physiotherapy help.

Methods: Tourettes Action, held a survey between March 2018 and March 2019 of its members to gain an understanding into the individual's experience of pain and access to support for pain and physical problems caused by tics. People were asked to describe injuries, physical problems or pain subsequent to their tics and if there was a particular problem they experienced regularly.

Results and Conclusions: 295* people with TS completed the survey; we did not collect details about their age or gender. Almost 100% reported pain from tics. Results highlighted some less well-known tics and their painful consequences;

- Mouth tics causing sores around the mouth
- Recurrent head and neck flicking tics resulting in whiplash
- Abdominal tics causing nausea and heartburn
- Head shaking resulting in regular nosebleeds
- Eye rubbing leading to eye damaged and loss of sight
- Gulping tics making swallowing food difficult

87% of respondents said that physical discomfort resulting from tics affects daily living from a 'moderate' amount to a 'great deal'. Many used painkillers on a daily basis to manage pain.

Patients tend to practice self-care to minimise or prevent issues such as injuries, physical problems and pain due to tics. In the survey many indicated that they were unaware they could seek professional intervention but would

welcome it. Painful tics can be addressed using behavioural therapy as recommended as the first-line treatment^{3,4}.

We suggest that painful tics could be helped by pain management and physiotherapy. Issues such as waxing and waning of tics, and repetitive movements create unique challenges to physiotherapy and occupational therapy professionals. It is clear that research is needed regarding use of physiotherapy to help establish an evidence base and clear outcomes for people with TS to get from physiotherapy.

*at time of abstract submission 20th March 2019, survey still open.



Missed diagnosis of ADHD in children referred to a Tic Disorder Clinic

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Background: Attention Deficit Hyperactive Disorder (ADHD) is a common comorbid disorder in Tourette's Syndrome (TS) which significantly impacts quality of life, in some cases more than the tics. Referrals to tic disorder clinics can be focused on the motor disorder, delaying management of ADHD. We aimed to examine how often a later diagnosis of ADHD has not already made in referrals to our service..

Methods: Referral letters and first clinic attendance reports for 119 new patients aged between 4-17 that attended a national tic disorder clinic between 2015-2017 were analysed to see how many new diagnoses of ADHD were made at first consultation that were not included in the referral letters. Other variables that were noted for each patient included age, sex, if referrer had a suspicion of ADHD (rather than established or firm diagnosis), medication for ADHD and the main treatment target decided at the tic disorder clinic.

Results and Conclusions: Out of 119 patients 13 (11%) already had a diagnosis of ADHD, which is in line with the prevalence of comorbid ADHD in the general population but not with the known increased prevalence in patients with TS (up to 80% in some studies). The assessment at the Tic Disorder Clinic found 46 new cases of ADHD (38%). Referrals were from paediatricians (51%), general practitioners (35%) and from mental health services (10%).

As the prevalence of comorbid ADHD is high in Tourette's patients and this can sometimes be obscured by the presentation of the tic disorder, referrers should have a low threshold for suspecting and managing ADHD in cases where specialist input for tics is awaited. It is likely that child psychiatry referrals were under-represented in the sample and it may be expected that prior ADHD diagnoses would be more likely from that source.



E-POSTER: ABSTRACTS (in alphabetical order)

At ease with your tics: A Guided Relaxation (GR)

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Background: Behavioural interventions for Tourette Syndrome (TS) and Chronic Tic Disorder (CTD) are recommended as first-line treatments and often preferred by patients 1, 2. Relaxation is a commonly used behavioural technique which are included in evidence-based packages of treatment such as Exposure with Response Prevention (ERP)² and Comprehensive Behavioural Intervention for Tics (CBITS)³. A guided relaxation (GR) aimed to help patients with TS access a mindfulness/relaxation technique. Underlying mechanisms of tic-alleviating processes are not known but evidence exists for relaxation reducing muscular tension, as in Habit Reversal Therapy (HRT) and relaxation training⁴⁻⁶. Researchers have reported favorable effects of mindfulness-based reduction on tics for adults with TS/CTD⁷. This third wave behavioural therapy has been gaining empirical support across a range of conditions⁸.

Methods: A clinical formulation model was used to script a guided relaxation (GR) steered by a group of experts. Two concepts were incorporated into the script: setting 'intention' and exploring neural pathways from within the body during meditation⁹. The focus was on 'mindful movement' to allow 'individuals who would struggle to sit still to complete the more commonly taught mindfulness practices'⁹. The script was adapted to fit with tic treatment by tolerating tic urges and stress reduction. An online survey gathered feedback about changes during and after the relaxation. It was anticipated that GR might decrease the intensity and frequency of tics, during or after practice.

Results and Conclusions: The GR was released in March 2018. 220 relaxations were downloaded and 35 people completed the survey.*

During relaxation

- 60% of people reported changes in tic frequency/intensity during GR.
- 41% reported tic **frequency** decreased during GR, 59% found tic intensity decreased during GR.
- 36% felt the urge to tic decreased, 31% stayed the same and 18% urge increased.

After relaxation

- 43% of people reported changes in tic frequency/intensity after GR.
- 33% reported tic **frequency** decreased after GR, 44% found tic **intensity** decreased after GR.
- After GR 34% urge to tic decreased, 37% stayed the same and 16% reported urge increased.

48% used words or phrases from GR ('calm and relaxed'). 82% said they would recommend to help with tic symptoms.

Conclusions: This technique decreased intensity of tics after the participants listened to the recording and reported satisfaction by the users was positive. We hope to plan a larger trial to evaluate the intervention fully, possibly as part of an existing evidence-based intervention. Plans are underway to make an adapted version for children with pre and post measures such as extent of change in tic frequency and intensity, anxiety, depression, QoL and acceptability.

*at time of abstract submission 20th March 2019, survey still open.



Clinical and cost-effectiveness of Internet-delivered behaviour therapy for children and adolescents with Tourette syndrome: Protocol for a single-blind randomised controlled trial in Sweden

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Background: Behaviour therapy (BT) for Tourette syndrome (TS) and chronic tic disorder (CTD) is effective but rarely available. To increase its availability, we developed a therapist- and parent-guided Internet-delivered BT programme for young people with TS/CTD, named BIP TIC. Preliminary results from a pilot study suggest that BIP TIC is a feasible and highly acceptable treatment. We now plan to evaluate BIP TIC in a full-scale randomised controlled trial in Sweden to determine its clinical efficacy, long-term durability, and cost-effectiveness. This poster outlines the trial protocol.

Methods: We plan to conduct a single-blind parallel-group randomised controlled superiority trial, where participants (N=220) are randomised to either 10 weeks of BIP TIC (therapist- and parent-guided Internet-delivered exposure and response prevention) or a control condition (therapist- and parent-guided Internet-delivered education on tics). The trial will be coordinated at a single site in Stockholm, Sweden, but will recruit nationally. Eligibility criteria will include a diagnosis of TS/CTD, age between 9 and 17 years, and stable medication for tics, if on medication. Participants are assessed at post-treatment and at 3, 6, and 12 months follow-up. The primary outcome will be tic severity as measured by the Total Tic Severity Score of the Yale Global Tic Severity Scale at the 3-month follow-up, which will be assessed by raters blind to the treatment condition. A full health economic evaluation will be conducted. Data will be analysed using a pre-specified intention-to-treat statistical analysis plan.

Results and Conclusions: Recruitment is planned to start in March 2019. If BIP TIC is superior to tic education alone, as well as cost-effective, we will aim to implement it in routine clinical care in Sweden.

Antibodies to neuronal surface proteins in Tourette Syndrome: lack of evidence in a European paediatric cohort

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Background: In Tourette Syndrome (TS) a role for autoantibodies directed against neuronal proteins has long been suspected, but systematic studies are sparse. The aim of this study was to look for antibodies to specific or undefined neuronal proteins that could be involved in the aetiology of the disease.

Methods: Sera from children with Tic Disorders or Tourette syndrome (TD/TS), collected as part of a pan-European EMTICS consortium were investigated. Patients included siblings of TD/TS before the development of TD/TS (pre-clinical cases) (n=30), the same children when they developed TD/TS (n=30), and those in the more chronic phase undergoing relapses (n=158). Tests included looking for antibodies binding to rodent brain tissue sections by immunohistology, and to the surface of live hippocampal neurons. Live cell-based assays (CBAs) were used to look for antibodies to NMDAR, D2R, CASPR2 and LGI1.

