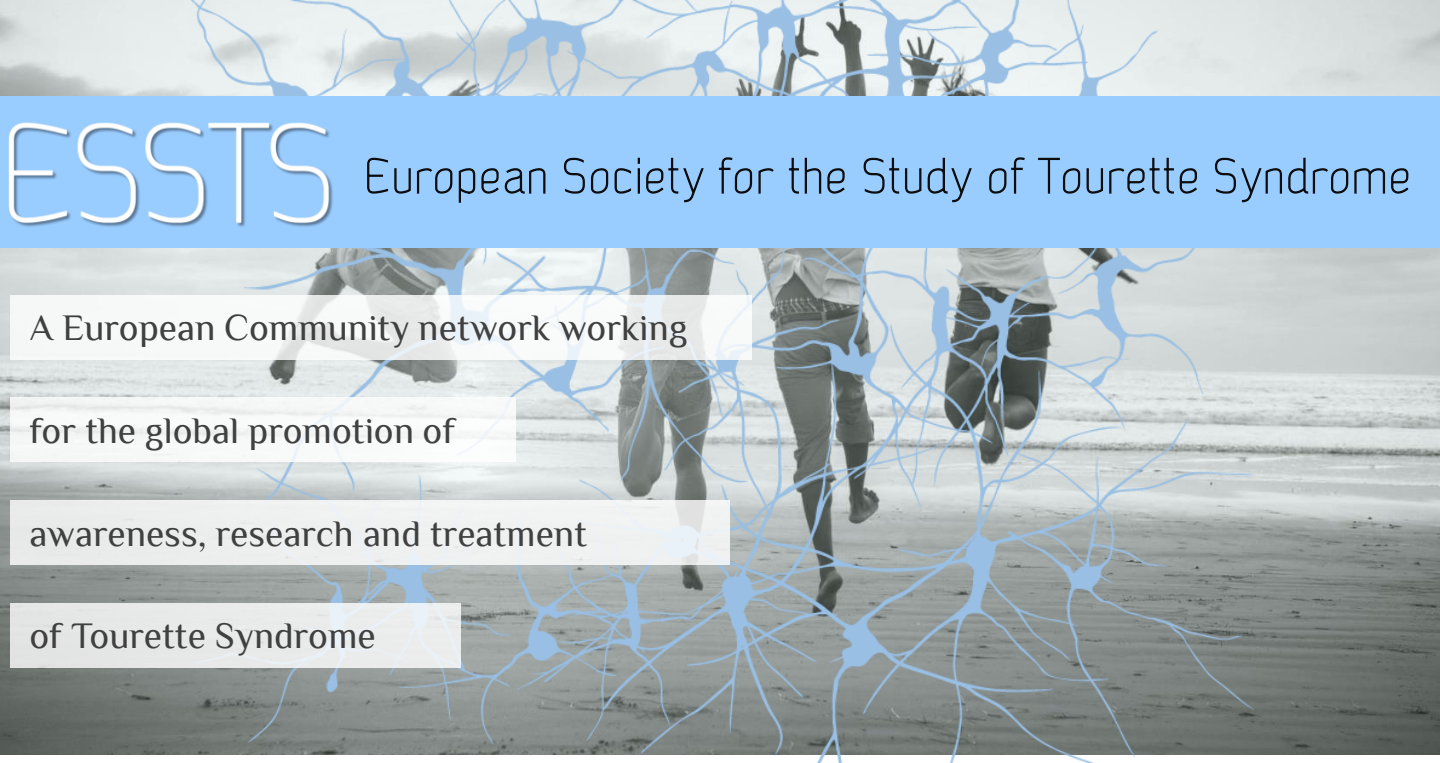
ESSTS European Society for the Study of Tourette Syndrome



