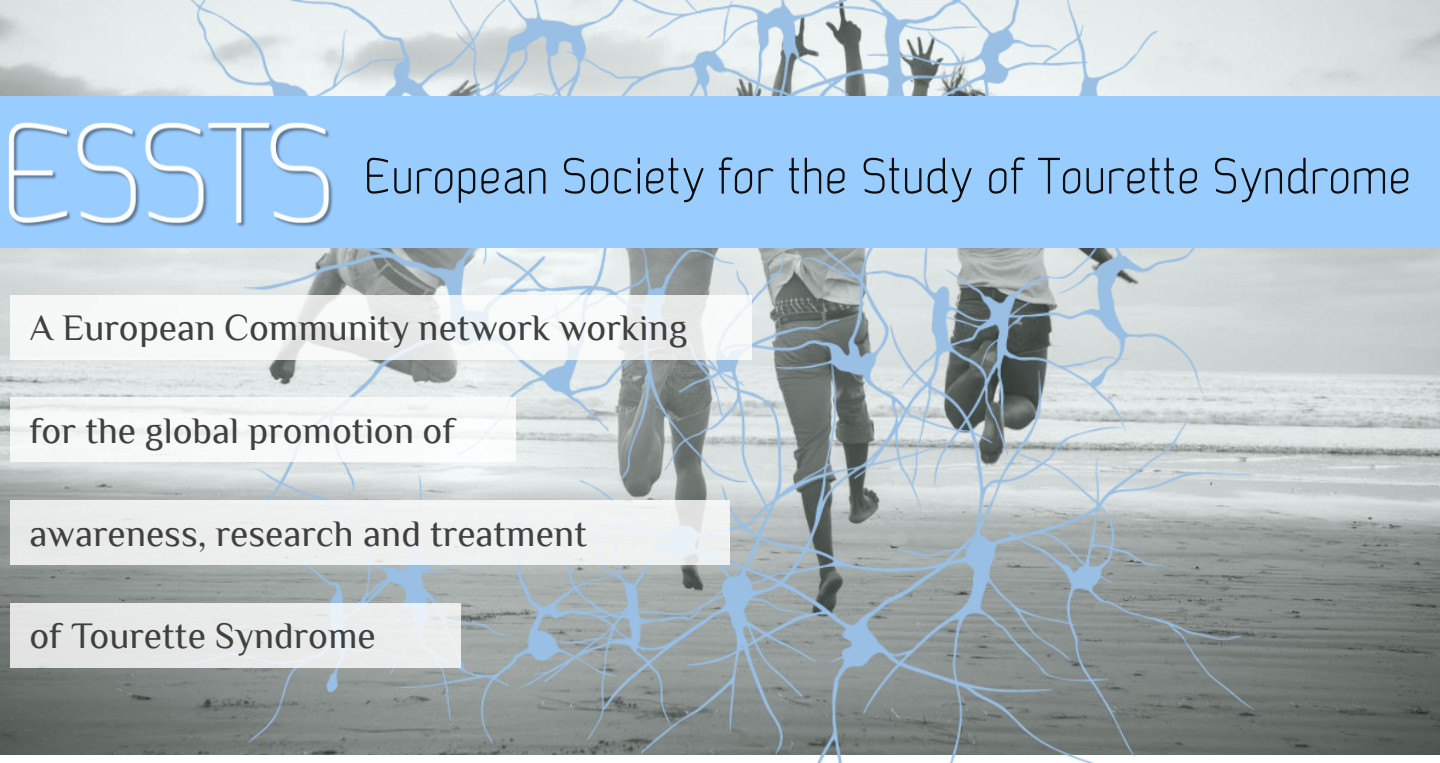
ESSTS European Society for the Study of Tourette Syndrome



Catania, ITALY 2012

Start Time: 8 June 2012
End Time: 9 June 2012
Where: University of Catania - Catania, Italy

5th European Conference on Tourette Syndrome and Tic Disorders

The European Society for the Tourette Syndrome and the "European Network for the Study of Gilles de la Tourette Syndrome" (COST Action BM 0905) are pleased to announce the 2012 ESSTS Annual Meeting and COST International Conference for Tourette Syndrome.

This year's meeting will take place in Catania, on June 8-9 2012, hosted be the University of Catania, will feature presentations from leading researchers and clinicians in the field of Tourette Syndrome and will be preceded by the 2012 COST Action Clinical Training School on the diagnosis and assessment of TS.

The inaugural ESSTS 2012 Lifetime Achievement Award will be presented to Prof. Mary Robertson (University College London, UK).

Scientific Committee:
Hartmann Andreas (France)
Hoekstra Pieter (Netherlands)
Müller Vahl Kirsten (Germany)
Rizzo Renata (Italy)
Robertson Mary (United Kingdom)
Paschou Peristera (Greece)

ESSTS Board members:
Chair: Paschou Peristera (Greece)
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ESSTS 2012 Annual Meeting Awards

2012 ESSTS Lifetime Achievement Award

Mary Robertson, University College London, United Kingdom

Best Oral Presentation by an Early Stage Researcher

Elif Weidinger, Vinzenz von Paul Hospital Rottweil, Germany

Best Poster Presentation by an Early Stage Researcher

Eleanor Crossley, University of Birmingham, United Kingdom

Tammy Pilowsky, Schneider Children's Medical Center of Israel, Israel

Friday, June 8th 2012, University Hospital

Aula Magna – Policlinico COST Action BM0905 Training School

9:00-10:30 Invited Session I

Neurobiology and Genetics (Chair: Andreas Hartmann, University Pierre and Marie Curie, France)

L1. The immune system in Tourette Syndrome. Davide Martino, Queen Mary University, UK

L2. The genetic basis of Tourette Syndrome. Peristera Paschou, Democritus University of Thrace, Greece

L3. Reinforcement learning and Tourette Syndrome. Stefano Palminteri, University Pierre and Marie Curie, France

11:00-12:30 Invited Session II

Comorbid and coexistent psychopathology (Chair: Kirsten Müller-Vahl, Hannover University, Germany)

L4. Learning disorders and Tourette Syndrome. Andrea Ludolph, University of Ulm, Germany

L5. Impulse control disorders and Tourette Syndrome. Andrea Cavanna, University of Birmingham, UK

L6. Personality Disorders in Tourette Syndrome. Stefanie Bokemeyer, Hannover University, Germany

L7. Prevalence of Tourette Syndrome comorbidities and their development over the time. Nanette Mol Debes, Herlev University Hospital, Denmark

11:00-12:30 Invited Session III

Patient Support and Advocacy Groups (Chairs: Suzanne Dobson, Tourettes Action UK; Michele Dunlap, Tourette Association Germany; Daniel Weber, NEMO, Germany)

L8. Overview: Activities of TS Foundation of Canada. Lynn McLarnon, TS Foundation, Canada

L9. What do patients want/need to know from health professionals. A UK perspective. Jeremy Stern, Suzanne obson, Tourettes Action UK

L10. Planning a European Tourette Day. Kirsten Mueller-Vahl, University of Hannover, Germany; Zsanett Tarnok, Vadaskert Clinic for Child and Adolescent Psychiatry, Hungary

17:30-18:00 Opening Ceremony

Aula Magna Catania University

Honorary Presidents: F. Basile (Italy), L.Pavone (Italy)

Prof. A. Recca: Dean Catania University

Prof. E. Fiore: Chair Dipartimento di Scienze Mediche e Pediatriche

Dott. A. Giacalone: Direttore Generale AOU Policlinico OVE

Dott. A. Lazzara: Direttore Sanitario AOU Policlinico OVE

Prof. P. Paschou ESSTS Chair

18.00-19.00 Invited Session IV

ESSTS Lifetime Achievement Award 2012 (Chairs: R. Bernardini, Italy; P. Curatolo Italy)

Recipient and keynote speaker: Mary Robertson, University College London, UK

The Gilles de la Tourette Syndrome. The current status with regards to Phenomenology and Aetiology.

Friday, June 9th 2012, University Hospital

Aula Magna – Policlinico

9:00-10:30 Oral Presentations – Session V

Basic Science Research for Tourette Syndrome

O1. Searching for the genes of Tourette's: the TIC genetics project Heiman GA(1), Dietrich A(2), Hoekstra PJ(3)

(1)Rutgers University, Department of Genetics, Piscataway, NJ 08854-8082, USA, (2)University Medical Center Groningen, Department of Child and Adolescent Psychiatry, University of Groningen, Netherlands, (3)University Medical Center Groningen, Department of Child and Adolescent Psychiatry, University of Groningen, Netherlands

The Tourette's International Collaborate Genetics (TIC Genetics) Study unites a group of highly experienced clinicians specializing in Tourette's disorder (TD) with statistical and molecular geneticists with a strong record of collaboration across the United States, Europe, and South Korea. The goal is to conduct a comprehensive genomics study of

TD concentrating on the potential contribution of rare and structural variants. We will ascertain over 1500 individuals over three years, focusing on the identification of TD pedigrees with 3 or more affected members and familybased association trios for pedigree-based gene discovery. The DNA and cell lines will become part of the National Institute of Mental Health (NIMH) Repository at Rutgers University as an international resource. The samples will be initially analyzed by TIC Genetics Study researchers and later made public by the NIMH to qualified scientists around the world to study how genes cause TD. In this presentation, we will specifically highlight (1) the structure and clinical assessments of the TIC genetics collaboration, (2) first published results by the TIC genetics collaboration, and (3) the research objectives, with a focus on identification of rare versus common genetic variants, gene expression and gene*environment interactions. We will also explore the potential for collaborative genomic research within the framework of ESSTS.