Results: Immunohistology indicated some evidence of antibodies reactive with brain tissue, binding mainly to the hippocampus, the basal ganglia or the cerebellum in 26/218 (13%). Only two individuals (one pre-clinical, one chronic) had antibodies binding the NMDAR and the binding was only weakly positive. There were no antibodies to D2R, CASPR2 or LGI1 detected.

Conclusions: Despite an increased immunoreactivity towards neuronal antigens on brain tissue, this was not mirrored by antibodies binding to live neurons which suggest non-specific antibodies or those that bind non-pathogenic intracellular epitopes. Neither NMDAR or D2R antibodies were common in these patients. The evidence for pathogenic antibodies that could be causative is weak.

ESSTS Patient Groups: The whole is greater than the sum of its parts

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Background: Since 2008, the European Society for the Study of Tourette Syndrome (ESSTS) has organised annual meetings to coordinate pan-European efforts for the study of Tourette Syndrome (TS). These meetings provide a platform for global outreach and educational activities. As part of the annual meeting representatives of the patients associations from European countries are invited to attend (also known as advocacy groups). Usually the representatives of the patients associations meet for half a day as well as attending the conference and its social events. The goals of the ESSTS association are to understand the prevalence and impact of TS and find effective treatments for TS. It also aims to help stimulate worldwide collaboration in research. ESSTS has fostered the establishment of the European-wide network of TS support and advocacy groups. However, collaboration between advocacy groups and researchers and clinicians can be improved, as well as the collaboration between different advocacy groups. It would be beneficial if the patients advocacy groups could set an agenda and create a mission statement themselves. This would help define the purpose and reason for the group as well as helping it outline what support it can give to member countries and what collaboration it can offer to the researchers and clinicians who attend the ESSTS annual meetings. It has the potential to make collaboration more effective.

Methods: The aim was to gather information from different sources to assist in setting an agenda and create a mission statement for the patients associations from European countries. This involved examining statistics for members of a closed Facebook group called ESSTS Patient Groups. Also under examination was the numbers of previous attendees at the ESSTS advocacy groups showing which countries sent patient representatives. Another source of information was from pre-existing collaboration initiatives between the central ESSTS annual meetings and the ESSTS Patient Groups to help steer future projects.

Results and Conclusions: It was found that the ESSTS Patient Facebook group had 62 members representing over 19 countries. There had been some previous collaboration during the ESSTS conference with the patient representatives invited to speak to the main conference on patient perspectives and research collaboration. The 2018 meeting also resulted in the production of two leaflets 'Guidelines for patient's participation in research'

and 'Information on TS related characteristics leaflet for patients'. Since the first ESSTS conference where patient representatives were present, Dresden in 2010, to Copenhagen in 2018, there has been an average of 10 countries in attendance at the ESSTS advocacy groups.

The ESSTS Patient Groups would like to put forward the idea that they could be more involved in the conference and have a role to play. This year (2019) the patient's advocacy groups aim is to set an agenda and create a mission statement. This will outline what support it can give to member countries and what collaboration it can offer to the researchers and clinicians who attend the ESSTS annual meetings.



Effectiveness of a psychotherapy for managing explosive outbursts in children with Tourette syndrome on the perception of their parents' stress

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Background: Parental stress is defined as parents' distress with their child's behaviors, their perceived ability to manage their child's needs, and the perceived quality of parent-child interactions (Abidin, Jenkins, & McGaughey, 1992 ; Mash & Johnston, 1990 ; Webster-Stratton, 1990 ; Wilkinson et al., 2008). Studies of children with TS have shown that manifestations such as explosive outbursts (EO) have an impact on family stress (Robinson et al., 2013, Wilkinson et al., 2008, Wilkinson et al. 2001), generating additional health care and education needs (Debes, Hjalgrim & Skov 2010, Kurlan 2010, Olfson et al., 2011, Sasnett 2008). EO refer to violent and uncontrollable outbursts of anger that occur suddenly and recurrently (Budman et al., 2000). The aim of this study is to examine changes in parents' perceptions of their own stress as a result of an intervention to reduce EO in their child.

Methods: The children were all randomly assigned to one of the two modalities of treatment, including a specific psychotherapy for managing EO and an active control group. Questionnaires on parental stress level were completed by 33 parents of TS children who were assigned to one of the two modalities of treatment.

Results and Conclusions: Pretreatment and post-treatment analyzes showed no significant difference in overall improvement in parental stress. However, when we analyze the different components of parental stress, the parents' distress with their child's behaviors shows a significant reduction. Moreover, by comparing the evolution of the two modalities of treatment, the results showed a significant improvement of the control group compared to the specific psychotherapy for managing EO group on their perceived quality of the parent-child interactions. This may be explained by the fact that the interventions proposed in the control group were more generalizable to other symptoms, since no specific intervention targeted the reduction of the EO. Thus, the control group have been exposed to tools that could also be applied for managing tics or other related disorders, compared to the experimental group that focused more on EO events. To this end, the addition of specific components for managing tics or other disorders associated with TS seems promising in order to improve parents' perception of their own stress.

Developing a Recruiting Database for Patients with Tic Disorders

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Background: The purpose of this project was to develop a database and managing tool for storing patient contact information and to enable an easy way to handle the recruitment of participants for upcoming tic-related studies at the Clinic of Psychiatry, Social Psychiatry, and Psychotherapy, Hannover Medical School.

Methods: We first investigated the current state of stored data at our specialty clinic, including the process of data storage for new patients, the recruitment of patients for research studies, the standard questionnaires used by study personal and the available IT infrastructure. We then designed a MySQL Database for storing patient data in connection with a custom Microsoft Access FrontEnd for accessing and managing data.

Results: The database schema was optimized in the process of several iterations. We started by including moderately complex (i.e. establishing family relationships between patients) and elaborate information (i.e. all ICD-10 diagnoses, full medication history) and after a selection and optimization process we arrived at a more simple approach including only contact information, a communication protocol (with Outlook integration for appointments), tic-related diagnoses, medication, study participation, as well as optional notes on the patients (i.e. regarding future recruiting).

Conclusions: Continuous feedback with the study personal throughout development and deployment showed that minimizing the amount of stored information led to a higher quality of information stored and a better utility of the managing tools for the study personal.

Development of a database for research needs should provide easier recruiting for ongoing and especially upcoming studies. Using an industry standard (SQL) for storing provides longevity of all data. This enables the clinic to integrate and examine the data with ease for various future projects.



Mindfulness, Self-Compassion, Parental Stress, Well-Being and Child Behaviour in Tourette syndrome, Autism and ADHD

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Background: Parents of children with neurodevelopmental disabilities (such as Tourette Syndrome (TS), Autism Spectrum Disorder (ASD) and Attention Deficit Hyperactivity (ADHD) report increased parental stress compared to parents of typically developing children. Caring for children with comorbid neurodevelopmental disabilities is likely to be more challenging due to the nature and severity of impairments. Mindful parenting (MP) has been defined as “applying practices of paying attention in a non-judgmental manner to one’s child and parenting over time” and has been found to play an important role in parent’s coping.

Methods: This cross-sectional, correlational study aimed to: a) explore relationships between facets of MP, self-compassion, parental stress, wellbeing and child externalizing difficulties, b) explore whether MP mediated the relationship between child externalizing difficulties and parental stress and c) explore any differences between levels of MP, self-compassion, parental stress, well-being and child externalizing difficulties, amongst parents of children with primary diagnoses of TS, ASD and ADHD.

Eighty-four parents of children with TS, ASD and ADHD (54% rate of comorbidities) completed self-report questionnaires measuring mindfulness, mindful parenting, parental stress and wellbeing and perceived child behaviours.

Results and Conclusions: Mindful parenting and self-compassion were significantly negatively correlated with parental stress. Of the MP facets, greater self-regulation was significantly related to lower child externalizing difficulties, whilst greater compassion was significantly related to lower child internalizing difficulties. Mindful parenting mediated the relationship between child externalizing difficulties and parental stress. Parents of children with a primary diagnosis of ASD had significantly lower levels of MP, self-compassion and reported higher rates of child internalizing and externalizing difficulties compared to those with a primary diagnosis of Tics/TS.

Results suggest that MP interventions may be beneficial to parents of children with comorbid neurodevelopmental disabilities. Increasing parent’s self-regulation skills and compassion may have important implications for children’s emotional and behavioural outcomes.

Microbiological characterization of Group A streptococci isolated from children in the EMTICS study.