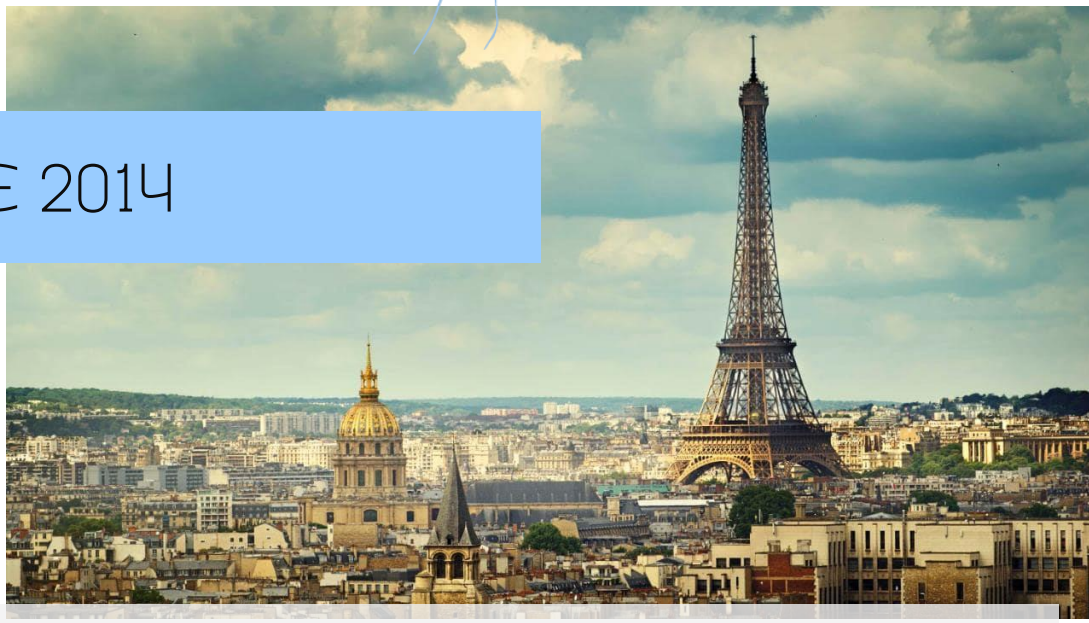
A European Community network working

for the global promotion of

awareness, research and treatment

of Tourette Syndrome

Paris, FRANCE 2014



Start Time: 25 April 2014
End Time: 26 April 2014
Where: ICM, Pitié-Salpêtrière Hospital, Paris, France

7th European Conference on Tourette Syndrome and Tic Disorders

The 2014 COST International Conference for Tourette Syndrome and Annual meeting of the European Society for the Study of Tourette Syndrome will take place on **April 25-26, 2014**, at the historic **Pitié-Salpêtrière Hospital in Paris**, home to Jean-Martin Charcot and one of his most famous students, Georges Gilles de la Tourette. The conference venue will be the newly built Brain and Spine Institute – ICM, which also houses the Charcot Library. Invited speakers are expected both from European countries and the US to make this the largest ESSTS meeting ever, bridging psychiatry and neurology, basic and clinical research.

ESSTS European Society for the Study of Tourette Syndrome

Invited Speakers include:

Bradley Peterson, Columbia University, USA

Flora Vaccarino, Yale University, USA

Frank Sharp, University of California Davis, USA

Jeremiah Scharf, Harvard University, USA

Marie-Laure Welter, Université Pierre et Marie Curie Paris VI, France

Andrea Cavanna, University of Birmingham, UK

Kirsten Mueller-Vahl, University of Hannover, Germany

Thomas Foltynie, University College London, UK

Yulia Worbe, Pôle des Maladies du Système Nerveux, France

Danielle Cath, Utrecht University, Netherlands

Organizers:

Andreas Hartmann, Local Host, Département de Neurologie, Pôle des Maladies du Système Nerveux, France

ESSTS Board members:

Peristera Paschou, ESSTS Chair, Democritus University of Thrace, Greece
Kirsten Mueller-Vahl, ESSTS Vice-Chair, University of Hannover, Germany
Renata Rizzo, ESSTS Secretary, University of Catania, Italy
Pieter Hoekstra, ESSTS Treasurer, Unversity of Groningen, Netherlands
Hugh Rickards, ESSTS Past Chair, University of Birmingham, UK

The meeting featured presentations from world renowned experts on Tourette Syndrome, who presented current advances in basic research as well as clinical practice.

With the support of COST Action BM0905, satellite events included a three-day Clinical Training School for Tourette Syndrome, focused on Behavioural Therapies for Tic Disorders (April 23-25), The 1st European Workshop on Neuroimaging for Tourette Syndrome (April 23-24), A TS-EUROTRAIN introductory training workshop on the Phenotype and Neurobiology of Tourette Syndrome (April 24), and The 3rd COST International meeting of Tourette Syndrome Support and Advocacy Groups (April 26).

Valerie Brandt, a PhD student from the Institute of Neurogenetics, University of Lubeck, was the recipient of the *2014 Prof. Mary Robertson Award for Research Contribution*.

The TS-EUROTRAIN Marie Curie Initial Training Network (FP7-PEOPLE) met in Paris as part of the 2014 ESSTS Annual Meeting.

The 2015 1st World Congress of Tourette Syndrome and Tic disorder will be held in London, June 24-26.

Looking forward to seeing you there!