O2. Investigation of the possible involvement of the Histidine Decarboxylase Gene (HDC) in Tourette Syndrome etiology

Karagiannidis I(1), Stathias V(1), Anastasiou Z(1), Rizzo R(2), Tarnok Z(3), Dehning S(4), Zill P(4), Heberbrand J(5), Noethen MM(6), Lehmkuhl G(7), Barta C(8), Farkas L(3), Nagy P(3), Ligda P(1), Androutsos C(9), Koumoula A(9), Madruga-Garrido M(10), Mir P(10), Szymanska U(11), Wolanczyk T(11), Mueller N(4), Sandor P(12), Barr C(12), TSGeneSEE(13), EUNetGTS(14), Paschou P(1)

(1) Dept. of Molecular Biology and Genetics, Democritus University of Thrace, Greece (2) Materno-Infantile and Radiological Science Department, University of Catania, Italy (3) Vadaskert Clinic for Child and Adolescent Psychiatry, Hungary (4) Department of Psychiatry, Ludwig-Maximilians-University Munich, Germany (5) Department of Child and Adolescent Psychiatry, University of Duisburg-Essen, Essen, Germany (6) Institute for Human Genetics, University of Bonn, Germany (7) Department of Child and Adolescent Psychiatry of the University of Cologne, Germany (8) Department of Medical Chemistry, Molecular Biology and Pathobiochemistry, Semmelweis University, Hungary (9) Department of Child and Adolescent Psychiatry, Sismanoglio General Hospital of Attica, Greece (10) Sección de Neuropediatría. Instituto de Biomedicina de Sevilla (IBiS), Seville, Spain (11) Department of Child Psychiatry, Medical University of Warsaw, Poland (12) Toronto Western Research Institute, University Health Network, Toronto, Ontario, Canada
(13) Tourette Syndrome Genetics Southern and Eastern Europe Initiative (14) European Network for the Study of Gilles de la Tourette Syndrome

The etiological background of Gilles de la Tourette Syndrome (GTS) is complex, with multiple genes interacting with environmental factors to lead to the onset of symptoms. Recently, analysis of linkage in a two-generation pedigree led to the identification of a a rare functional mutation in the HDC gene encoding L-histidine decarboxylase, the rate-limiting enzyme in histamine biosynthesis. However, the participation of this gene in GTS etiology, has not yet been studied extensively, and is, up until now, considered rare. We present here our results on the investigation of the HDC gene in association to GTS in a large multi-centered study of eight populations. This is the largest study of the HDC gene in relation to HDC reported to date. A total of 521 trios with GTS were

studied, originating from Canada, Germany and Spain, as well as the TSGeneSEE consortium (Greece, Poland, Hungary, Albania, Italy, supported by the Tourette Syndrome Association, USA and COST Action BM0905). In order to cover variation across the HDC gene, 12 tagging Single Nucleotide Polymorphisms (SNPs) were selected from the HapMap database, using the CEPH Europeans as reference. The transmission test for linkage disequilibrium was run as implemented in HAPLOVIEW. Joint analysis of all 521 trios yields significant association results that withstand correction for multiple testing (both with single markers and multi-marker haplotypes) . It should be noted that, individual population analysis reveals some heterogeneity among observed LD patterns. Our results indicate that the HDC gene may play a role in GTS etiology. Interestingly, the patterns of association may vary in different populations. Our findings warrant further investigation of the intriguing histaminergic pathway hypothesis in relation to GTS.

O3. Brain activity in the Supplementary Motor Area dissociates volitional and automatic motor control mechanisms in Tourette syndrome Jackson GM (1), Parkinson A (2), Fisher M (2), Jackson SR (2)

(1)Division of Psychiatry, University of Nottingham, UK (2)School of Psychology, University of Nottingham, UK

Tourette syndrome [TS] is a neurodevelopmental disorder characterised by chronic vocal and motor tics. TS is associated with dysfunctional volitional (inhibitory) control, however the evidence for this, beyond the occurrence of tics, is scant. We used functional brain imaging to investigate, in children with TS, how brain activity within the Supplementary Motor Area (SMA] varied during the execution of two tasks previously associated with volitional and automatic motor control. We show that activation in motor cortex predicts both behavioural measures of volitional control and also clinical measures of tic frequency. More importantly, we demonstrate that comparable behavioural performance to controls is associated with increased SMA activation for the TS group during automatic motor control, but decreased SMA activation during volitional motor control. We propose that motor behaviour in TS may reflect dysfunctional short-range, automatic, motor control that can be compensated for by long-range volitional control mechanisms.

O4. Altered activity of dorsal premotor cortex during externally determined inhibition in Gilles de la Tourette syndrome Ganos C (1), Kühn S (2), Kahl U (1), Schunke O (1), Feldheim J (3), Haggard P (4), BüchelC (5), Götz T (1), Münchau (1)

(1)Department of Neurology, University Medical Center Hamburg-Eppendorf (UKE), Hamburg, Germany (2)Center for Lifespan Psychology, Max Planck Institute for Human Development, Lentzeallee 94, 14195 Berlin, Germany (3)Brain Imaging and Neurostimulation Laboratory, Department of Neurology, Universitätsklinikum Hamburg-Eppendorf, Hamburg, Germany (4)Institute of Cognitive Neuroscience,

University College London, UK (5)NeuroImage Nord, Department of Systems Neuroscience, University Medical Center Hamburg-Eppendorf, Hamburg, Germany.

Background: Gilles de la Tourette syndrome (GTS) is a prototype disorder of motor inhibition. Here, we evaluated neural correlates of inhibition in an adult, pure GTS patient sample during a stop-signal reaction-time task.

Methods: 14 pure GTS patients (mean age 30.5, SD: 8.7), diagnosed according to the DSM-IV criteria and 15 healthy Controls (mean age 32.3, SD: 8.7) were included. Tic severity was evaluated using the Yale Global Tic Severity Scale and the modified Rush videotape Rating Scale. Lifetime tic severity was assessed with the Diagnostic Confidence Index (DCI) and premonitory urges with the Premonitory Urge for Tics Scale (PUTS).

Results: Both groups had similar inhibitory task performance. Within group analysis showed wider inhibitory task-related activations (stop versus go) for the control group. Between-group analysis revealed stronger activations of the dorsal premotor cortex (Brodmann area 6) for the control group. Post hoc statistics for this region showed a significant interaction for the main effects of condition x group. While controls activated the region during the stop task, GTS patients deactivated it. Percent signal changes during the stop task in patients were found to be inversely correlated to the DCI.

Conclusion: Altered task-related activity in the dorsal premotor cortex in pure adult GTS patients may compensate for inhibitory deficits in other regions ensuring normal inhibitory task-performance. Its inverse correlation with the DCI, a lifetime-GTS trait scale, lends support to the notion that this deviant functional interplay represents a core feature of the pure GTS syndrome, rather than a state feature.

O5. Comparative Genomic Hybridisation -suggesting a possible role for NRXN1 in Tourette Spectrum Woods M (1), Bunton P (1), Grose C (1), Hindley P (1), Hedderly T(1)

(1) TANDeM, Paediatric Neurosciences, Evelina Children's Hospital, Guy's & St Thomas' NHS Foundation Trust, Lambeth Palace Road, London SE1 7EH

Introduction: The CGH array finding of 2p16.3 has been shown to be implicated in autism spectrum (ASD), schizophrenia and neurodevelopmental disorders. To our knowledge it has not yet been reported in association with Tourettes. NRXN1 is a gene located in this region and it is highly expressed in the brain. The proteins coded by this gene play a role in synaptic development and function.

Method : A 13yr boy presented with multiple phonic and motor tics to TANDeM for assessment and management advice. His neuro developmental phenotype was complex. He had been assessed for ASD including observational assessment (ADOS). He did not reach cut off for diagnosis but was noted to have some features in addition to learning difficulties. His mother has a diagnosis of schizo-affective disorder and inheritance studies are pending.Video consent is being obtained.

Results: The results of the neurological, cognitive , behavioural and social assessment will be presented. His genetic CGH Array analysis revealed a 2p16.3 x 3, 12q12 x3.

The duplication in the short arm of chromosome 2 lies within an intron of the NRXN1 Gene.