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Background: Tic disorders during childhood have a detrimental effect on quality of life of patients and families. Genetic and environmental risk factors, including exposure to *Streptococcus pyogenes* (group A *Streptococcus*, GAS) are poorly understood and were investigated in the FP7 project “European Multicentre Tics Study” (EMTICS) study.

Methods: EMTICS comprised two longitudinal observational studies: the COURSE study consisting in a cohort of 715 tic-affected children, aged 3-16 years, followed for 16 months; the ONSET study that included 260 high-risk children (having a first degree relative with a diagnosis of Tourette syndrome and no tics at study entry), aged 3-10 years, followed for three years.

EMTICS children were throat swabbed both at the time of enrolment and at planned visits. Swabs were processed following a common validated microbiological protocol for GAS detection and isolation.

Microbiological characterisation of bacterial strains included the emm typing as the GAS molecular typing gold standard, the screening of virulence genes (superantigens and surface protein R28 genes) including their allelic variants, the clonal genetic GAS population structure using both Multiple Locus Variable-number of tandem repeats Analysis (MLVA) and Multi Locus Sequence Typing (MLST) methods. Susceptibility to erythromycin and clindamycin was also assessed.

Results: GAS positivity of children largely varied between centres ranging from 0% to 46.6%. In total, 296 GAS strains were collected. As a control population, 42 GAS strains from pharyngitis were received and typed.

There were not striking differences in the serotype distribution, virulence and clonal relationships between GAS strains isolated from ONSET and COURSE children. In both populations, emm28 and emm89 were the most diffuse serotypes. Noteworthy, these emm types don't produce capsule because of missense mutations (emm28) or absence of the has gene (emm89), respectively, which encodes an enzyme required for hyaluronic acid capsule biosynthesis. Further unidentified frameshift mutations in the has gene are being identified in EMTICS bacterial collection. At present, the incidence of non-capsulated strains in EMTICS study is 43.1%, more frequent in ONSET than COURSE (49.4% vs 40.6%).

The most diffuse serotypes in pharyngitis were the capsulated emm1 and emm3; the proportion of non-capsulated strains was 30.9%.

When GAS was isolated during exacerbation of tics symptoms, in severe tic symptoms or persistent throat colonisation, an enrichment of emm12 strains was noted.

The superantigen speC gene was abundant in both ONSET and COURSE isolates (68.2% vs 58.9%) but SpeC1 allele was significantly more present in COURSE isolates (Fisher's exact test: 0.04). Surface adhesin R28 was associated to certain emm types (emm 2, 28, 48, 77).

Resistance to erythromycin was 9.9% (3.5% and 12.5% in ONSET and COURSE, respectively).

Conclusions: It is not evaluable how much the difference in the incidence of GAS positive children between participating centres could have affected the microbiological analysis. A large proportion of non-capsulated GAS strains is represented in EMTICS, more in ONSET than in COURSE. Moreover, emm type 12, speC1 allele and erythromycin resistance were asymmetrically represented in GAS strains from the ONSET and COURSE studies.



Attentional dimension in Tourette Syndrome

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Background: Attention is a multidimensional phenomenon based on the existence of several processes of selection. These subsystems perform different functions, which are interconnected in the concepts of orienting, shifting, selective, divided, and sustained attention (or vigilance). The aims of this review is to study the different profile in attentional dimension of TS, explain how various confounding factors can affect TS patients' performance in attentional tasks and differences between TS and ADHD.

Methods: 43 children with a diagnosis of TS with no comorbid ADHD and 51 age and sex matched children with ADHD (both conditions according to the DSM5 classification) were assessed by experienced child neuropsychiatrist. The assessment battery included evaluation of IQ using either Raven's Progressive Matrices or WISC-IV and a structured neuropsychological battery using NEPSY-II (processing speed, inhibitory control, selective attention, vigilance, and cognitive flexibility).

Results: "Visual Attention test" 33% of the ADHD group scored -1.5 SD from mean scoring compared to 12% of TS group; in the "Design Fluency test" 42% ADHD versus 37% TS; in the "Auditory attention test" 72% ADHD versus 30% TS; in the "Naming Test" 58% ADHD versus 12% TS; in the "Inhibition Test" 61% ADHD versus 21% TS; in the "Switching Test" 72% ADHD versus 14%. The ADHD group scored worst in all the items analyzed. Nevertheless only in the auditory response (1.94 vs 0.52), the naming (1.17 vs 0.21), the inhibition (1.17 vs 0.35) and the switching test (2.42 vs 0.30) showed a statistically significant difference with the TS ($p < 0.05$).

Conclusions: We have shown how both ADHD and TS fail in the attentional dimension with a different discrepancy profile. TS particularly fail in the design fluency test, a nonverbal fluency task during which the child must draw as many unique designs in a given time limit from both structured and unstructured dot arrays. This shows a specific difficulty with initiation and productivity and a poor cognitive flexibility. ADHD group compared to the TS scored worst in the three items of the inhibition test (naming, inhibition and switching). In conclusion, TS patients show a poor attentional neuropsychological functioning even though they do not meet the DSM5 criteria for ADHD.



Motor timing and time perception in children with Tourette Syndrome

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Background: Time processing is regulated by several basic cognitive functions. Distortion in time perception is present in many neurological-psychiatric conditions such as TS. Tourette syndrome (TS) is a neurodevelopmental disease characterized by dysfunctional connectivity between prefrontal cortex and subcortical structures with an impaired dopaminergic network.

Methods: 27 TS patients were recruited and age-matched with 21 healthy controls. All subjects underwent a structured neuropsychological evaluation. A computer based neuropsychological assessment was performed analysing motor timing and time perception. Comparison between groups were performed by using ANOVA or ANCOVA (where appropriate). Data were analysed with MYSTAT software.

Results: Motor timing, the temporal organization of motor behaviour, was measured by using three tasks: (Finger tapping test: TS group resulted more impaired than controls considering both dominant ($p<0.001$) and non-dominant ($p=0.013$) hand; Sensorimotor synchronization test: no statistical difference found between the two groups; Sensorimotor synchronization and continuation test: statistical significance for 2000ms timing response ($p<0.001$).

Time perception: (1) Duration discrimination task (temporal discrimination between a short -100 ms- and a longer-1000 ms auditory stimuli): a statistically significant difference was found between TS and controls (respectively 0.663 vs 0.324, $p<0.001$) in distinguish 1000 ms while no significance was found for the 100 ms;(2) Temporal reproduction task: ability to reproduce previously presented tones (duration 1000, 2000, 3000, 4000 and 5000 ms). TS group resulted less accurate than controls for 3000 and 4000 ms ($p<0,001$);(3) Prospective Time Estimation task: report the duration of an auditory stimulus (53 sec). No significant difference was found between the groups.(4) Time wall Estimation: estimate when a moving object reaches a target point. A higher coefficient of error was evident for TS group ($p<0.010$).

Conclusions: Timing functions are associated with poorer results in TS group and our data suggest an altered perception of time.

“Tic Attacks” in Tourette Syndrome

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Background: Tourette syndrome is a childhood-onset neuropsychiatric disorder characterized by motor and vocal tics that are sudden, recurrent, and involuntary¹. Some individuals with Tourette syndrome have reported explosive and continuous bouts of tics that can last up to several hours². These have been commonly referred to as “tic attacks”, “tic fits”, or “tic status”. They are frequently mentioned in clinical settings and online forums for Tourette syndrome, but there is limited agreement as to how these bursts of tics should be defined. A recent publication has described the episodes as incorporating tics and tic-like movements (which they term ‘functional tics’) in the context of high anxiety². This study aims to shed light on what these events are, their triggers, and maintaining factors, through reviewing the literature and integrating online personal accounts.

Methods: This paper uses two approaches to gain further understanding of the episodes. The first approach involved conducting a systematic literature search of three scientific databases using “tic attacks” as a search term, along with other synonymous terms. The second approach involved conducting a thematic analysis of posts from three internet forums to provide a detailed description of the episodes.

Results and Conclusions: The literature review yielded three papers relating to continual bouts of tics^{2,3,4}. Two of these papers took a neurological perspective, describing the events in detail along with medication management. The third described these events as functional tic-like movements, conceptualized and treated with current CBT models for functional symptoms. Preliminary qualitative analysis indicated that these events cause high levels of distress, with particular fears of self-injury. Management of the events frequently included presentations to hospital emergency departments. The data suggests that people experiencing these events are conscious, despite their appearance being compared to an epileptic fit. The current research highlights the need to conduct further research alongside the Tourette community.