UEMS-EACCME® accredited event

Funded by COST Action BM0905 (coordinated by Democritus University of Thrace) **Thursday, April 24, 2014** (ICM entrance Hall)

13:00-18:00	Registration – pick up conference material

Friday, April 25, 2014 (Auditorium)

8:00-9:00	Registration
9:00-10:30	**Invited Session I** (COST Action Training School) ***Updates on the neurobiology of Tourette Syndrome***
10:30-11:00	Break/Poster presentations
11:00-12:30	**Invited Session II** (COST Action Training School) ***Updates on deep brain stimulation in Tourette syndrome***
12:30-13:30	Light lunch/ Poster presentations
13:30-14:15	**Invited Session III** ***Genetics of Tourette Syndrome and related disorders***
14:15-15:45	Oral presentations I - *Genetics*
15:45-17:00	Break / Walk to the Saint-Louis Chapel
17:00-17:30	Opening Ceremony
17:30-18:30	**Keynote Speaker: Bradley Peterson, Columbia University, USA** ***Brain-Based Vulnerability and Compensation in Tourette Syndrome ?***
19:00	Welcome reception/cocktail (Tour Zamansky, Jussieu)

Saturday, April 27, 2014 (Auditorium)

8:30-10:00	**Invited Session IV – *The history of Tourette Syndrome***
10:00-10:30	Break/ Poster presentations

10:30-11:15	**Keynote Speaker: Flora Vaccarino, Yale University, USA.** ***Reduced basal ganglia interneurons and increased inflammation as revealed by transcriptome analysis in TS brains***
11:15-12:45	Oral presentations II – *Neuroimaging and Therapies*
12:45-13:15	Break/ Poster presentations / Light lunch
13:15-14:30	Oral presentations III - Clinical Research
14:30-14:45	The Mary Robertson Young Investigator award - Presentation
14:45-15:00	Break
15:00-15:45	Best Poster Presentation Award - Best Oral Presentation Award ESSTS general assembly
16:00-19:30	***3ND European Tourette Syndrome Patient Groups Meeting (COST Action BM0905)***

Satellite Events

2014 Clinical Training School for Tourette Syndrome; Clinical Assessment and Behavioural Therapies (COST Action BM0905)

April 23-24, 2014 (Room 01/02)

European Workshop on Neuroimaging for Tourette Syndrome (COST Action BM0905)

April 23-24, 2014 (Auditorium)

2014 COST Action BM0905 Management Committee Meeting

April 24, 2014 (Room 04)

TS-EUROTRAIN Training Session

April 24, 2014 (Auditorium)

TS-EUROTRAIN Annual Retreat

April 26, 2014 (Room 04)

Third European Tourette Syndrome Patient Groups Meeting (COST Action BM0905)

April 26, 2014 (Room 01/02)

Awards

Valerie Brandt, a PhD student from the Institute of Neurogenetics, University of Lubeck, was the recipient of the ***2014 Prof. Mary Robertson Award*** for Research Contribution.

Best Oral presentation award was won by **Dr. Bertelsen** from Applied Human Molecular Genetics, Copenhagen University Hospital, Denmark. ***Second best Oral presentation award*** was won by **Dr. Huys** from University of Cologne, Department of Psychiatry and Psychotherapy, Germany.

European Accreditation Council for Continuing Medical Education (UEMS/EACCME): The 2014 ESSTS Annual Meeting and COST International Conference for Tourette Syndrome has been accredited by the European Accreditation Council for Continuing Medical Education (EACCME) to provide the following CME activity for medical specialists. The EACCME is an institution of the European Union of Medical Specialists (UEMS): www.uems.net. The Conference is designated for a maximum of, or up to, **9 European CME credits** (ECMEC). Each medical specialist should claim only those hours of credit that he/she actually spent in the educational activity. CME credit claim forms are available at the Conference Registration Desk as well as with the conference material received upon registration. Completed forms should be submitted to the Conference Registration Desk after the end of the Conference.

Certificates of Attendance: Certificates of Attendance will be provided at the Conference Registration Desk on Friday, April 25, and Saturday, April 26, 2014. All participants are required to sign the COST Action attendance forms on each day of attendance.

Thursday April 24

(13:00-17:00) TS EUROTRAIN TRAINING SESSION: – Introduction to the Phenomenology and Neurobiology of Tourette Syndrome

L1. Everything you have always wanted to know about the phenotype of tics and GTS. *Müller-Vahl K* - Clinic of Psychiatry, Socialpsychiatry and Psychotherapy, Hannover Medical School, Carl-Neuberg-Str. 1, 30625 Hannover, Germany.

Tourette syndrome (TS) is defined as a childhood-onset chronic neuropsychiatric disorder characterized by multiple motor and one or more vocal tics. According to DSM-5, tics are sudden, rapid, recurrent, non-rhythmic motor movements or vocalizations. Although tics can include almost any muscle group or vocalization, certain tic symptoms are more common (such as eye blinking or throat clearing) than others. Tics can be divided into simple and complex (motor and vocal) tics. Most patients suffer from many more simple than complex tics. Complex motor tics are of longer duration (sometime similar to dystonic movements and then called “dystonic tics”), often include a combination of simple tics, often include different groups of muscles, or appear purposeful. Copropraxia (sexual or obscene gestures) and echopraxia (imitation of someone else's movements) represent special forms of complex motor tics. Complex vocal tics include coprolalia (uttering socially unacceptable words and obscenities), echolalia (repeating the last-heard word or phrase) and palilalia (repeating one's own sounds or words, sometime like stuttering). The majority of patients with TS suffers from mild to moderate tics. Severe or extreme tics occur only in a minority of patients. Tics fluctuate spontaneously, are influences by different environmental factors, and have a characteristic age dependency with typical onset between the age of 6-8 years and a maximum between the age of 10-12 years. Tics can occur as individual tics, but also in bouts. Tics are generally experienced as involuntary. However, there is evidence that tics are not “abnormal” but “physiological” movements that are only misplaced both in time and context. Most (adult) patients are able to suppress their tics voluntarily. Only recently, it became clear that voluntary tic suppression does not result in a paradoxical tic increase, although most patients believe in such a tic rebound. With increasing age, patients report about a feeling that precedes the occurrence of a tic. At present, it is unclear whether these premonitory urges are a prerequisite of successful tic inhibition.