Discussion: NRXN1 is a neurexin, cell surface receptors that bind neuroligins. Complexes are formed which are Ca (2+) –dependant and which are important for efficient neurotransmission. A clinical case will be demonstrated to highlight the importance of careful clinical phenotyping when identifying potential contributing genetic anomalies in neuro-developmental disorders. This approach should l allow for targeted intervention in management in the future. Further work is planned.

O6. 9p24.1 as a possible contribution to genetic myoclonus in a girl referred with sudden onset florid ?Tics Hedderly T(1), Bunton P(1), Goyal S(1), Woods M(1), Grose C(1), Criddle J(1)

(1) TANDeM, Paediatric Neurosciences, Evelina Children's Hospital, Guy's & St Thomas' NHS Foundation Trust, Lambeth Palace Road, London SE1 7EH

Objective: We will present the case of a girl with a sudden onset florid movement disorder presenting to our A and E department. This case will allow for discussion of differential diagnosis and highlight the probable wide (as yet unknown) genetic aetiologies in children with non-epileptic myoclonus

Methods: We will show videos at presentation and discuss investigations performed including video EEG and neuro-imaging.

Results: To date after extensive investigation the only finding is the 9p24.1 array anomaly. Interesting rare associations in the literature have recently linked obsessive and repetitive symptoms in Autism Spectrum (ASD) to this region. There are glutamate transporter genes in this region (SLC1A1 and SLC1A2) which may be explored. Inheritance studies are pending. We will discuss the association of myoclonus with OCD and ASD in more detail and compare with a previous video case from ESSTS 2010 of a young girl with myoclonus now managed with the addition of Deep Brain Stimulation.

Conclusions: Copy number variants are reported commonly in the children we are investigating in TANDeM , a service for children with tics and other presumed neurodevelopmental movement disorders. We are continuing to try and determine the relevance of the CNV in this population. It is our hope that by careful clinical phenotyping, genotype correlation and by collaboration with ESSTS and USA colleagues we may be able to contribute to the further understanding about the neurobiological mechanisms of these interesting conditions.

O7. Dysfunctional fMRI patterns of Tourette syndrome beyond the ticking territories.

Zapparoli L (1), Porta M (2), Invernizzi P (1), Gandola M (1), Colajanni V (1), Banfi G (2,3), Santis A (2,3), Servello D (2), and Paulesu E (1,2)
(1) Dipartimento di Psicologia, Università degli Studi di Milano Bicocca, Milano, Italia (2) IRCCS *Galeazzi*, Milano, Italia (3) Università degli Studi Statale di Milano,

Italia.

Introduction: The physiopathology of Tourette Syndrome (TS) has not been fully clarified yet. Previous imaging studies revealed dysfunctions in thalamo-cortical and basal ganglia networks (review in 2,3) but also of cortico-cortical connectivity. Only few studies investigated the neurofunctional correlates of voluntary action in TS patients, with inconsistent findings. We used fMRI to investigate the neurophysiological correlates of motor control of the hands in TS patients with dominant orobuccal tics. We tested the hypothesis that in TS functional differences of cortical/subcortical activation can be observed even for motor acts of body segments not directly involved by the ticking manifestations.

Methods: Eight adult TS patients (mean age: 32 sd:11 yrs; median Y-GTSS 53, sd:22) and 24 age-matched controls (mean age: 27 years; sd:5.7), half males and half females, were studied. Tic distribution was orofacial for all patients.

The fMRI conditions involved cued hand movements or cued motor imagery for the same movements, both alternated with resting state in a block-design paradigm for the collection of 316 fMRI brain volumes analyzed with SPM8.

Results and comments: There was a large pattern of shared activations for the controls and the TS patients in both tasks. However, we also found hyperactivation in dorsal premotor/prefrontal cortices in TS patients. Surprisingly, the dorsal premotor/prefrontal regions had a relative reduction of grey matter as revealed by a voxel-based morphometric analysis. This evidence supports the hypothesis of a different structural and neurofunctional organization in patients with TS than in healthy subjects that generalizes for motor behaviours in territories outside those involved by the tics.

O8. Imaging the When and Where of Tic Generation Neuner I (1,2,3), Werner CJ (1,4), Stöcker T (1,3), Kellermann T (2,3), Ehlen C (2), Wegener HP (2), Schneider F (2,3), Shah JN (1,3,4)

(1)Institute of Neuroscience and Medicine - 4, Forschungszentrum Jülich GmbH, 52425 Juelich, Germany (2)Department of Psychiatry, Psychotherapy and Psychosomatics, RWTH Aachen University, 52074 Aachen, Germany (3)JARA – Translational Brain Medicine, Germany (4)Department of Neurology, RWTH Aachen
University, 52074 Aachen, Germany

Background: Tourette's Syndrome (TS) is a neuropsychiatric disorder mainly characterized by tics. Previous imaging research has identified a widespread neuronal network involved in either the suppression or occurence of tics. However, the precise spatiotemporal sequence of brain activation prior to tics is unknown.

Methods: We employed functional magnetic resonance imaging (fMRI) in 10 adult Tourette outpatients. Tics were allowed to occur freely and were acquired using a MR-compatible video system while patients rested in the scanner. We used tic onset times as regressors and added two preceding time-bins of 1s duration each to detect prior activation. Standard statistical analyses were performed on the data using publicly available software.

Results: A spatio-temporally distinct pattern of activation was found, at two seconds before a tic SMA (BA6 mesial), ventral primary motor cortex (BA6 lateral), primary sensorimotor Cortex (BA3+4) and parietal operculum were active. At one second before a tic the anterior cingulate, the putamen, the insula, the amygdala, the cerebellum and the extrastriatal-visuell cortex were active. With ticonset, the thalamus, primary motor and somatosensory cortices and the central operculum were active..

Conclusion: We demonstrate that the temporal pattern of a tic follows the corticostriato-thalamo-cortical circuit. Its origin does lies in cortical not in subcortical structures.

O9. Haematological Features of Neuro-Akanthocytosis in Tourette's Syndrome

Weidinger E (3), Gruber R (1), Resch R (1), Matz J (1), Dehning S (1), Riedel M (3), Schwarz M (1) and Müller N (1)

(1)University Hospital for Psychiatry and Psychotherapy of the Ludwig-MaximiliansUniversity, (2)Synlab laboratories Munich and (3)Vinzenz von Paul Hospital Rottweil, Germany

Objective: Clinical similarities between patients suffering from Tourette's syndrome (TS) and neuo-acanthocytosis (NA) syndromes were described repeatedly. The core findings of NA syndromes are the acanthocytic morphology of erythrocytes, associated with other haematological abnormalities. Due to phenomenological parallels between both disorders, we suggested that haematological characteristics of NA can also be found in a subgroup of TS.

Methods: To test the hypothesis of haematological abnormalities in patients with TS, we analysed major blood parameters for haemolytic and iron deficiency anaemia, such as complete blood count, haptoglobin, soluble transferrin receptor (sTfR), erythropoietin (EPO) and lactate dehydrogenase (LDH) in patients with TS (n = 48) and sex- and age matched healthy controls (n = 43).

Results: TS patients had significant elevations of mean corpuscular haemoglobin concentration (MCHC), LDH activity and EPO concentration compared to agematched controls.

Conclusion: The haematological alterations in TS patients are in accordance with a slight chronic haemolysis and in parallel with haematological findings in NA. Due to these parallels in clinical symptoms and laboratory findings it has to be discussed whether TS and NA share common pathological mechanisms.

10:30-12:00 Oral Presentations – Session VI

Clinical Research for Tourette Syndrome

O11. The relationship of epilepsy in Tourette syndrome to comorbid learning difficulties and autism Williams D (1), Grabeki K (1), Stern JS (1,2), Simmons H (2), Robertson MM (1,2,3)

(1) St. George's, University of London (2) Department of Neurology, St. George's Hospital, London (3) Department of Mental Health Sciences, University College, London

Background: Tourette syndrome is usually associated with common co-morbidities such as OCD and ADHD but also other neurodevelopmental conditions including Learning Difficulties (LD) and Autism Spectrum Disorder (ASD). Both LD and ASD are associated with high rates of epilepsy. A large sample of children with epilepsy found co-morbid tics in 19%. The TIC international consortium reported epilepsy in 9% of TS patients without ADHD and 21% of patients with ADHD. It is not clear if epilepsy in TS can be attributed to the presence of comorbidities.

Methods: Clinical details of 349 patients of all ages that had attended the St. George's Tic Disorder Clinic over the last 7 years was reviewed. Epilepsy diagnoses were reviewed by a consultant neurologist. Clinical characteristics including tic severity (YGTSS and MOVES), and comorbidities were compared.

Results: 6.1% of TS patients had epilepsy with a non-significant trend to more severe tics. They were more likely to have ADHD (71% v 53%), OCD (48% v. 22%), LD (29% v. 9%), ASD (24% v. 9%) and more comorbid conditions (5.8 v. 3.4).