Tackle your Tics: a unique and innovative cooperation between researchers, therapists and patient representatives

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Background: The research norm has long been that research was conducted by academically educated researchers only. Over the last few years, there has been a shift towards involving patients representatives. By collaborating with experts by experience, research can be better attuned to patients' and parents' needs, and can therefore become more effective.

Methods: Different kind of patients representatives (adults with Tourette Syndrome and parents of children with TS) are highly involved in the Tackle your Tics study, a feasibility study into brief intensive group based behavioral therapy for tics in children and adolescents (9-17 years). This study was funded by the British patient organization Tourette's Action. The psychologist conducting the research (AH) and a co-researcher (LB) are both patient representatives. This co-researcher and another patient representative (IV), both licensed educational professionals, provided psychoeducation during this brief therapy. A forth patient representative (EC), trained in coaching and counseling support groups, provided peer support for parents. Parental meetings were accompanied by both patient representatives and experienced therapists. Patient representatives were involved in every phase of the study, from identifying the problem, to development of the study, design of the protocol and conducting the study all the way to evaluation.

Results and Conclusions: Initially, the main research goal in the Tackle your Tics study was tic reduction. Quality of Life was added, as patient representatives emphasized its importance. Innovative workshops on coping mechanisms were included in the treatment protocol. These workshops were taught by patient representatives (adults with TS). This was seen as very valuable by patients, parents and the research and treatment team. Via parent meetings, led by patient representatives (an adult with TS and a parent of a child with TS), parents were involved, which was evaluated as very helpful by parents. Tackle your Tics is a unique and innovative cooperation between researchers, experienced therapists and patient representatives. An evidenced-based treatment was provided and additional elements were added. This led to a 'total package' of treatment with a focus on both tics and quality of life. According to parents, this was one of the main reasons to participate in this study. Considering our positive experience in this worthwhile collaboration in the Tackle your Tics project, we recommend to use patient representatives during the whole research project.

No need to treat tics in adults? The effects of anxiety, depression and obsessive compulsive symptoms on tic severity and quality of life in Tourette's Disorder

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Background: In patients with Tourettes' Disorder (TD), anxiety, depression, obsessive-compulsive (OC) and tic symptoms all have the potential to result in reduced Quality of life (QoL). However, mutual relationships between the various comorbid symptoms and QoL are unclear. The aim of this study is to gain more insight in the differential contributions of anxiety, depression and OC symptom severity to QoL and tic severity in adults with TD.

Methods: Self-reported OC, anxiety and depression symptom severity measures were used to investigate their predictive value on QoL and Tic severity in adult TD patients (N=187), using correlation, regression and mediation analyses.

Results and Conclusions: Tic symptom severity has no direct or indirect effect on QoL. Depression symptom severity directly negatively influences QoL, whereas both anxiety and OC symptom severity have an indirect effect on QoL, mediated by depression symptom severity. OC symptom severity directly and negatively affects tic severity, whereas depression and anxiety symptom severity do not have a direct effect on tic or OC symptom severity. Finally, anxiety symptom severity indirectly impacts tic symptom severity, with OC symptom severity functioning as a mediator.

Discussion/conclusion: In line with and extending previous reports on the impact of comorbidity on QoL in TD patients, these findings indicate that OC symptom severity directly influences tic symptom severity whereas depression severity directly influences QoL in TD. The findings imply that to improve QoL in TD patients, treatment should primarily focus on diminishing OC and depressive symptom severity rather than focusing on tic reduction.

Thalamic Deep Brain Stimulation for Tourette syndrome

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Background: Since its first application in 1999, the potential benefit of deep brain stimulation (DBS) in reducing symptoms of otherwise treatment-refractory Tourette syndrome has been documented in several publications. However, there is still a lack of controlled studies to prove efficacy and the underlying mechanisms remain elusive.

Meta-analytic investigations of available literature along results from international registries showed significant reductions of tics after stimulation of the thalamus and globus pallidus internus. There is increasing evidence that deep brain stimulation for Tourette syndrome exerts both local and distributed effects on brain regions, but the exact networks that carry out clinical improvement remain unclear.

Methods: In this single-centre trial, 8 patients with severe and medically intractable Tourette syndrome were treated with DBS of the thalamus at the University Hospital of Cologne. To assess tic-severity, clinical comorbidities, and self-perceived quality of life, patients underwent repeated psychiatric assessments at baseline and 6 and 12 months after DBS onset. Additionally, the trial included two short periods of double blinded randomized and sham-controlled conditions.

In a secondary analysis, individual stimulation-dependent connectivity was correlated with clinical outcome to assess optimal stimulation networks.

Results and Conclusions: DBS significantly decreased tic-symptoms and improved quality of life. Connectivity to both motor and sensory networks correlated with tic reduction. Trading off motor effects and desirable side effects against surgery-related risks and negative implications, stimulation of the thalamus seems to be a valuable option when considering DBS for Tourette syndrome.

Thus, deep brain stimulation for Tourette syndrome may have left its experimental character, but difficulties in designing larger controlled clinical trials and the numerous targets used by different centres are relevant obstacles to prove efficacy and study mechanisms of action. Relevant topics for future investigations include treatment predictors, augmentation techniques, building up international registries and a better understanding of adverse events.

ABX-1431, A First-in-Class Endocannabinoid Modulator, Improves Tics in Adult Patients with Tourette Syndrome

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Background: ABX-1431 is a first-in-class, oral, highly selective inhibitor of the enzyme monoacylglycerol lipase (MGLL) that raises nervous system concentrations of the endocannabinoid 2-arachidonoylglycerol (2-AG), which acts as an agonist on presynaptic central cannabinoid (CB1) receptors. Since 2-AG exerts feedback inhibition on neurotransmitter release, and MGLL is abundant in the basal ganglia, ABX-1431 may improve tics and comorbidities in TS.

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), and premonitory urges according to the Premonitory Urge for Tics Scale (PUTS).

Results: 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.

Conclusions: Our data suggest that modulation of the endocannabinoid system by selective inhibition of MGLL improves tics in TS. ABX-1431 may provide a unique treatment profile for TS, and holds promise as a novel mechanism to treat movement disorders and neuropsychiatric conditions.



Employment and quality of life in a sample of adults with Tourette syndrome

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Background: Work participation is considered to be important for an individual's health and quality of life. In adults with Tourette syndrome (TS) still little is known about what impacts occupational status and quality of life. The aim of this study was to investigate employment status and quality of life in a sample of adults with TS.

Methods: An anonymous questionnaire survey was performed among adults with TS. Eligible for the study were adult members of the Norwegian Tourette Association with a diagnosis of TS. Tic severity was measured with a subset of items from the GTS-QOL (Cavanna et al, 2008). QoL and current health were measured with two items from the WHOQOL-BREF, respectively. Logistic and linear regression analyses were performed to identify variables associated with better outcome.

Results and Conclusions: The sample consisted of 78 adults with TS of whom 45% were females. Mean age of participants was 39.3±13.7 years (20-80 yrs) with no significant difference on gender. Mean age for TS diagnosis was 23.1±13.8 years (6-61 yrs). Women were significantly older when diagnosed with TS compared to men (27±14.4 vs 19.3±12.2 years; $p=.01$). Overall, 41% of the sample had completed college/university. Almost 60% of participants were living together with a partner (married or cohabited). The current employment rate was 71%. Experience of unemployment over a period of at least six months was reported by 35% of the sample. Mean tic severity score was 8.1±5.9 (0-28). Tic severity was found negatively correlated to current health and QOL. Those employed reported significantly better current health (3.5±0.9 vs 2.7±1.2; $p=.008$) and QOL (3.9±8.0 vs 3.1±1.1, $p=.003$) compared to the unemployed group. When adjusted for gender, age and significant variables, regression analyses revealed that current health ($p=.02$) and time for TS diagnosis ($p=.04$) were associated with occupational status. Current health ($p\leq.001$) was associated with better QOL.

In this study on adults with TS we found a relatively high employment rate. Self-reported tic severity was moderate. Women were significantly older when diagnosed with TS. Current health was associated with employment and QOL. The impact of occupational status on QoL has to be investigated further.

The complex picture of comorbidity in children with Tic Disorders: Associations with Obsessive-Compulsive Disorder and Attention-Deficit/Hyperactivity Disorder- an EMTICS study.