L2. Everything you have always wanted to know about the co-morbidities of GTS (including videos and epidemiology). *Cath D C* - Utrecht university, department of clinical & health psychology.

GTS affects between 0.3% [10] and 1% of the population, a.o. depending on age of the group under study and on the sampling method used. Tics occur predominantly in young people (before age 18), and tend to have a waxing and waning course. Interestingly, a GTS diagnosis is twice more likely to occur in non-Hispanic white persons than in Black persons or in Hispanics. There is a male to female preponderance of between 3:1 and 4.3:1. In clinical series the large majority of cases (79%) have co-morbid psychopathology, with attention deficit/ hyperactivity disorder (ADHD) predominantly of the inattentive or combined subtype, being the most frequent co-morbid disorder in up to 60% of the cases in both children and adults (Stewart et al., 2006), followed by Obsessive-Compulsive Disorders (OCD; Robertson, 2000), anger control problems, sleep disorder, learning disorders, mood disorders, anxiety disorders, and conduct and oppositional defiant disorders (CD/ODD). Sex differences occur with respect to this co-morbidity, with predominance of males over females for ADHD, CD/ODD, anger control problems and learning disorders, and a female preponderance for OCD and self-injurious behavior. Other co-morbidities include impulsive, self-injurious and aggressive behaviour, autism spectrum disorders and sleep disorders (Robertson, 2000) . Especially in adults, comorbidity often forms the main reason to seek help. In this lecture, we will provide an overview of the epidemiology of GTS co-morbidities across the lifespan, and illustrate the co-morbidity issue using video examples, and invite participants to comment on the diagnostic in an interactive way.

L3. Neuroimaging in Tourette's Syndrome. *Veltman D J* - Department of Psychiatry, VU University Medical Center.

Although non-invasive methods for in-vivo imaging have been available at least since the '90s, imaging patients with Tourette Syndrome has proved to be difficult and early results were inconsistent, due to factors such as clinical heterogeneity of TS and technical obstacles during scanning, in particular patients' movements. Over the last decade, however, a considerable number of imaging studies in TS has been published, both anatomical and functional, and also including molecular imaging studies. Anatomical (morphological) studies have provided evidence for increased subcortical hyperintensities in TS, coupled with cortical thinning in various prefrontal regions and alterations in sensorimotor white matter tracts. Findings with regard to the motor system have been inconsistent, as both increased and decreased motor cortex volume has been reported, as well as increased and reduced white matter integrity. Functional imaging studies have shown involvement of sensory and limbic regions in premonitory urges, together with increased motor and premotor activity during tics. Activity in prefrontal-striatal-thalamocortical circuits effecting top-down control over motor pathways is likely to be reduced during tics, but tic inhibition may result in worse performance during e.g. impulse control tasks. Molecular imaging studies are still scarce in TS but available data point to

involvement of both dopaminergiv and GABA-ergic transmission in the disorder. Overall, imaging data support the notion of TS as a nerurodevelopmental disorder characterized by functional and morphological changes predominantly affecting striatal-frontal circuitry, which may reflect both underlying pathogenetic and compensatory mechanisms .
Inconsistent findings across studies may be explained by various methodological issues as well as clinical heterogeneity within TS and associated comorbidity.

L4. Neuroimaging in Obsessive-Compulsive Disorder. *Van den Heuvel O A* -
Department of Psychiatry and Department of Anatomy & Neurosciences, VU University Medical Center, Amsterdam, The Netherlands.

I will give an overview of 20 years brain imaging research in OCD, by discussing structural studies (voxel-based morphometry, cortical thickness, diffusion tensor imaging) and functional imaging studies (at rest and during task performance). I will present the results of some individual studies (including our own work), some meta-analyses and two recent mega-analyses of pooled MRI data of the OCD Brain Imaging Consortium (OBIC). I will also discuss overlap and differentiation within OCD (OCD symptom dimensions) and between related disorders (anxiety disorders and obsessive-compulsive spectrum disorders, including Tourette's syndrome). I will present the endophenotype studies (including unaffected 1st degree relatives of OCD patients) on executive functioning in OCD and discuss the implications for future imaging-genetics studies. Finally, I will present some OCD 'disease models' and it's relevance for future research on Tourette's syndrome.