Discussion: Epilepsies are at least 6 times more common in this TS cohort compared to background rates. Patients with seizures are more likely to have comorbidities including those which are known themselves to have an increased epilepsy rate i.e. LD, ASD and ADHD. Epilepsy may act as a marker for greater neurodevelopmental abnormalities, and perhaps underlying common aetiologies e.g. epileptogenesis genes. Alternatively, seizures or anticonvulsants during development could themselves lead to modulation in phenotypic severity.

O12. Tourette-related Tourettism: A Proposed Concept Bunton P(1), Hindley P(1), Hedderly T(1)

(1) TANDeM, Paediatric Neurosciences, Evelina Children's Hospital, Guy's & St Thomas' NHS Foundation Trust, Lambeth Palace Road, London SE1 7EH

Objective: To present a description of the phenomenology of Tourette-related Tourettism (TRT) and a debated aetiological framework. Three video case studies will be presented to illustrate this new concept.

Methods: We compare a proposed phenomenology of 'Tourette-related Tourettism' (TRT) with the literature surrounding non-epileptic seizures in children with epilepsy, discussing a biopsychosocial model and specifically highlighting the biological vulnerabilities underlying TRT.

Results: All patents presented with abnormal non-tic movement disorders in addition to tics. Tics, which are a defining feature of Tourette syndrome (TS), are sometimes termed 'Tourettism' when they arise as a (presumed) secondary phenomena to drugs, basal ganglia lesions or in association with other medical conditions. So-called 'psychogenic' Tourettism has previously been considered as a differential diagnosis for

TS, however, our clinical experience suggests that Tourettism and TS are not mutually exclusive disorders. We propose that the presence of the underlying tic disorder may actually predispose an individual to the development of Tourettism and so-called psychogenic movements, in parallel with emerging evidence which suggests that pre-existing epileptic disorder may predispose individuals to the development of non-epileptic seizures.

Conclusions: We debate the term psychogenic movement disorder in this group of children, finding it both pejorative and misleading in masking biological vulnerabilities, and instead propose the term Tourette-related Tourettism (TRT), defined as the presence of both movements or sounds that do not qualitatively appear like or fulfil diagnostic criteria for tics, but occur in the presence of organic tic disorder and appear to be driven by psychosocial stressors.

O13. Data presentation of a survey among ESSTS members into the application of behaviour therapy for tics Verdellen C (1) Griendt J (1) (1) HSK Group Inc.

In September 2011, a questionnaire was send by email to all ESSTS members (N=103) assessing the application of behaviour therapy for tics in Europe. Members were asked to complete the questionnaire and forward it to professionals in the field of tic disorders. The questionnaire contained 18 questions and took about 10 minutes to complete. After 3 months, 49 professionals from 11 European countries had responded and 40 professionals had completed the questionnaire. Most responders recommended psychological treatment as first-line intervention for tics. Habit reversal was the preferred behavioural method for tics, and exposure and response prevention was the behavioural method of second choice. The main reason to advise or initiate psychological treatment instead of medication for tics was the preference of the patient. The main barrier to advise or initiate psychological treatment instead of medication was difficulty finding a knowledgeable treatment provider. The results of this survey suggest that behaviour therapy for tics should be made more available in Europe.

O14. A functional MRI study of children with Tourette syndrome reveals activation in areas in the brain involved in psychiatric disorders Debes NM (1) , Skov L (1) , Hansen AE (2), Larsson H (2)

(1) Paediatric Department, Herlev University Hospital and (2) Functional Imaging Unit, Glostrup University Hospital, Denmark

Background: There is evidence that cortico-striato-thalamo-cortical pathways are involved in the pathophysiology of Tourette syndrome (TS). During performance of neuropsychological tests in subjects with TS, there are suggestions for increased activity in the sensimotor cortex, supplementary motor areas, and frontal cortex.

Aim: The purpose of this study was to confirm the hypothesis that cortico-striatothalamo-cortical pathways are involved in the pathophysiology of TS.

Methods: We have examined 22 medication-naive children with TS-only, 17 medication-naive children with TS and co-morbidity, and 39 healthy controls using functional MRI during performance of Stroop-test, a Go/no-go test, and fingertapping.

Results: There were no differences in brain activation between the children with TS (divided into a TS-only, TS+Attention Deficit Hyperactivity Disorder (ADHD), and TS+Obsessive Compulsive Disorder (OCD) group) and healthy controls after correction for the confounders age, sex, and intelligence. We did find activation patterns during performance of Go/No-go task and fingertapping that were statistically significant correlated to the OCD-score in areas in the brain that are known to be involved in OCD and other psychiatric disorders (cingulate gyrus, temporal gyrus, and medial frontal gyrus). We did not find any statistically significant correlations between the activation patterns during performance of the three tests and the covariates age, sex, duration of disease, intelligence, severity of tics, and ADHDscore.

Conclusion: There were correlations between activation patterns in areas in the brain involved in psychiatric disorders and OCD-score. There were no differences in brain activation between the children with TS and healthy controls.

O15. Depressive symptoms in Tourette syndrome and affective disorders: A controlled study Piedad CJP (1), Gordon-Smith K (2) Jones LA (2), Cavannaa AE (1,3)

(1) Michael Trimble Neuropsychiatry Research Group; University of Birmingham & BSMHFT, Birmingham, UK (2) Department of Psychiatry; University of Birmingham, Birmingham, UK (3) Sobell Department of Motor Neuroscience and Movement Disorders; University College London & Institute of Neurology, London, UK

Background : Tourette syndrome (TS) is a neuropsychiatric condition characterised by multiple motor and vocal tics, as well as a spectrum of behavioural problems. In particular, it is estimated that 76% of patients with TS experience depressive symptoms, with 13% fulfilling diagnostic criteria for affective disorder.

Objectives : We set out to compare the severity of affective symptoms in patients with TS, patients with primary affective disorders (recurrent major depressive disorder [rMDD], bipolar affective disorder types I and II [BPAD-I/II]), and healthy controls.

Methods : Patients with affective disorders and controls completed the Beck Depression Inventory (BDI)-IA, and those with TS the BDI-II. Total BDI-II scores were transformed using an equipercentile equating method for converting raw total BDI-II to BDI-IA scores. Only items (14/21) with corresponding anchor points between the two versions of the BDI were analysed.

Results: Three-thousand-and-sixty-six individuals were included in this crosssectional study: TS (N=65), rMDD (N=696), BPAD-I (N=1515), BPAD-II (N=497), and controls (N=293). Depressive symptoms did not associate with ethnicity or age. There were statistically significant differences in BDI scores across gender (female patients reported higher BDI scores than males, P=.013) and diagnostic groups, with patients with TS scoring significantly lower than patients with rMDD (P=.030), but higher than healthy controls (P=<.001).

Conclusion : Female patients attending specialist TS clinics present a particularly high risk to develop severe depressive symptoms. This has relevant clinical implications in terms of screening, management and prognosis of this patient population.

O16. Cardiovascular safety of aripiprazole and pimozide in young patients with Tourette syndrome Gulisano M (1), Calì PV (1), Cavanna AE (2), Eddy C (2), Rickards (2), Rizzo R (1)

(1)Section of Child Neurology, Department of Pediatrics, Catania University, Catania, Italy (2)Department of Neuropsychiatry, University of Birmingham Birmingham and Solihull Mental Health NHS Foundation Trust, Barberry Building, Birmingham B152FG, UK

The pharmacotherapy for tic management in Tourette syndrome (TS) relies on neuroleptics, which have been associated with electrocardiographic abnormalities, including QTc interval prolongation. This study assessed the cardiovascular safety of the newer antipsychotic aripiprazole in comparison with the neuroleptic pimozide among young patients affected by TS. Fifty patients aged 6–18 years were assigned to either pimozide (n = 25; mean daily dose 4.4 mg/die) or aripiprazole (n = 25; 5.3 mg/die) treatment for up to 24 months. All patients underwent five serial cardiovascular assessments (baseline, 6, 12, 18 and 24 months). The group treated with pimozide showed significant changes in blood pressure (decreased), QT and QTc (both prolonged). The aripiprazole group showed changes from baseline to peak values in blood pressure (increased), whilst modifications in QT and QTc were not statistically significant. At equivalent doses, aripiprazole is characterised by a safer cardiovascular profile than pimozide, being associated with a lower frequency of QTc prolongation.

O17. Measuring anger expression in young patients with Tourette s syndrome Selvini C (1), Luoni C (2), Cavanna AE (3,4), Blangiardo R (1), Gagliardi E (1), Balottin U (5), Termine C (1)

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AIMS : Tourette syndrome (TS) is a neurodevelopmental disorder characterized by multiple tics and co-morbid behavioural problems. It has been observed that young TS patients can exhibit a peculiar personality organization, with increased indicators of poor emotional control and aggression compared to healthy controls (Balottin et al., 2009). Anger could play a central role in the expression of behavioural problems in TS. We set out to evaluate this aspect using the State-Trait Anger Expression Inventory (STAXI).