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Background: Tic disorders (TD) are neuropsychiatric disorders that usually begin during childhood, Research shows that comorbidity rates of these disorders are extremely high, with TD-OCD and TD-ADHD being the most common comorbidities. Although the comorbidity of tic disorders with these disorders has been well documented, not much is known about the contribution of each comorbidity to the severity of TD itself. In addition, comparisons between different levels of comorbidity (e.g., two vs. three comorbid disorders) have been scarce. Finally, research on psychological factors associated with TD comorbidity has been limited. The suggested research aims to bridge these gaps in the literature by presenting preliminary findings from the first wave of the EMTICS, a unique longitudinal study of TD in children and adolescents.

Method: The EMTICS study includes 715 children and youths aged 3 to 16 years (mean=10.65, SD=2.83) with TD according to DSM-IV-TR .They were evaluated via a clinical interview for ADHD and OCD, and also completed semi-structured interviews to assess tic severity (YGTSS) and Premonitory Urge for Tics Scale (PUTS). The children were assessed at 5 total time points with 4 month gap between them, The current findings addresses data from first visit.

Results: The reported prevalence of TD+ADHD in the sample was 27.5% and the prevalence of TD+OCD was 27%. Interestingly, 10.5% of the participants in the sample had a "triple comorbidity" of TD+ADHD+OCD. 55.3% of the participants has TD alone. For the entire sample, a positive correlation was found between comorbidity and tic severity. Participants with TD+OCD\TD+ADHD have shown higher tic severity and impairment than participants without comorbidity. Furthermore, children with TD+ADHD+OCD presented the highest tic severity of all comorbidity groups. Age and Premonitory Urge for Tics were significantly associated with TD comorbidity. Results show that the prevalence of comorbidities was higher among older children and that participants with comorbidities has shown higher puts scores than participants with TD alone.

Conclusions: Comorbidity of TD with ADHD/OCD may be associated with severe distress. Comorbidity level is associated with risk factors such as like age and Puts level. While TD, ADHD and OCD have been widely studied, this



research indicates that much more needs to be done to understand comorbidity patterns. As far as we know, there are only few longitudinal studies that systematically examined the way in which these disorders affect each other across time. This kind of research has, in our view, a potential to expand the clinical understanding of comorbidity in tics disorders, an understanding that may serve as a basis for developing customized treatment interventions for TD patients with a variety of clinical profiles. These preliminary findings presented here are thus the first step towards a longitudinal model that will eventually assess comorbidity over time, through the EMTICS study platform. Our future plans are to examine the way in which each disorder affects the other across time, based on 5 longitudinal assessments.



Sexuality and Tourette Syndrome: The impact of sexual self-esteem on sexual practices. Pilot study.

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Background: Sexuality is an essential part of life, very interrelated with general self-esteem and the way we express ourselves and relate to others. In Tourette Syndrome (TS) we know that general self-esteem or self-confidence may be affected, especially when the severity is high or there are comorbid disorders, but the affection that it can specifically involve in the sexual sphere is unknown.

Methods: The objective is knowing the sexual self-esteem in people with TS. We hypothesized that there is a negative impact on sexual self-esteem in people with TS interrelated with their level of perception of TS severity.

A total of 30 people, 11 women and 19 men, with an average of 34.7 years ($SD = 11.03$). All of them answered the Sexual Questionnaire (Snell, Fisher y Walters, 1993) online. The criteria to be selected was that they had been diagnosed with TS. Considering the severity of the disorder, 30% is considered mild, 46.7% moderate and 23.3% severe.

Results and Conclusions: It is observed that 56.7% have no self-confidence as a sexual partner. In the same way, 66.7% do not consider themselves a fairly good sexual partner, 76.7% do not classify themselves as a very favourable sexual partner and 83.3% do not feel better than other people practicing sex.

When we came trust in sexual encounters, it can be seen that 60% report having problems. In this section, differences are observed between men ($M = 3.52$; $SD = 1.57$) and women ($M = 4$; $SD = 1.34$), although they do not reach statistically significant values ($t = -0.87$; $p = .411$). When assessing the differences between severity, it is observed that the list the perception of TS severity, the higher the sexual self-esteem with the means in each of the groups: mild TS ($M = 4.33$; $SD = 1$), moderate TS ($M = 3.64$; $SD = 1.55$) and severe TS ($M = 3$; $SD = 1.73$).

In general, we observed lower sexual self-esteem in men than in women, even lower in those with more severe TS. There is a need to specifically address the problems of sexuality that may be present in people with TS, especially in the case of men who suffer, for cultural reasons, more pressure for higher standards at the sexual level.



A graph theory study of resting-state functional connectivity in children with Tourette syndrome

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Background: Little is known about the brain's functional organization during resting-state in children with Tourette syndrome (TS). We aimed to investigate this with a specific focus on the role of comorbid attention-deficit/hyperactivity disorder (ADHD).

Methods: We applied graph theory analysis to resting-state functional magnetic resonance imaging data of 109 8-to-12-year-old children with TS (n=46), ADHD without tics (n=23), and healthy controls (n=40). First, we compared these three groups, and in a second comparison four groups, distinguishing TS with (TS+ADHD, n=19) and without comorbid ADHD (TS-ADHD, n=27). Weighted brain graphs were constructed for both comparisons to investigate global efficiency, local efficiency, and clustering coefficients in the whole-brain and per acquired network.

Results and Conclusions: Local efficiency and clustering coefficients were significantly lower in children with TS-ADHD in the default-mode network compared with healthy controls, and in the fronto-parietal network compared with ADHD; we also found associations with higher tic severity. We did not find group differences in whole-brain organization, although we observed a significant positive relationship between tic severity and whole-brain global efficiency. Our study supports a different functional brain network organization in children with TS-ADHD, independent from comorbid ADHD, compared with healthy controls and children with ADHD.

Rage Attack Questionnaire (RAQ): Comparison of Rage Attacks in Tic Disorders to other Psychiatric Populations

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Background: Rage attacks are common in patients with chronic tic disorders (CTD) occurring in 25–70% of patients. Typically they are short-lasting, intense, impulsive and emotional reactions on situations or stimuli that cannot be controlled willingly. The affected person is completely aware of this inadequate behavior often resulting in shame. Since, there is no standardized assessment instrument available, we developed the Rage Attack Questionnaire (RAQ), the first self-assessment to measure rage attacks in GTS. This study aimed to investigate frequency and intensity of rage attacks using the RAQ in a large sample of adult patients with CTD compared to both healthy controls (HC) as well as a general psychiatric population including an inpatient (acute psychiatric care as well as more specialized treatment units for drug abuse and borderline personality disorder) and an outpatient population. We aimed to 1) validate the RAQ and 2) compare the prevalence of rage attacks in CTD to those in both HC and other psychiatric populations.

Methods: The RAQ consists of 22 items given on a 4-point Likert scale (0 - 3). The total score is calculated by summing the scores (0-66). 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, both the Barratt Impulsiveness Scale-short version (BIS-15) and the Scale of Impulsive Behavior (I-8) for impulsivity, and the Gilles de la Tourette Syndrome–Quality of Life Scale (GTS-QoL) for disease specific quality of life.

Results and Conclusions: For this study we recruited 127 (89m, 38f) patients with CTD, 645 age- and sex-matched HC, and XX patients from general psychiatry. Compared to HC, patients with CTD demonstrated significantly more rage attacks using the RAQ (CTD: 25+15.36, HC: 10.37+9.48, $p<0.001$). Based on our findings rage attacks represent a clinical phenomenon distinct from ADHD and impulsivity that impairs patients' quality of life. Further results compared to general psychiatric patients will be presented to investigate whether rage attacks as assessed by the RAQ represent a specific symptom for patients with CTD.



Web platform and SQL tools to facilitate data integration from questionnaires

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Background: The Emtics project, European multicenter pan-European Tics Study, funded by the European Commission seventh Framework programme (FP7) required an instrument to collect data from the participating centers, located in different countries. The most important aim was to develop a database able to respond to new research questions, new questionnaires, for further data “just in time”. It was necessary to have a flexible tool to allow rapid responses. A reliable platform in a secure environment, establishing an effective electronic data capture system for the cohort studies and the treatment study enabling the coupling of measurements with the electronic data capture system having as result a Europe-wide database for the longitudinal cohort studies and the associated measurements obtained from the participants.

Methods: The platform, an integrated e-CRF (Electronic-Case Report Form), based on a web platform with patient data, related visits and a large number of questionnaires.

Through this methodology, it was possible to provide a web-based data system to host all the variables necessary for EMTICS, highly customized.