Friday, April 25

(9:00-10:30) INVITED SESSION I: – Updates on the neurobiology of Tourette Syndrome

Chairs: *K. Müller-Vahl (University of Hannover, Germany), D. Cath (Utrecht University, Netherlands)*

L5. Goal-directed and habitual controls in Gilles de la Tourette syndrome. *Worbe Y* – [1] Neurology Department, Pitié-Salpêtrière Hospital, APHP, Paris, France, [2] CR-ICM, Spine and Brain Institute, Pitié-Salpêtrière Hospital, Paris, France.

In humans and animals, optimal behavioural performance results from a balance between adaptive flexible and more rigid repetitive choices, which are supported by goal-directed and habitual systems, respectively. Goal-directed and habitual systems may act synergistically or competitively and so far, their abnormal interactions could potentially lead to neuropsychiatric disorders. In pathological conditions, such as Gilles de la Tourette syndrome (GTS), the balance could be shifter towards the habitual system leading to a repetition of certain actions without achieving a specific goal. Such an aberrant habit formation could potentially underlie both abnormal movements (tics) and behaviours (compulsions) characteristic to GTS patients. As brain habitual control system is submitted to the mesostriatal dopaminergic control, in GTS the use of dopamine antagonists could alleviate the clinical symptoms, probably via the disruption of habit formation mechanism. To test this hypothesis, we employed the 3-stages instrumental learning paradigm that included an initial instrumental learning stage, a subsequent outcome devaluation test and a 'slip-of-action' stage where participants were asked to selectively respond to stimuli that signalled the availability of still- valuable outcomes, whereas they should withdrawal the response to the devalued stimuli. This task stage directly tests the balance between goal directed and habitual systems: if goal-directed system exerts the control over behaviour, this results in a selective responding towards valuable as opposed to devalued outcomes. The dominance of the habitual control system leads to commission errors on trials with the devalued outcomes. Three groups of subjects completed this task: unmedicated and medicated GTS patients and healthy controls. Subsequent statistical analysis with mixed-measures ANOVA showed that all groups successfully learned from the instrumental learning stage of the task (Main effect of Learning: $F_{(2,48)} = 161.00$, $p < 0.0001$), with no difference in the learning rate at the end of this stage. Similarly, there was no difference in the performance in the outcome devaluation test, suggesting that both groups of GTS patients and healthy volunteers learned the action-outcome associations. By contrast, there was a significant statistical difference (Main effect of Group: $F_{(248)} = 4.47$, $p = 0.024$)) in the 'slip-of-action' stage, where unmedicated GTS patients showed the highest rate of the response on the devalued stimuli on post-hoc comparisions ($F_{(248)} = 4.86$, $p = 0.020$), whereas the performance of the medicated GTS patients was similar to those of controls.

These still preliminary results suggest the dominance of habitual system of behavioural control in drug naive GTS patients. Such aberrant mechanisms of behavioural control could play a key role in the GTS symptoms formation and maintenance.

L6. Changes in functional MRI following Habit Reversal Training. *Mohammadi B* - Klinik für Neurologie INI - Hannover, Germany.

Objectives: Tourette syndrome (TS) is a neuropsychiatric disorders characterized by motor and vocal tics. Behavior therapy, based on habit reversal training (HRT), offers a new promising approach to tic reduction. Randomized controlled trials in both children and adults demonstrated that HRT results in a tic reduction that even last for months after therapy was stopped. The aim of this study was to investigate whether treatment with HRT results in significant functional and structural brain changes.
Methods: Functionally connected brain networks during rest were defined by independent component analysis (ICA) to assess differences between TS patients and healthy controls. Analysis was carried out using FSL (FMRIB's Software Library).
Results: Using ICA we found different networks as described in previous studies. Increased connectivity was found in TS patients in a number of networks such as default mode network, sensori-motor network and central executive network. Some of these changes correlated with clinical scores. These changes were partially reversed after HRT.
Conclusions: We found significant changes in different networks involved in cognition, motor- and behavioral-control and monitoring in TS patients. The significant clinical development after HRT in TS and its correlation with partial reversal of changes at rest show the affectability of described networks after therapy in TS.

L7.Neuroimaging in OCD: tic-related circuits? *Van den Heuvel O A* - Department of Psychiatry and Department of Anatomy & Neurosciences, VU University Medical Center, Amsterdam, The Netherlands.