METHODS : Twenty-five patients diagnosed with TS (age 15.4±2.6 years) and 41 matched-healthy controls (age 16.3±2.9 years) participated in this study. All recruited participants completed the STAXI. Participants' parents completed the Child Behaviour Checklist (CBCL) and Conners' Parent Rating Scales-Revised (CPRS-R), teachers completed the Conners' Teacher Rating Scales-Revised (CTRS-R). Results were compared with similar data obtained from controls.

RESULTS : Sixteen patients (64%) fulfilled DSM-IV-TR criteria for at least one comorbidities: obsessive-compulsive disorder (OCD, n=9; 36%): attention deficithyperactivity disorder (ADHD, n=3; 12%); OCD+ADHD (n=4; 16%). Scores on STAXI failed to show any significant differences between TS and controls, as well as between TS+ADHD and TS-ADHD subgroups. However, most subscores of the CBCL, CPRS-R and CTRS-R were significantly higher for the TS group than controls (CPRS-R-Oppositional, CBCL-Externalizing, Rule-Breaking and Aggressive Behaviour subscales).

CONCLUSIONS : Specific self-report measures of anger such as the STAXI appear to have limited usefulness in measuring anger expression of young TS patients. However, proxy-rated instruments differentiate this patients from healthy subjects on measures of oppositional and aggressive behaviours and should always be included in the multidimensional assessment of TS.

O18. Preliminary findings about effects of music on motor tics frequency in Tourette Syndrome

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(2)Department of Neurology, Tourette Centre, IRCCS "Galeazzi", Milan, Italy

Tourette syndrome (TS) is a neurodevelopmental disorder consisting of multiple motor and one or more vocal/phonic tics. Various behavioral patterns are usually also existent in TS patients. The clinical assessment of TS is done by quantifying and classifying its clinical manifestation (frequency, number of tic-types, intensity, complexity, body distribution, suppressibility, and interference with normal activities). Wearable technology (WT) was recently proposed for monitoring and quantifying motor-tics caused by the TS and for studying correlations with psycho-physiological states. The system is based on a compact 1-lead ECG and one 3D accelerometer placed on the patient's trunk. During the experimental activity we found a correlation between motor tics frequency and sound stimulation. Thus we investigated the possible role of music in TS treatment through a structured protocol on a small subjects population.From the methodological point of view the assessment of TS combining video and WT data demonstrated to be reliable and effective. Clinically,the administration of environmental music seemed to produce in patients the execution of large movements - tics synchronized with rhythm. The presence of the examiner forced the patient to control this behavior thus increasing the number of low intensity tics; while the patient is alone in the laboratory, music induces a reduced but synchronized and high intensity motor tics. Through a more direct sound stimulation by earphones we found a tic occurrence rate reduction of 30%, and specifically the subjects kept the high intensity

tics.Music administration produced also HR decrease, i.e. a stress reduction.These factsseem to suggest that music can play a role in TS management.

12:30-13:30 ESSTS GENERAL ASSEMBLY

14.00-19.00 Satellite Meeting

Aula Magna University Hospital

1st International Meeting of Tourette Syndrome Support Groups (supported by COST Action BM0905)

Chairs: Z. Tarnok (Hungary), K. Muller Vahl (Germany)

14.00-16.20 Presentation by each group attending

(Canada, Denmark, Finland, Germany, Hungary, Israel, Italy, Norway, United Kingdom)

16.20-17.00 The changing role of self/help groups in the future (K. Malish, M. Dunlap, Germany)

17.00-17.30 Coffee Break

17.30-19.00 The future for joint working (S. Dobson, United Kingdom)

POSTERS

P1. The role of 5-alpha-reductase inhibitors in TS neurobiology. Preclinical evidences.

Bini V (1,2,4), Frau R (1,2), Pillolla G (4), Paba S (2,4), Saba P(1), Devoto P (1), Bortolato[2] M (2,3,4)

(1) Dept. of Biomedical Sciences, Division of Neuroscience and Clinical Pharmacology, "Guy Everett Laboratory", University of Cagliari, Italy (2) Tourette

Syndrome Center, University of Cagliari, Italy (3) Dept. of Pharmacology and Pharmaceutical Sciences, University of Southern California, USA (4) Dept. of Cardiovascular and Neurological Sciences, University of Cagliari, Cagliari, Italy

The pathophysiology of Tourette Syndrome (TS) remains poorly understood. Rich evidences suggest a functional role of androgen steroids in this neuropsychiatric illness. TS afflicts men much more than women, and androgens are known to exacerbate tic severity. Although androgen receptor antagonists have been shown to significantly improve severity of TS symptoms, their therapeutic efficacy is partial and limited by severe side effects. An alternative approach to reduce androgen signaling in the brain might be offered by the 5-alpha-reductase inhibitors (5ARIs). Our studies were aimed at testing the effect of 5ARIs, such as finasteride (FIN), in animal models validated for TS, such as the deficits in prepulse inhibition (PPI) of the startle, the hyperlocomotion and the stereotyped behaviors induced by dopamine receptor manipulations. We then investigated the specific contributions of D1- and D2-like family receptors and the brain areas involved in FIN pharmacological actions. FIN dose-dependently antagonized PPI deficits mediated by the dopamine indirect agonists, apomorphine and amphetamine, and reduced hyperlocomotion and stereotyped behaviors induced by these dopaminergic agents. Notably, FIN did not induce catalepsy in either bar and paw test, a common consequence of dopaminergic signaling blockade. PPI deficits produced by systemic apomorphine administration were countered by FIN infusions in the brain ventricles and specifically in the Nucleus Accumbens area, but not in the other brain regions investigated. Finally, FIN was able to reverse PPI impairments observed after D1, but not D2 receptor manipulations. These results suggest that 5ARIs may exert therapeutic actions in TS disorder without eliciting extrapyramidal effects.

P2. Attachment Style and Anger in Individuals with Tourette-Syndrome Burger MB, Buchheim A, Meyer S, Yundina E, Müller N, Zill P Dehning S

Klinik für Psychiatrie und Psychotherapie, Nußbaumstr. 7, 80336 München

Introduction: The present study explores the degree to which individuals diagnosed with TS exhibit particular attachment styles, and the degree to which the underlying attachment dimensions of relationship anxiety and avoidance are themselves associated with forms of aggression: physical aggression, verbal aggression, anger, and hostility.

Method: The 47 patients included in the present analysis were all diagnosed with TS based on the ICD-10 criteria and were compared to 27 healthy controls (HC), matched with respect to gender and age. *Measures:* Experiences in Close Relationships-R Scale (ECR-R), Aggression Questionnaire (AQ)

Results: TS patients had a strongly elevated relationship anxiety when compared to HC (TS=3.5 ± 1.04; HC=2.7 ± 1.11); p=.003. Those TS patients showing selfinjurious behavior were especially associated with a fearful attachment style (p=.013).
TS patients showed a highly elevated AQ total compared to HC (TS=71.8 ± 18.36; HC=61.4 ± 15.94); p=.012, particularly the dimensions anger and hostility differed significantly from HC.

Discussion: We could show higher levels of anxiety in intimate relationships in TS patients as well as a greater tendency of anger and hostility to occur. The first clinical implication of this findings could be to have a closer look at patient's relationships and self-management. To what extent the attachment style might be contributing to TS's pathogenesis should be the subject of further studies.

P3. Pharmacodynamic and pharmacogenetic assessment in TS patients treated with Aripiprazole. Preliminary results.

Cardona F (1), Silvestri P (1), Baglioni V (1), Chillemi G (2) , Lionetto L (4), Gentile G (3,4), Simmaco M (3,4)

(1) Pediatrics and Child Neuropsychiatry Department (2) CASPUR (3) NESMOS Department- Sapienza University of Rome (4) Sant'Andrea Hospital of Rome

Introduction: This open study was aimed to gather information on the relationship between pharmacodynamic and pharmacogenomic profiles and clinical response to treatment with Aripiprazole in patients affected by Tourette Syndrome (TS).

Introduction: Aripiprazole (ARI) is an atypical antipsychotic characterized by partial dopaminergic agonism, antagonism at 5HT2A and partial agonism at 5HT1A. Several studies suggested the efficacy of ARI in the treatment of tics. ARI is metabolized in the liver by the cytochrome P450 isoenzymes 3A4, 3A5 and 2D6, highly polymorphic. Dehydroaripiprazole (DARI) is the active metabolite of ARI.

Sample: We examined 26 children and adolescents, aged 9-18, with TS, followed at the outpatient division of Child Neuropsychiatry Department of Sapienza University of Rome. Patients had been treated with ARI from 4 years to 1 month (mean time: 20 months).

Methods: A clinical assessment was performed in all patients. Serum levels of ARI, DARI and prolactin were measured. Patients were genotyped for CYP2D6, CYP3A5 and CYP3A4 polimorphisms. Serum ARI and DARI levels were measured using a high performance liquid cromatography- tandem mass spectrometry (HPLC-MS/MS) method. CYP2D6, CYP3A5 and CYP3A4 genes were genotyped using DNA microarray and pyrosequencing.