Quality checks performed at different stages. During the data entry phase, real time checks: automatic verification of missing data, format of input data; data out of bounds, interval. Lastly also backoffice analyses: statistical checks on data to verify significant differences in relation to expected values. The platform has also been set up for biological data linked to patient data. Export tools of raw data implemented in various format according to the most widespread statistical packages.

Results and Conclusions: The developed solution fully responded to the need of the project and suitable in other context with the same characteristics.

A relational database with specific technical solutions developed for this purpose. This allowed the modification/implementation of new questionnaires using only SQL tools, ensuring a substantial reduction of time.

Immune system involvement in Tourette's syndrome: a study of brain metabolites and antigen-presenting cells

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Background and aims: There is evidence that Tourette's syndrome (TS) physiopathology, as well as other neurodevelopmental disorders, could involve a dysfunctional neural-immune crosstalk. This might lead to altered maturation of brain pathways controlling different behavioural domains and differences of immune and stress responses (Martino, 2015). Dendritic cells are major players in innate immunity and have important functions in the phagocytosis of pathogens, antigen presentation, activation of naïve T cells, induction of tolerance and cytokine/chemokine production. Changes in their number have been observed in several autoimmune conditions (Jego, 2003). Magnetic resonance spectroscopy (MRS) offers the opportunity to explore neuro-inflammation and glial cells by measuring brain metabolites. The elevation of total choline (tCho), representative of membrane turnover, and myo-inositol (mI), a marker of glial cells and inflammatory changes, has been interpreted as glial activation (Breece, 2013). With this study we aim to better understand in vivo aspects of neuro-inflammation in TS patients exploring the possible relationship between brain metabolites and peripheral markers of immune dysregulation.

Methods: So far, we have studied 10 patients and 10 age and gender matched controls healthy volunteers (31 +/-7 yr; 6 males with TS, 5 male controls). Subjects with known inflammatory or auto-immune disease were excluded. We collected patients' demographic and clinical data as well as measures of disease severity included adult ADHD Self-Report scale (ASRS), Yale Global Tic Severity Score (YGTSS), Yale-Brown Obsessive Compulsive Scale (Y-BOCS) and Beck anxiety and depression score (BAI, BDI-II). Flow cytometry of venous blood was used to study myeloid dendritic cells type 1 and 2 (mDC1, mDC2). Proton magnetic resonance spectroscopy (1H-MRS) was acquired in frontal white matter (FWM) and putamen (PUT) to measure total choline (tCho), myo-inositol (mI), total creatines (tCr) and N-acetylaspartate (NAA) levels.

Results and Conclusions: The two groups were similar for demographic and clinical characteristics. Only FWM Cho/Cr was significantly different between



groups with significance $p = 0.008$ for a t-test and $p = 0.014$ for GLM analysis with age and gender as covariates. We also observed a trend for a greater percentage of mDC type 1 in TS patients, $r = 0.763$, $p = 0.028$. Moreover, there was a significant correlation of FWM tCho/tCr with mDC type 1 cells for TS patients, with a similar but weaker correlation for healthy volunteers (Fig.1). Our data suggests potential signals of metabolite changes in TS patients' brain, particularly in the FWM, which could be proportional to the degree of neuro-inflammation. Similarly, the trend for greater frequency of mDC type 1 in TS patients might support the hypothesis of a relationship between innate immune cells over-activation and metabolic brain changes. This is an ongoing study, we are aware of the limitation due to the small number of subjects, in fact we are aiming towards a final target of 25 subjects per group.

Decreased Transfer of Value to Action in Tourette Syndrome

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Background: Tourette syndrome (TS) is associated with a dysfunctional dopaminergic system, putatively best explained by dopaminergic hyperinnervation. The ability to learn based on rewards and punishments might be altered in TS, as midbrain dopaminergic activity acts as a teaching signal for learning from both factual and counterfactual outcomes.

Importantly, medial frontal and parietal EEG deflections are well suited to capture reinforcement learning processes. We hypothesized impaired probabilistic learning in TS and expected these changes to be reflected in decreased interrelations between model-derived parameters and neural activity.

Methods: We tested whether adult TS patients exhibited altered reinforcement learning and corresponding feedback-related EEG deflections using a reinforcement learning task providing factual and counterfactual feedback. The paradigm presented various reward probabilities to enforce adaptive adjustments. We employed a computational model to derive estimates of the prediction error, which we used for single-trial regression analysis of the EEG data.

Results and Conclusions: The behavioral results show that model-derived learning rates of TS patients did not differ from healthy controls indicative of unaltered value update. We did observed significantly altered choice temperature TS patients, implying a weakened influence of established values on choices. On a neural level, the feedback-related negativity represented an axiomatic prediction error for factual feedback and did not differ between groups. Importantly, TS patients showed reduced coding of factual feedback in the P3a and P3b implying diminished attentional capture and disrupted tracking of the stimulus values, respectively. In short, our findings indicate that cortical prediction error coding is unaffected by TS but the transfer of learned values into choice formation is attenuated.

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

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Background: Clinical observations as well as neuroanatomical characteristics of Gilles de la Tourette Syndrome (GTS) indicate the possibility of social cognition impairment in patients with GTS. It could result difficulties in emotion recognition or formulation of mental representations. The main goal of this study was to assess possible theory of mind (ToM) deficits in children and adolescents with GTS and an identification of potential connection between ToM deficits and type and severity of the tics.

Methods: Participants: 35 children and adolescents with GTS, 35 healthy control participants, and 35 participants diagnosed with ASD. The study group mainly consists of children and adolescents aged 9 to 16 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 ToM Task Battery, Strange Stories Test, and Faux Pas Recognition Test, YGTSS, ASRS (Autism Spectrum Rating Scale), Stanford - Binet Intelligence Scale (SB-5), and optionally K-SADS-PL (Schedule for Affective Disorders and Schizophrenia for School-Age Children Present and Lifetime Version).

Results and Conclusions: There is connection (negative correlation) between severity of the vocal tics and altered social cognition in terms of understanding non-literal language. Understanding of false belief (first, second and third order), understanding of hints, white lie and joke appeared to be intact. Patients with GTS may show small differences in interpretations of humorous stimuli (unconventional interpretations). The findings of our study are coherent with structure of social cognition impairments reported by previous studies. GTS may be associated with changes in reasoning on tasks involving social, emotional, and non-literal language aspects. There are numerous limitations associated with our study, especially methodological issues related to the sample selection and size.

Dystonic tics in patients with Gilles de la Tourette syndrome

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Background: Gilles de la Tourette syndrome (GTS) is a childhood onset disorder characterized by motor and vocal tics. Different types of motor tics may occur in GTS, among other, dystonic tics (DTs). Although DTs have been recognized as part of GTS symptomatology, little is known about their risk factors and how often and at which age they appear in affected individuals. The aim of our study was to investigate lifetime prevalence and clinical correlates of DTs in Polish cohort of GTS patients.

Methods: We performed a prospective, one-registration study in a cohort of 207 consecutive ambulatory patients (mean age 16.5 ± 9.4 , 76 adults and 131 children, 162 males) with GTS. Duration of GTS was 9.0 ± 8.0 years (range: 1-39 years). DTs were diagnosed during the interview. DTs were defined as lasting longer than clonic tics, that were characterized by abnormal dystonia-like movements that lead to sustained but not fixed posture.

Results: DTs occurred at some point in the lifetime of 73.9% ($n=153$) patients. In 41.2% of patients ($n=63$) DTs was only present in the past, but not at the time of evaluation. The prevalence of DTs in adults and children was almost the same ($p=0.963$, 75%, $n=57$ vs 73.2%, $n=96$, respectively). Age at onset of DTs was known only in 57% ($n=86$) of patients with the most frequent onset in children (7-11 years, 74.4%, $n=64$), followed by adolescence (12-18 years; 17.4%, $n=15$) and adulthood (≥ 18 years, 8.1%, $n=7$). DTs occurred 3.7 ± 4.2 years after the tic onset and mean age of DTs onset was 9.9 ± 5.2 years. On average patients suffered from 1.8 ± 1.7 types of DTs. The most frequent manifestations of DTs were: eyes (tightening resembling blepharospasm 84.3%, $n=129$ and oculogyric crisis 45.8%, $n=70$), trunk (dystonic postures 59.5%, $n=91$), jaw (bruxism 34.6%, $n=53$), neck (30.7%, $n=47$), upper limb (26.1%, $n=40$) and foot (20.9%, $n=32$). Multivariate logistic regression analysis showed significant associations of DTs with total number of simple and total number of complex tics.