Although non-invasive methods for in-vivo imaging have been available at least since the ’90s, imaging patients with Tourette Syndrome has proved to be difficult and early results were inconsistent, due to factors such as clinical heterogeneity of TS and technical obstacles during scanning, in particular patients’ movements. Over the last decade, however, a considerable number of imaging studies in TS has been published, both anatomical and functional, and also including molecular imaging studies. Anatomical (morphological) studies have provided evidence for increased subcortical hyperintensities in TS, coupled with cortical thinning in various prefrontal regions and alterations in sensorimotor white matter tracts. Findings with regard to the motor system have been inconsistent, as both increased and decreased motor cortex volume has been reported, as

well as increased and reduced white matter integrity. Functional imaging studies have shown involvement of sensory and limbic regions in premonitory urges, together with increased motor and premotor activity during tics. Activity in prefrontal-striatal-thalamocortical circuits effecting top-down control over motor pathways is likely to be reduced during tics, but tic inhibition may result in worse performance during e.g. impulse control tasks. Molecular imaging studies are still scarce in TS but available data point to involvement of both dopaminergiv and GABA-ergic transmission in the disorder. Overall, imaging data support the notion of TS as a nerurodevelopmental disorder characterized by functional and morphological changes predominantly affecting striatal-frontal circuitry, which may reflect both underlying pathogenetic and compensatory mechanisms . Inconsistent findings across studies may be explained by various methodological issues as well as clinical heterogeneity within TS and associated comorbidity.

L8. The course of GTS in adults: prospective findings. *Cath D C* - Utrecht university, department of clinical & health psychology.

Generally, tics onset at the age of primary school, and tend to wane in adolescence, with up to 70% of TS individuals reporting significant decrease in frequency and intensity of tics by age 18 (Leckman JF *et al.* 1998). In clinical series about one third of children with TS report co-morbid OCD. Further, up to 60% of TS individuals experience co-morbid ADHD symptoms (Khalifa and von Knorring, 2003). In addition to this, TS individuals may onset with OC (and other psychiatric) symptoms for the first time in adulthood (Bloch *et al.* 2006). Especially in adults, psychiatric co-morbidity -in contrast to the tics- often forms the main reason to seek help. The course of tics and their co-morbidities into adulthood in individuals with GTS has not been widely investigated. The topic of this talk is to get some answers to the follwing questions: What are the characteristics of those adults in whom tics do not remit in adolescence or early adulthood? How do co-morbidities develop with age? And how does persistence of tics and of comorbidities impact a person's adult outcome with respect to symptom persistance and quality of life? On overview of the current literature is given, and outcomes of two naturalistic course studies in adult individuals are presented, i.e. one in TS individuals and one on the impact of tics on outcome in OCD subjects.

(10:30-11:00) Break - POSTERS

(11:00-12:30) INVITED SESSION II: Updates on on deep brain stimulation in Tourette syndrome

Chairs: *T. Foltynie (UCL, UK), M. L. Welter (Pitié-Salpêtrière, France)*

L9. Animal models of tic expression. *Bar-Gad I* - Gonda Brain Research Center, Bar Ilan University, Ramat Gan, Israel.

Motor tics are brief, repetitive, involuntary muscle contractions that interfere with ongoing behavior and are a symptom of several neural disorders, most notably Tourette syndrome. While the pathophysiology of tics is still largely unknown, multiple lines of evidence suggest the involvement of the cortico-basal ganglia loop, and specifically the striatum, in tic formation. The striatum is a major input structure of the basal ganglia, which contains a complex internal inhibitory (GABAergic) network comprised of interneurons and projection neuron collaterals. We transiently induced motor tics in freely behaving rats and primates by local microinjections of the $GABA_A$ antagonist bicuculline into the dorsolateral striatum. Acute multi-electrode (primate) and chronic multi-wire (rat) recordings were used to assess tic related neuronal activity following the injections. We characterized these tic related changes in neuronal activity and their modulation by multiple pharmacological agents. Our results indicate an intricate dopaminergic and glutamatergic modulation of the striatal GABAergic disinhibition leading to profound behavioral and neurophysiological changes. The results of this study shed light on the basic mechanisms underlying the generation and expression of motor tics and their association with the cortico-basal ganglia system.

L10. Anteromedial pallidal stimulation in patients with Gilles de la Tourette Syndrome : a multicentric double-blind randomized study. *Welter M L,[1,2] Houeto J L,[3] Karachi C,[2] Bataille B,[3] Thobois S,[4] Mertens P,[4] Burbaud P,[5] Cuny E,[5] Durif F,[6] Jalenques I,[6] Derkinderen P,[7] Raoul S,[7] Borg M,[8] Fontaine D,[8] Karck P,[9] Chabardes S,[9] Tezenas du Montcel S,[10] Worbe Y,[1,2] Hartmann A,[1,2] Yelnik J,[2] Mallet L[2]* – [1] Neurology Department, Pitié-Salpêtrière Hospital, APHP, Paris, France, [2] CR-ICM, Spine and Brain Institute, PitiéSalpêtrière Hospital, Paris, France, [3] Neurology and Neurosurgery Department, CHU Poitiers, Poitiers, France, [4] Neurology and Neurosurgery Department, CHU Lyon, Lyon, France, [5] Neurology and Neurosurgery Department, CHU Bordeaux, Bordeaux, France, [6] Neurology and Psychiatry Department, CHU Clermont-Ferrand, Clermont-Ferrand, France, [7] Neurology and Neurosurgery Department, CHU Nantes, Nantes, France, [8] Neurology and Neurosurgery Department, CHU Nice, Nice, France, [9] Neurology and Neurosurgery Department, CHU Grenoble, Grenoble, France, [10] Biostatistics and Medical Informatics Unit and Clinical Research Unit, Pitié–Salpêtrière Hospital, Paris, France.