Results: No correlation was found between clinical response to treatment with ARI and both serological levels of ARI and DARI, as well as the different cytochrome genotypes. It's worth to be mentioned two data: the low level of prolactin in most of the patients and the high value of DARI/ARI ratio (from 80 to 250). This inversion of the DARI/ARI ratio was in contrast with literature data concerning adults, so drug/metabolite levels were also assessed in 75 adult patients. In this cohort, the DARI/ARI ratio was similar to that reported in the literature.

Conclusions: These preliminary data seem not support the usefulness of pharmacodynamic and pharmacogenetic assessment in the management of TS patients treated with ARI, possibly due to the low number of examined subjects. The reversal of DARI/ARI ratio found in children and adolescents, compared with the data in adults, is an interesting feature to be further investigated.

P4. Sensory phenomena: clinical correlates and impact on quality of life in adult patients with Tourette syndrome Crossley E (1), Cavanna AE (1,2)

(1) Michael Trimble Neuropsychiatry Research Group, Department of Neuropsychiatry, University of Birmingham and BSMHFT, Birmingham, UK (2) Department of Neuropsychiatry, Institute of Neurology, UCL, London, UK

Background: Sensory phenomena (SP) are unpleasant bodily sensations or discomforting feelings, which result in involuntary urges to tic in patients with Tourette Syndrome (TS). Despite the high prevalence of these subjective experiences and their central role in TS phenomenology, little is known about the clinical characteristics of SP or their possible impact on Health-Related Quality of Life (HRQoL) in adult patients with TS.

Methods: A cross-sectional observational study of 72 adult outpatients with TS at a specialist tertiary clinic. Participants completed a comprehensive battery of psychometric measures, including the Premonitory Urge for Tics Scale (PUTS) to measure SP.

Results: SP were very common (97.2%), with a median PUTS total score of 28.0 (IQR=10; range=10-40). Bivariate analyses found that SP were most significantly correlated with self-report measures of vocal tic severity ($p<0.001$), compulsivity ($p<0.001$) and attentional difficulties ($p=0.001$). SP were also significantly correlated with GTS-QOL scores (a measure of quality of life in TS), most notably with the psychological subscale ($p<0.001$). Stepwise multiple linear regression analysis found MOVES total score was associated with PUTS total score ($B=0.241$, $t=4.214$, $p<0.001$).

Conclusions: SP are frequently reported by adult patients with TS and can be associated with specific aspects of perceived tic severity and co-morbid behavioural symptoms. SP can significantly affect patients' psychological well-being and treatment interventions for adults with TS should take SP into consideration for more comprehensive management of the condition.

P5. TOURETTE SYNDROME AND COMORBID CONDITIONS DOC/OCB IN A SAMPLE OF 42 CHILDREN AND ADOLESCENTS.

Giraudo MC (1), Davico C (1), Gerardi S (1),. Massucco C (1), Notari D (1) , Osello E (1), Ruffino C (1), Torta F (1), Anichini A (1)

(1) Childhood and Adolescence Science Department-University of Child and Adolescent Neuro-Psychiatry

Background: Tourette Syndrome (TS) is frequently associated (30-60%) with the obsessive-compulsive symptoms (DOC / OCB). Various interesting studies (Robertson, Rizzo 2006), support the hypothesis that obsessivecompulsive symptoms are an integral part of TS.

Objective: This study investigates the comorbidity OCD/OCB in a sample of 42 children and adolescents. Data are collected from 2006 to present and the comorbid

conditions are analyzed in relation to age and type of obsessive compulsive symptoms. The aim of the study is also to verify the test consistency in detecting obsessive compulsive symptoms in children with TS.

Methods: The diagnosis of TS was done according to *TSCSG* criteria. We used the following psychometric scales: CBCL,YSR,YGTSS,CY-BOCS, and the follow-up was carried out by a multidisciplinary team.

Results and discussion: In our sample we found DOC in 26.19%, OCB in 33.33% , OCD and ADHD associated in 9.52%; OCB and ADHD in 4.76% and ADHD only in 2.38%, without any statistically significant difference in relation to age. We found a high frequency of contamination (68.18%), somatic (59.09%) and aggressive (54.55%) obsessions.

The prevalent compulsions were "various" in 68.18%. We didn't highlight any difference in symptom's quality in relation to age, while we found significant differences in relation to the presence of OCB versus DOC. The tests used (CBCL, YSR and CY-BOCS) have a high concordance in the assessment of obsessive-compulsive symptoms.

P6. Functional Outcome and Quality of Life after Deep Brain Stimulation of the Globus Pallidus internus in Tourette's Syndrome Patients Leitner B (1), Dehning S (1), Bötzel K (2), Müller N (1) and Mehrkens JH (2)

(1) Department of Psychiatry and Psychotherapy, Ludwig-Maximilians-University, Munich, Germany (2) Department of Neurosurgery, Ludwig-Maximilians-University, Munich, Germany

Objective: Lately deep brain stimulation (DBS) in therapy resistant patients with Tourette syndrome (GTS) has been in the focus of research with over 60 cases published. While most reports concentrate on the improvement of symptoms after DBS, there is hardly any data on "psychosocial" outcome of patients. Therefore we conducted a naturalistic observational study in six GTS patients. In addition to symptoms we also determined the psychosocial changes by measuring functional outcome and quality of life after DBS of the Globus Pallidus internus (GPi).

Methods: Six patients suffering from therapy-refractory GTS had undergone GPiDBS (posteroventrolateral, motor part). The Yale Global Tic Severity Scale (YGTSS) was used to evaluate the symptomatic outcome. Moreover, "psychosocial changes" were assessed using the Global Assessment of Functioning Scale (GAF), and the GTS-Quality-of-Life scale (GTS-QOL). Any "major psycho-social event" was recorded.

Results: Four of the six patients were responders and had a significant (p=0.001) tic improvement with different response times. The significant tic-improvement in the YGTSS was between 60% (Pat VI, after 10 month) and completely tic free (Pat I, after 12 month). Certain psychosocial "life-events" could not be assessed by the applied scales. For example patient IV became pregnant and gave birth to a healthy boy. In all responders significant social functional improvement was found, showing an increase in the GAF and quality of life.

Conclusions: GPi-DBS seems to be a promising option in a selected group of therapy resistant GTS. Treatment success should be defined as improvement of symptoms, functional outcome and quality of life.

P7. Tourette Syndrome and Quality of life in Developmental Age. Follow-up at 12 and 24 months in a 44 patients sample

Massucco C (1), Notari D (1), Davico C (1), Gerardi S (1), Giraudo MC (1), Osello E (1), Ruffino C (1), Torta F (1), Anichini A (1)

(1) Childhood and Adolescence Science Department-University of Turin Child and adolescent Neuro-Psychiatry

Scientific Background: medical literature counts rare studies concerning the followup of Tourette Syndrome patients' treatment; specific tools assessing life quality in the developmental age are still in a validation phase (Cavanna 2008). There isn't any systematic study comparing the various treatment's effectiveness, even if the importance of a multidisciplinar approach is commonly aknowledged.

Objective: monitoring quality of life with follow-up at 12 and 24 months of TS patients in developmental age.

Methods: we analyzed a sample of 44 patients referring our Structure with a diagnosis of TS DSM IV-TR and TSCSG oriented. We applied a **6 step** protocol for TS diagnosis and follow-up (> 24 months): first examination, differential diagnosis, comorbibity survey, psychodiagnostic assessment, restitution conference; follow-up in a multidisciplinary taking charge. We monitored the progress of YGTSS (alla subscales), CBCL and YSR (internalizing and externalizing disorders, cross-informant agreement), both in the total sample and in various subgroups we selected according to the treatment (no therapy, drug therapy and supportive psychotherapy alone or combined).

Results and Discussion: we collected preliminary results; in spite of its many limits (need to increase sample number; identification of new subgroups according to morbidity) this study offers a contribution toward following the evolution of Tourette patients in response to different interventions. Our interest is not only to estimate the symptom course, *but to assess the person's quality of life*

P8. Citation Classics in Tourette Syndrome Neethu M (1), Cavanna AE (1,2)

(1) The Michael Trimble Neuropsychiatry Research Group, Department of Neuropsychiatry, BSMHFT and University of Birmingham, United Kingdom

(2) Sobell Department of Motor Neuroscience and Movement Disorders, Institute of Neurology and University College London, United Kingdom

The impact of scientific articles is proportional to the citations they have received. In this study, the most cited works ("citation classics") related to Tourette syndrome (TS) were identified as articles with more than 100 citations according to the Web of Science. We retrieved 89 highly cited articles, which were published in 26 journals: 54 clinical studies, 27 laboratory studies, 7 reviews and 1 classification article. Clinical studies

consisted of phenomenological evaluations of TS and co-morbid behavioral problems (n=22), studies on pharmacotherapy (n=16) and clinical genetics (n=13), whilst laboratory studies covered basic genetics, cellular and molecular biology (n=11) and neurobiology (neuroimaging, neuropathology and neurophysiology) (n=16). The majority (58%) of citation classics were published after
1990, when laboratory studies (especially neuroimaging, immunological and genetic studies) became widely cited. These articles are able to reach the highest numbers of citations in a short time span and suggest potential directions for future research.