Conclusion: DTs are early and frequent symptoms of GTS. They tend to localize in the face area. DTs occur more frequently in individuals with the higher number of tics and probably add to global impairment caused by tics.

How familial is GTS?

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Background: Genetic factors play an important role in Gilles de la Tourette syndrome (GTS). The aim of our study was to investigate family history (FH) of GTS, tics, obsessive-compulsive disorder (OCD) and obsessive-compulsive symptoms (OCS) in probands with GTS.

Methods: We performed a prospective, one-registration study in a cohort of 207 consecutive ambulatory patients (131 children, 162 males) with GTS. The information about FH was taken during the interview from the parents or patients themselves. The affected members of family were not personally interviewed except those who attended the patient clinical evaluation.

Results: 158 patients (76.3%) had positive FH either for tics or GTS, and 73 subjects (35.3%) had positive FH for OCD or OCS. 48 patients (23.2%) had at least one person with GTS in his/her family and 110 patients (53.1%) had positive FH for tics others than GTS. Particularly, in group of patients with positive FH (n=158) of tics or GTS, 71 patients (44.9%) had relatives with tics from maternal side, 71 (44.9%) from paternal side, 35 (22.2%) had siblings with tics and 6 (3.8%) had children with tics (multiple answers possible). On average there were 4.2±1.8 (range 1-10) relatives with tics or GTS. 57 (27.5%) patients had positive FH for OCS and in 16 cases (7.7%) there was a positive FH for OCD. In this group, 42 patients had relatives with OCD or OCS from maternal side (20.3%), 20 (9.7%) from paternal side, 16 (7.7%) had siblings with OCD or OCS and 1 GTS patient had children with OCS or OCD (multiple answers possible). Limitations included recall bias from persons who delivered the data on family history.

Conclusion: Two third of probands with GTS had positive family history of tics or GTS and more than one third of obsessive-compulsive symptoms which suggests strong heritability of GTS.

Meta-Analysis: Adulthood Prevalence of Tourette syndrome

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Background: Tourette syndrome (TS) is estimated to have a prevalence of 0.30-0.77% in school aged children. Longitudinal studies suggest that roughly half-to-two-thirds of children with TS experience a substantial improvement in tic symptoms during adolescence. By contrast, few studies have examined adulthood prevalence of TS. Accurate prevalence estimates across the lifespan are needed to support regulatory and public health decisions in the area.

Methods: We searched PubMed and EMBASE for studies that examined the prevalence of TS in adults. We conducted a random-effects meta-analysis of logit event rates to estimate prevalence of TS across studies. Too few studies are available to conduct moderator analysis or examine publication bias.

Results: Three studies involving 2,356,485 participants were included. There were significant differences in TS adulthood prevalence estimates between studies ranging from 49 to 657 cases of TS per million adults. Overall prevalence of TS in adulthood was estimated to be 118 cases of TS per million adults (95%CI: 19-751 cases per million adults). There was a large amount of heterogeneity between studies ($I^2=99\%$) that was likely related to differences in their methods of identification of TS cases. By contrast, the male:female ratio of risk of adulthood TS was similar between studies with a Risk Ratio=2.33 (95% CI: 1.72-3.16).

Conclusion: Estimates of adulthood prevalence of TS are sparse and likely highly affected by differences in method of case identification. Diagnosis and diagnostic estimates of TS could be aided by including a requirement for impairment as well as potential remission criteria similar to other psychiatric conditions.



Serotonin transporter binding is increased in Tourette syndrome with Obsessive Compulsive Disorder*

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Background: While the importance of the serotonergic system in psychiatric disorders such as obsessive compulsive disorder (OCD) is well established, its role in Tourette syndrome (TS) is still uncertain. In patients with “pure OCD”, most studies demonstrated reduced brain serotonin transporter (SERT) binding capacity in different brain regions. In TS, available data from a small number of imaging studies also suggested a reduction of SERT availability. However, so far it is unclear, whether alterations in SERT availability are related to tics or to comorbidities such as OCD (TS+OCD).

Methods: Here, we investigated for the first time SERT binding in TS patients with (TS+OCD) and without OCD (TS-OCD) compared to both healthy controls (HC) and OCD patients. using the selective, high affinity SERT imaging ligand [¹²³I]2-((2-((dimethylamino)methyl)phenyl)thio)-5-iodophenylamine ([¹²³I]ADAM) and single-photon emission computed tomography (SPECT). In addition, we investigated the influence of treatment with the selective serotonin reuptake inhibitor (SSRI) escitalopram on binding capacities. We included 33 adult subjects (10 HC, 10 TS-OCD, 8 TS+OCD and 5 OCD). After baseline data acquisition, all patients suffering from OCD (patients with TS+OCD and OCD) received oral treatment with escitalopram. Starting dose was 10 mg/day. Dose was increased gradually by 10 mg/week, if well tolerated up to a maximum dose of 30 mg/day, followed by a maintenance phase. In patients with OCD and TS+OCD investigations including [¹²³I]ADAM SPECT were repeated after 12-16 weeks treatment with escitalopram.

Results: At baseline, SERT binding was normal in patients with OCD and TS-OCD, but significantly increased ($p < 0.05$) - particularly in caudate and midbrain - in those with TS+OCD compared to both HC and TS-OCD. In both, patients with OCD and TS+OCD, treatment with escitalopram resulted in a significant overall reduction in SERT binding (range, 19 to 79%, p values between 0.0409 and < 0.0001) without any correlation with clinical improvement.

Conclusions: Our results provide further evidence that alterations in the serotonergic system in TS are related to comorbid OCD, are unrelated to tic severity and do not represent the primary cause of the disease. In contrast to recent SPECT studies, but in line with a study using [¹⁸F]altanserin PET, we found increased SERT binding in patients with TS+OCD. Differences might be related to small sample sizes and different imaging techniques.

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A case study of a child with complex TS treated with intensive CBIT and close school liaison

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Background: Tourette Syndrome (TS) is a neurological condition affecting ~1% of school-age children in the general population¹. Around half of young people diagnosed with TS have comorbidities² with the most common including Attention Deficit Hyperactivity Disorder (ADHD)³ and Obsessive Compulsive Disorder⁴.

Tic expression can be stimulated by both external reinforcers (e.g. responses from others, environment) and internal motivators (strong feelings)⁵. These reinforcers can therefore make TS even more impairing⁶ to a child's daily functioning⁷ and quality of life⁸. Behavioural treatments are considered first-line in the treatment of TS^{9,10} and the role of environmental reinforcers also shows potential benefits¹¹, but little is known about how this should be integrated into treatment. The purpose of this case report was to shed light on the key factors that led to a successful outcome for one child with severe TS.

Methods: Jacob was referred due to his severe and enduring TS, and associated difficulties of additional 'tic-like' movements, anxiety and OCD. These symptoms impaired his daily functioning/ school attendance. Jacob attended a group psycho-education session and individual behavioural treatment for TS. Comprehensive Behavioural Intervention for Tics^{12,13} was delivered through a combination of three intensive sessions (3.5 hours) and three telemedicine sessions (1 hour). School staff attended part of Jacob's treatment and functional analyses were completed with parents, education and local mental health services.

Results: Clinically meaningful improvements were seen on all measures including Yale Global Tic Severity Scale (YGTSS), Children's Global Assessment Scale (CGAS) and Goal Based Outcomes (GBOs).

Conclusions: Several factors impacted on successful treatment, including:

- Putting Jacob at the centre of his treatment enabling him to identification of triggers, consider perpetuating factors and empowering him to take charge in implementing strategies.
- Supporting the family to identify key reinforcers (home/school) and develop alternative methods of rewarding Jacob, without reinforcing tics.
- Close liaison and involvement with school, to create a cohesive plan used by all adults involved.

We argue the functional component was central to Jacob's positive outcome, illustrating it is fundamental to behavioural tic treatments.



Developmental Motor Profile in Preschool Children with Primary Stereotypic Movement Disorder

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Background: Different neuropsychological dysfunctions have been described in children with primary Stereotypic Movement Disorder (SMD), mainly attention or motor coordination problems. Up to now no study has evaluated psychomotor functions in preschoolers primary SMD. The aim of this observational study was to gather information on the motor profiles of SMD patients in this age range in comparison with typically developing children.