Gilles de la Tourette syndrome (GTS) is thought to result from dysfunction of the associative-limbic territory of the basal ganglia (BG). High frequency stimulation of the BG has recently been applied in severe GTS patients medically refractory using the centromedian-parafascicular complex (CM-Pf) of the thalamus, the internal part of the

globus pallidus (GPi) within the dorsolateral portion (motor) or ventromedial portion (associative-limbic) in open and/or small double-blind studies. Here we report the effect of high-frequency stimulation of the anteromedial part of the GPi in 19 patients with GTS (age=31±12, mean Yale Global Tic Severity Scale-YGTSS=75±11, mean Global Assessment of Functioning-GAF=63±16) in a randomized parallel double-blind study. Patients were assessed one month before surgery, 3, 6, 9 and 12 months after. Of these 19 patients operated for GPi stimulation, 7 were randomly assigned to undergo active GPi stimulation and 9 to undergo sham stimulation, 3 were not randomized. The primary outcome measure was the severity of tics as assessed by the YGTSS at the end of the 3-month randomized period. General psychopathologic findings, functioning and neuropsychological tests were also assessed. At the end of the randomized double-blind period, the YGTSS score was not significantly different after active pallidal stimulation than the score after sham stimulation (P=0.32). In patients with active stimulation, the motor tic, clinical global impression, Yale-Brown Obsessive Compulsive scale (YBOCS), anxiety and depression scores were significantly lower than before surgery, and the GAF was significantly higher, however. Conversely, no significant change was observed in patients with sham stimulation. Six months after surgery, all patients received pallidal stimulation. One year after surgery, the YGTSS was significantly reduced by 39%, obsessive-compulsive symptoms, anxiety and depression scores were also significantly decreased and the GAF score significantly increased. No neuropsychological or behavioural side effects occurred. Five patients presented infections requiring removal of the electrode with re-implantation in 2. These preliminary findings suggest that stimulation of the anteromedial part of the GPi reduce symptoms of severe forms of GTS one year after surgery but is associated with high risk of infections.

L11. Thalamic and pallidal deep brain stimulation in patients with severe Tourette Syndrome.

Ackermans L, Duits A, Smeets A, Temel Y – University of Maastricht, The Netherlands.

Background: Deep Brain Stimulation (DBS) seems a promising treatment for severe therapy refractory Tourette patients. A major controversial issue is the choice of the brain target that leads to optimal outcomes within a dysfunctional network of the basal ganglia and related thalamocortical circuits. We compare the effects of stimulation of the centromedian nucleus – substantia periventricularis – nucleus ventro-oralis internus (CmSpv-Voi) crosspoint of the thalamus with the limbic part of the globus pallidus internus (GPi).

Methods: Eleven patients were selected for bilateral DBS surgery, six targeting the CmSpv-Voi crosspoint of the thalamus and five targeting the limbic GPi. All patients were evaluated twice, before and after surgery, on all primary and secondary outcomes, as well as on cognition. Follow-up duration was 12 months in the thalamic group and variable in

the pallidal group (range seven – 38 months). Primary outcome measure was tic severity, evaluated with the Yale Global Tic Severity Scale (YGTSS), the modified Rush Video-Based Tic Rating Scale (mRVRS) and the amount of video-tics. Secondary outcome measures were associated behavioural disorders and mood. Possible negative effects on cognition and adverse events were monitored.

Results: Thalamic and pallidal stimulation produced a significant improvement in tic severity in comparison with preoperative assessments (YGTSS 49.2% vs. 67.%, mRVRS 35.5% vs. 46.2%, video-tics 72.0% vs. 78.4%, respectively). No significant differences between both groups were found on tic severity measures,however, a positive trend towards limbic GPi stimulation was seen. No significant differences between groups were found on the secondary outcome measures and on cognition. Side-effects were more pronounced in the thalamic group, being lack of energy and visual disturbances in all patients.

Discussion and conclusion: The findings from this comparative study suggest that there are no significant differences in effect between stimulation of the Cm-Spv-Voi crosspoint of the thalamus and stimulation of the limbic GPi. However, a positive trend in improvement of tics and OCb towards limbic GPi stimulation was seen. Moreover, the risk of stimulation induced side-effects seemed higher in the thalamic group.