P9. SELF INJURIOUS BEHAVIOURS (SIB) AND SUICIDE ATTEMPT IN A POPULATION OF 64 CHILDREN AND ADOLESCENTS WITH TOURETTE SYNDROME (ST) Notari D (1), Davico C (1), Gerardi S (1), Giraudo MC (1), Massucco C (1), Ruffino C (1), Torta F (1), Toscano S (1), Tocchet A (1) , Anichini A (1)

(1) Childhood and Adolescence Science Department- University of Turin Child and adolescent Neuro-Psychiatry

Background: ST individuals frequently present various comorbid conditions affecting disease progression, prognosis, quality of life (*M.Robertson2006*). SIB (Self Injurious Behaviours) are common in ST, and precise diagnosis and typing is fundamental. SIB occur in 4% of the general psychiatric population and in 60% of ST patients (*Mathews 2004*).

Objectives: This study aims to assess prevalence of suicide attempt, age of onset of SIB, their severity in comparison to tic's severity, duration of disease and comorbid conditions (OCD,OCB, ADHD, mood disorders etc..)

Methods: The study stems from a multidisciplinary collaboration at Children's Hospital Regina Margherita in Turin. Our diagnostic protocol was applied from 2006 to present in 64 pediatric patients. ST diagnosis meets *DSM IV* and *TSCSG*. Comorbid conditions are carefully diagnosed on the base of clinical observations and psychometric tests (YGTSS, CBCL, YSR, CY-BOCS). We also explored risky behaviors such as: suicide attempts, SIB (*Mathews2004*), and Anger and Violence (*Comings and Comings 1985*).

Results: initial results (*in progress*) show that 35.9% of patients presented SIB (mild and moderate), 9.3% made suicide attempt. Identification of SIB predisposing factors is essential as they can adversely affect not only safety, but also psychopathological evolution and adaptability of our patients in relation to developmental tasks.

P10. Efficacy of finasteride in Tourette Syndrome therapy Paba S (2,4), Bini V (1,2,4), Corona M (1,2), Marrosu F (2,4), Bortolato M (2,3,4)

(1) Dept. of Biomedical Sciences, Division of Neuroscience and Clinical Pharmacology, "Guy Everett Laboratory", University of Cagliari, Italy (2) Tourette Syndrome Center, University of Cagliari, Italy (3) Dept. of Pharmacology and Pharmaceutical Sciences, University of Southern California, USA (4) Dept. of Cardiovascular and Neurological Sciences, University of Cagliari, Cagliari, Italy

Pharmacotherapy of Tourette syndrome (TS) is still limited: although antipsychotics are used for the attenuation of motor and vocal tics in TS, their therapeutic effectiveness is heavily restricted by significant side effects, such as sedation, weight gain and extrapyramidal symptoms. The marked male predominance of TS suggests that androgens play a key role in the pathophysiology of this disorder. Although androgen receptor antagonists attenuate TS symptoms, their efficacy is hindered by severe side effects. A valid alternative may be afforded by inhibitors of 5-α-reductase (5AR), the main rate-limiting enzyme in androgen metabolism. Finasteride, the prototypical 5AR inhibitor, is approved for the treatment of benign prostatic hyperplasia and alopecia and elicits very limited side effects. Following preclinical results indicating the efficacy of finasteride in TS animal models, we tested this drug in 16 adult male TS patients. Symptom severity was evaluated at the baseline and every 6 weeks, with the Yale Global Tic Severity Scale and the Yale Brown Obsessive and Compulsive Symptoms Scale. Finasteride (5 mg/day) reduced tic severity in a time-dependent fashion. In particular, significant declines in phonic and vocal tics were observed after 6 and 12 weeks of treatment, respectively. Compulsive, but not obsessive symptoms were also significantly reduced in all patients. No side effects were reported but a mild reduction in libido, which was deemed completely acceptable. Although further studies are warranted to confirm our observations, these findings highlight 5AR inhibitors as a promising therapeutic option for TS and related disorders.

P11. Blood Level Measurements of Pimozide in Tourette Patients: Pharmacokynetics, Efficacy and Compliance Preliminary Considerations Perego L (1), Porta M (1), Barassi A (2), Ghilardi F (2), Camerlingo M (1), Servello D (1) Melzi D' Eryl G (2)

(1) Tourette Center IRCCS Ist. Galeazzi Milano e Policlinico S. Marco Zingonia (2) Dep. Med. e Chir. Odont., Milano

In 30 Tourette patients, pimozide blood levels were measured. Pimozide is one of the oldest and routinely used drugs to correct tics (vocal and motor). Its efficacy on behavioural symptoms is less evident. Tourette patients have usually bad compliance. Often pimozide is associated to other drugs. Pharmacokinetics, efficacy and compliance are evaluated in relation to blood level of pimozide.

P12. ADHD and Epilepsy in children with Tourette Syndrome: a triple comorbidity?

Rizzo R (1), Gulisano M (1), Calì PV (1), Curatolo P (2)

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The comorbidity TS and epilepsy is rarely reported. We report a long term follow-up of 8 young patients presented a triple comorbidity : TS, ADHD and epilepsy. All the

patients had TS (typical onset) and idiopathic benign seizures (good response to the therapy and obtained the complete resolution of the seizures); 6 patients presented "combined ADHD" type, 2 showed predominantly hyperactive "ADHD-H" type. The relationship between TS , ADHD and epilepsy is not fully understood. Our study hypothesize that it could be a relationship in the aetiology of TS, ADHD and epilepsy.

The increased excitatory activity, DOPA and GABA mediated, could be the common aetiology than cause all the clinical symptoms.

P13. LEARNING DISORDERS IN CHILDREN AND ADOLESCENTS WITH TOURETTE SYNDROME: A RETROSPECTIVE STUDY IN A 52 PATIENTS SAMPLE.

Ruffino C (1), Davico C (1), Gerardi S (1), Giraudo MC (1), Massucco C (1), Notari D (1), Torta F (1), Siravegna D (1), Bassi B (1), Anichini A , Ciuti A (2)

(1) Childhood and Adolescence Science Department-University of Turin Child and Adolescent Neuro-Psychiatry (2) SCDU Child and Adolescent Neuro.Psychiatry, ASL 8, Carmagnola (Torino)

Scientific Background: Clinical observation and sperimental evidence in the neuropsychological field show that TS patients suffer a discrepancy between normal intellectual abilities, and an impaired inhibition of unappropriate or inadequate behavioral responses, with the consequent impossibility of and adaptive motor and behavioral output.

Objectives: assessment of presence, distribution and characteristics of learning disorders in a school-age sample of 52 children and adolescents who referred to our Department since 2006; detection of eventual neuropsychological differences between patients with both TS and Learning Disorders comparing to TS patients without

Learning Disorders; Learning Disorders evaluation in relation to patient's age. **Methods**: in the context of our diagnostic-therapeutic protocol, with repeated followup visits, we proposed a targeted interview concerning Learning Disorders, and we analyzed prophiles derived from WISC-III (Wechsler Intelligence Scale for Children – III) administration.

Results: TS has a strong impact on school malfunctioning in these children, regardless from tic severity. It determines a "*faceted spectrum*" of academic difficulties, with specific and non specific Learning Disorders, attentive deficits, conduct and socialization disorders, which may imply a decreased school performance and/or school refusal and dropout.

P14. Creativity in Tourette Syndrome Zanaboni C., Anasetti F., Porta M., Servello D

Tourette Center, Functional Neurosurgery IRCCS Galeazzi, Milan

Background: Creativity is *"the union of pre-existing elements that produce new and useful combinations"* (Poincaré H., 1999). The main features of creativity (Williams'

F., 1994) are thinking-cognitive divergent factors (fluidity, flexibility, originality, elaboration) and personality-emotional divergent factors (curiosity, imagination, complexity, risk taking). As Tourette syndrome (TS) does, also creativity and divergent thinking activate the dorsolateral prefrontal circuit and anterior cingulate circuit of the frontal cortex. In particular, the frontal lobe is linked with idea generation; this phenomenon is clearest in verbal creativity, but it also shapes nonlinguistic creativity. At the same time, creative personality is influenced by mesolimbic dopamine, especially when measured by Novelty Seeking and Creative Drive categories and TS presents an altered dopaminergic synaptogenesis. The assumption that TS is linked to creativity is first described in 1992 by Oliver Sacks, professor of Clinical Neurology at the Albert Einstein College of Medicine in New York.