Methods: Twenty-six children (four girls) aged 36 to 76 months (mean= 53 ±10) with primary SMD were assessed by a structured evaluation including the Movement Assessment Battery for Children-Second Edition (MABC-2), the Beery-Buktenica Developmental test of Visual-Motor Integration (VMI), the Repetitive Behaviour Scale-Revised (RBS-R), the Motor Severity Stereotypy Scale (MSSS), and the Child Behaviour Checklist (CBCL). The diagnoses of Intellectual Disability or Autism Spectrum Disorder were exclusion criteria from the study. A comparison group of twenty-seven (four girls) typically developing children without stereotypies aged 36 to 59 months (mean= 48 ±7) was also examined.

Results: The MABC-2 total score was lower than 15th percentile in fifteen children with SMD (58%); the worst performances were observed in Balance and Manual Dexterity subtests. The motor coordination score of VMI was lower than 15th percentile in ten children (38%). The majority of the children with low scores at MABC-2 also had low scores at the motor coordination subscale of VMI. MABC-2 standard scores of the clinical group were significantly lower than those of controls on MABC-2 Total, Balance, and Ball Skills subtests.

Conclusions: The finding of widespread dysfunction of gross and fine motor abilities in preschoolers with primary SMD seems to delineate a peculiar phenotype and could provide new approaches to the management of this neurodevelopment disorder.

Implementation and evaluation of a therapeutic online coaching using habit reversal training in children with chronic tic disorders

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Background: Habit reversal training (HRT) is an effective intervention for reducing tics, but the availability of this intervention is still limited. Furthermore cognitive-behavioral psychotherapeutic interventions often struggle with problems of implementation in daily routine, which is often essential for generalizing therapy effects.

Methods: Objective of this study is to evaluate a therapeutic online coaching (via videoconference) using HRT in the natural environment of children and adolescents with tic disorders in addition or alternative to face-to-face therapy. The patients are guided by the therapist to implement and practice HRT in critical situations (e.g. during increase of tics after school or in the evening).

In a single case study, the first results/trends are to be obtained for exploratory purposes, especially with regard to the questions:

- Can online coaching be implemented?
- Does online coaching reduce tic symptoms and functional impairment?
- Is online coaching experienced as helpful by the patient and the therapist?

It is expected that the effectiveness of the entire treatment is increased by the (additional) online coaching and the entire duration of treatment is shortened. The efficacy and applicability of online coaching is carried out in a single case study with multiple baseline design in a total sample of n = 4 children and adolescents aged 8-17. Online coaching takes place 2-3 times a week and a maximum of 12 weeks. In order to evaluate online coaching, various outcome measures are assessed (clinical rating (YGTSS), parent and self-ratings assessing severity of symptoms, psychosocial functional level, practical implementation and satisfaction). The change during a baseline phase is compared to the change during the intervention phase.

Results and Conclusions: Initial experiences show a good feasibility of online coaching.

Neural correlates of performance monitoring in adult patients with Gilles de la Tourette syndrome: A study of event-related potentials

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Background: Basal ganglia circuits are involved in the pathology of Gilles de la Tourette syndrome (GTS), but also play an important role in different cognitive processes. Specifically, we were interested in examining interference resolution (the ability to distinguish task-relevant and distracting stimuli) and performance monitoring (the ability to monitor responses and mistakes during a task) in adult patients with GTS. These can be assessed using the flanker task, which requires participants to indicate the direction of a ‘target’ arrow that is flanked by 2 ‘distractor’ arrows. The target and flanker arrows face the same direction in the congruent condition, but opposite directions in the incongruent condition, which typically produces slower reaction times and higher error rates.

Methods: We assessed N = 23 adult patients with GTS (mean age=32.78, SD=11.11, female=10) using the flanker task during an EEG recording session compared to N = 27 age- and sex-matched healthy controls (HC). We examined behavioural performance using reaction time and error rates, as well as the N2 event-related potential (ERP) as an indicator of interference resolution, and the error-related negativity (Ne/ERN) as an index of performance monitoring. The Ne/ERN is a negative frontocentral ERP that occurs when a mistake is made.

Results: Behavioural results showed significantly enhanced congruency effects on reaction times of patients with GTS compared to HC ($p = .032$). Error rates did not differ between groups ($p = .992$).

Electrophysiological data revealed a significantly larger Ne/ERN in patients with GTS compared to HC at the Fz electrode (GTS: $-9.00 \mu V$; HC: $-5.57 \mu V$; $p < .001$). The N2 and Ne/ERN were more frontally distributed in patients with GTS, while HC demonstrated central distributions.

Conclusions: Our data indicate neural alterations in error processing in adult patients with GTS compared to HC, which is not due to differential error probabilities.

The N2 and Ne/ERN data are consistent with literature, although this is limited in adults. Our data suggest that patients may compensate for insufficient task preparation by using attentional resources from frontal pathways to maintain behavioural performance. Alternatively, they may perceive mistakes as being more salient than controls, due to obsessive compulsive tendencies.

Abnormal thalamo-cortical functional connectivity patterns in Gilles de la Tourette Syndrome: a seed-based resting state fMRI study

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Background: Gilles de la Tourette Syndrome (GTS) is a neuropsychiatric disorder characterized by tics, which are recurring and unwanted movements or vocalizations. The disease is an example of dysfunctional motor control, with interferences in planning, selection and programming of voluntary actions. Pharmacological and imaging studies suggest that GTS is characterized by perturbed connectivity within cortico-sub-cortical motor networks.

Here we directly tested this hypothesis and we investigated the specific functional connectivity patterns of thalamic motor seeds in 24 GTS patients and 24 healthy controls, by means of a resting state fMRI approach.

Methods: To this end, we used a 3-steps methodology. We first identified the stereotactic coordinates of motoric thalamic seeds by selecting, with a univariate analysis, the most significant peaks of activation in the right and left thalamus recorded during the execution of voluntary finger opposition movements, in both healthy controls and GTS patients. Then, the functional connectivity maps of these regions of interest were calculated for each subject/patient by using a seed-to-voxel whole brain approach.

Finally, the individual maps were entered in a full factorial analysis with Group (Patients/Healthy Controls) and Seed (Left Thalamus/Right Thalamus) included as factors.

Results and Conclusions: The results showed significant differences between the two groups in the form of abnormally augmented functional connectivity in GTS patients between the right thalamic seed and the cortical motor areas (premotor and primary motor cortex).

This abnormal connectivity was positively related to the severity of the syndrome: the greater the abnormal connectivity, the more severe the disease in terms of tics manifestation. In turn, the strength of such connectivity was compensated for by neuroleptics whereby the larger the dosage of neuroleptics the smaller the value of such connectivity.

Our findings confirm the presence of an altered subcortical-cortical functional network in Gilles de la Tourette syndrome, highlighting the important role of the connections between the motor thalamus and premotor/primary motor cortex.



Group Comprehensive Behavioral Intervention for Tics (CBIT) vs. Educational Intervention for Tics (EIT): Effects on Parental Distress

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Background: Tourette syndrome and chronic tic disorders (TD) are associated with reduced quality of life (QoL) and may have adverse effects on family members, including high parental stress. Parents' training and active involvement in treatment have been reported to increase treatment gains in children with anxiety, ADHD, and behavioral problems. Comprehensive Behavioral Intervention for Tics (CBIT) is effective in reducing tic severity and concomitant symptoms in children with TD. However, no data exists for CBIT effect on parents, and the relation to their child's symptoms.

Methods: Children with TD (age 9-15, 45 boys) were randomly assigned to group-CBIT (n=23) or group-educational intervention for Tics (EIT; n=23). Children received eight weekly group sessions followed by three monthly sessions, while their parents received five group sessions, according to their child's assignment. Parents QoL, sense of competency, and depressive symptoms were explored in relation to children's symptoms and intervention contribution.

Results: Children's baseline emotional-behavioral problems correlated with parents' QoL, sense of competency, as well as their gain from intervention. Child's anxiety, somatic complaints, social and cognitive problems, and aggressive and rule-breaking behaviors correlated with parents' QoL. Similarly, child's anxiety, and aggressive and rule-breaking behavior correlated with parents' sense of competency. Neither CBIT nor EIT improved parental sense of competency. However, following CBIT (but not EIT), parental depressive symptoms significantly decreased. Lower baseline child obsessive-compulsive symptoms were associated with greater decrease in parental depressive symptoms following CBIT. Parental baseline anxiety negatively correlated with improvement in child tic impairment and decrease in child anxiety following both interventions.

Conclusions: Children's symptoms are indeed relevant to parents' QoL, sense of competency, as well as gain from intervention. While not improving sense of competency, CBIT contributed in decreasing parents' depressive symptoms. In turns, parental anxiety was relevant to children's gains from intervention.

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