Research in Europe : The hypothesis of the study was that TS patients are more creative than not-TS people. The study (Porta M., Zanaboni C., 2010) took place in Italy at IRCCS Galeazzi of Milan, it involved 23 TS children/adolescents (6-18 years old), their teachers, and parents, and a control group tested by TCD (Williams F., 1994). Results from the flexibility subtest of the Divergent Thinking Test confirm the initial hypothesis: creativity is statistically higher in the TS group than in the control sample (Fig.1). Flexibility is the ability to change your approach towards a stimulus, the capability to pass from one category to another, and change your mind set to avoid obstacles.

Research in the U.S. : The study was repeated at the Yale Child Study Center with a sample of 18 TS patients, and the main results confirm that flexibility is more likely to be developed in TS patients than in the control group. Additionally, the findings of this second study found fluidity to be more developed in the clinical sample than in controls (Fig.2). Fluidity is the ability to quickly consider a huge quantity of ideas and then generate a large number of valid responses.

Interventions Based on Creativity : As a treatment supplement to medications and/or other psychological techniques such as Habit Reversal Training, TS patients may benefit from therapeutic programs including visual arts, music, acting and dance. Actually, it could incorporate body activity to deal with ADHD and the practice of new cognitivebehavioral and interactive relationship styles to soften OC symptoms. It could also improve these patients' social skills and self-efficacy, bolstered by public approval from the final performance. This could cause a shift away from the immediate satisfaction given by the impulsive pleasure of tic manifestation towards a more gradual and controlled one given by the creative product and by extension of cognitivebehavioral patterns learned outside the therapeutic context.

The school environment is often a stressful context for TS patients. Ideally, by introducing psychoeducational classes for teachers, parents and students and a recreational lab for classmates of Tourette students, school could become a supportive or even therapeutic setting. A TS creative school lab could first take into account motor/ linguistic limitations in choosing activities, then include simple tasks to avoid feelings of failure on the part of the patients, as well as exclude tasks that may highlight symptomatology to prevent embarrassment or tiredness.

Conclusion: The correlation between psychopathology and creativity has already been explored in evolution theories (Huxley A., 1964). According to Huxley, because psychopathology has a genetic component, it must show some positive aspects; creativity is an example. Creativity is one's ability to use cognitive and aesthetic skills

and empathy towards cultural evolution (Csikzentmihalyi M., 1998). The link between TS and creativity has been verified empirically. Many TS patients have a strong expressive creative predisposition that treatment providers and caregivers may use to maximize therapeutic benefit. Special thanks to the following: Mauro Porta MD, Domenico Servello MD, James Frederick Leckman MD, Mary Robertson MD, Tammy Hedderly MD and Tourette Center of Milan, Yale Child Study Center, Evelina Children's Hospital of London.

Accomodations:

Grand Hotel Baia Verde

(http://www.grandhotelbaiaverde.it/)

Catania college residence (Campus d Aragora di Catania, http://www.campus.it/)

Social Event: Benedicte Monastery (founded in1558) Tour on 8th June 2012 (evening). Admission upon reservation and admission fee

Cocktail on 8th June 2012, University Main Building, Piazza Universita, 3 Catania

Friday 8th June

8.30-9.00 Registration

9.00-10.30

BASIC SCIENCES: NEUROANATOMY & NEUROCHEMISTRY, GENETICS, NEUROIMMUNOLOGY, PATHOLOGY

Chair: A. Hartman

9.00-9.20 Introduction (A. Hartman)

9.20-9.40 The immune system in Gilles de la-Tourette Syndrome (D. Martino)

9.40-10.00 The genetics of Gilles de la Tourette Syndrome (P. Paschou)

10.00-10.20 Reinforcement learning and Tourete Syndrome (S. Palminteri)

10.20-10.30 Discussion

10.30-11.00: ***Coffee-Break***

11.00-12.30

COMORBID AND COEXISTENT PSYCHOPATOLOGY

Chair: K. Müller– Vahl

11.00-11.20 Learning disorders (A. Ludolph)

Venue:

Aula Magna Facoltà di Medicina e Chirurgia

A.O.U. "Policlinico - Vittorio Emanuele" Catania

European Network for the Study of Gilles de la Tourette Syndrome
COST Action BM0905

cost
European Cooperation in Science and Technology

AOU Vittorio Emanuele-Policlinico
Presidio Gaspare Rodolico
Dipartimento di Scienze Mediche e Pediatriche

11.20-11.40 Impulse control disorders (A. Cavanna)

11.40-12.00 Personality traits in patients with Gilles de la Tourette Syndrome (S.Bokemeyer)

12.00-12.20 Prevalence of comorbidities and their development over the time (N. Mol Debes)

12.20-12.30 Discussion

Presidio "Gaspare Rodolico"

Neuropsichiatria Infantile

Via Santa Sofia, 78 – 95123 Catania, Italy

2012 Clinical Training School for TS

Catania, Italy 6-8 June 2012

Aula Magna Facoltà di Medicina

How to find A.O.U. "Policlinico - Vittorio Emanuele" :

By Plane:The nearest international airport is Catania Fontanarossa, Vincenzo Bellini Airport".
Arriving at the airport we recommend taking a taxi to your final destination.
In case no taxi is available at the airport please dial:
+39 095330966.
Taxi low cost company from Airport to Hotel Baia Verde fare 35 Euro. From Airport to Camplus (Via Ventimiglia 184) fare 20 Euro.

COST is supported by the EU RTD Framework Programme
ESF provides the COST Office through a European Commission contract
The Council of the European Union provides the COST Secretariat

SINPIA SOCIETA' ITALIANA DI NEUROPSICHIATRIA DELL'INFANZIA E DELL'ADOLESCENZA

List of Speakers

S.

Bokemeyer (Germany)

D. Cath (Netherlands)

Organisers:

Mary Robertson, UCL, United Kingdom
Renata Rizzo, University of Catania, Italy

F. Cardona (Italy)

A. Cavanna (United Kingdom)

A. Hartman (France)

P. Hoekstra (Netherlands)

A. Ludolph (Germany)

D. Martino (United Kingdom)

N. Mol Debes (Denmark)

K. Müller-Vahl (Germany)

T. Murphy (United Kingdom)

S. Palminteri (France)

P.Paschou (Greece)

M. Porta (Italy)

H.Rickards (United Kingdom)

R. Rizzo (Italy)

M. Robertson (United Kingdom)

Z. Tarnok (Hungary)

C. Termine (Italy)

J. Van de Griendt (Netherland)

C. Verdellen (Netherland)

Wednesday 6th June

8.00-9.00: Registration

9.00-9.30: My journey in GTS (M. Robertson)

9.30-10.00: Perinatal adversities and Gilles de la Tourette syndrome (P. Hoekstra)

10.00-10.30 : Neurobiology and functional anatomy (K. Müller-Vahl)

10.30-11.00: Diagnosis & Neuropsychological assessment (D. Cath)

11.00-11.30: *Coffee-Break*

11.30-12.00: Understanding co-morbidity in GTS (H. Rickards)

12.00-12.30: Natural History of GTS (R. Rizzo)

12.30-13.00: *Lunch*

13.30-14.00: Pharmachological treatment in GTS (P. Hoekstra)

14.00-14.30: Comorbidity pharmacological treatment (OCD, SIB, rage attacks, personality disorders) (F. Cardona)

14.30-15.00: Comorbidity in childhood and adolescence ADHD, OCD, anxiety, depression, autistic spectrum disorders (A. Ludolph)

15.00-15.30: Deep Brain Stimulation thereapy for treatmant of refractory Gilles de la Tourette's Syndrome (M. Porta)

15.30-16.00: Coffee-Break

16.00-16.30: Quality of life in adult with Gilles de la Tourette Syndrome (A. Cavanna)

16.30-17.00: QoL in children with Gillles de la Tourette syndrome (C. Termine)

17.00-17.30: Discussion

Thursday 7th June

8.00-8.30 Registration

8.30-10.00:

Introduction to Workshop (T. Murphy) Quiz (Z. Tarnok)

SDQ, SNAP, PUTS (T. Murphy)

PSS-10, ASSQ, QoL (Z. Tarnok)

10.00-10.30: *Coffee Break*

10.30-12.00

Introduce YGTSS (Background, scoring, pitfalls) (C. Verdellen, J. Van der Griendt)

YGTSS: Video materials (C. Verdellen, J. Van der Griendt)

YGTSS: group scoring and discussion (C.Verdellen, J. Van der Griendt, Z. Tarnok, T. Murphy)

12.00-13.00: *Lunch* 13.00-14.30

CYBOCS introduction : Background, scoring, pitfalls etc including Video materials (C. Verdellen, J. Van der Griendt)

View video material with scoring (C. Verdellen, J.Van der Griendt, Z. Tarnok, T. Murphy)

YGTSS and CYBOCS rating by participants (C. Verdellen, J. Van der Griendt, Z. Tarnok)

14.30-15.00

Discuss ratings of CYBOCs and YGTSS
Quick Quiz
(C. Verdellen, J. Van der Griendt, T. Murphy)