(12:30-13:30) Break - POSTERS

(13:30-14:15) INVITED SESSION III: Genetics of Tourette syndrome and related disorders

Chairs: *T. P. Paschou (Democritus University of Thrace, Greece), P. Hoekstra (Groningen University, The Netherlands)*

L12. Comparative Genomics of Tourette Syndrome and OCD. *Scharf J – Harvard Medical School, USA*

Tourette Syndrome (TS) and OCD are both highly heritable, and are thought to have shared genetic susceptibility based on twin and family studies. Emerging analytic methods now provide the ability to partition the human genome into different structural or functional units and to examine their relative genetic contributions to the overall heritability of a genetic disorder. Here, we present two complementary approaches to dissect the underlying genetic architecture of TS and OCD as well as their genetic relationship. Our results confirm that TS and OCD are both strongly heritable (TS h^2=0.58, p=5.6x10^{-12}; OCD h^2=0.37, p=1.5x10^{-7}) genetic evidence that the classic twin and family study estimates of TS and OCD heritability are not inflated. The data suggest that OCD is primarily a polygenic

disorder, consisting of a large number of genes of small effect distributed throughout the genome, though with a statistically significant concentration of heritability on chromosome 15. OCD and TS have some degree of shared heritability (r=0.41; p=0.002), though there is a clear distinct component as well. Furthermore, using a polygenic risk score approach, we provide evidence that OCD with TS/CT is genetically different than OCD without tics. Overall, these results advance our knowledge of TS and OCD genetics and have the potential to inform nosology, future strategies for gene discovery, and ultimately may provide new insights into pathophysiology and treatments of these disorders.

L13. Gene Expression and Splicing correlate with tics, drugs and ADHD symptoms in Tourette Syndrome. *Sharp F* - Department of Neurology, University of California at Davis, Davis, California**.**

Gene expression was examined in blood of Tourette Syndrome (TS) patients since it should reflect some interaction of genetic and environmental factors important in TS. Using whole genome microarrays we found that age affected genes associated with interferon response, viral processing, Natural Killer Cells and cytotoxic T lymphocytes. Because tics tend to abate with age we examined genes that correlated with tic severity, and of these many were catecholamine-(DRD2,HRH3, MAOB, BDNF, others), GABA- and acetylcholine-related. These were of interest given dopamine receptor blockers are used to treat tics, and GABA and acetylcholine neurons have been found to be decreased in TS brain. We also found over 1000 genes in blood that correlated with inattention and over 1000 that correlated with hyperactivity/impulsivity and 262 that correlated with both in attention and hyperactivity/impulsivity. Thus, the genesis of ADHD like symptoms in TS might result from a complex genetic interaction. Over 20 of the genes have been identified in previous GWAS studies of ADHD. Medications were found to have a profound effect on peripheral blood gene expression including dopamine, norepinephrine and GABA pathways. Finally, using whole genome exon microarrays, several hundred genes were predicted to be differentially alternatively spliced in TS compared to healthy control children, and these differences in splicing might be sensitive and specific enough to diagnose TS. Future studies are needed to confirm and extend these findings, and perhaps provide novel pharmacological targets for treating specific TS symptoms.

(14:15-15:45) ORAL PRESENTATIONS I: Genetics

Chairs: *T. P. Paschou (Democritus University of Thrace, Greece), P. Hoekstra (Groningen University, The Netherlands)*

O1. A Second Genome Wide Association Study for Tourette Syndrome. *Tsetsos F[1]*, Yu D[2,6]*, Sul J H[3]*, TSAICG, GGRI Consortium, Coppola G[4], Paschou P[1], Mathews C[5],*

Scharf J[2, 6-8] - [1] Department of Molecular Biology and Genetics, Democritus University of Thrace, Alexandroupoli, Greece, [2] Psychiatric and Neurodevelopmental Genetics Unit, Center for Human Genetics Research, Department of Psychiatry, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA, [3] Computer Science Department, University of California, Los Angeles, California, USA, [4] Department of Psychiatry and Semel Institute for Neuroscience and Human Behavior, David Geffen School of Medicine, University of California Los Angeles, Los Angeles, California, United States of America; Program in Neurogenetics, Department of Neurology, David Geffen School of Medicine, University of California Los Angeles, Los Angeles, California, United States of America, [5] Department of Psychiatry, University of California at San Francisco, San Francisco, CA, US, [6] Stanley Center for Psychiatric Research, Broad Institute of Harvard and MIT, Cambridge, Massachusetts, USA, [7] Department of Neurology, Massachusetts General Hospital, Boston, MA, USA, [8] Division of Cognitive and Behavioral Neurology, Brigham and Womens Hospital, Boston, MA, USA.

Tourette Syndrome (TS) is a common neurodevelopmental disorder characterised by the occurrence of multiple chronic motor and vocal tics. Despite evidence for a strong genetic contribution, TS inheritance is complex, and risk alleles have proven difficult to identify. A previous Genome Wide Association Study has not identified common variants associated with Tourette Syndrome at genome-wide significance thresholds, although several interesting hits of indicative association were observed. Here, we present a preliminary report on the second GWAS for TS. We analysed 1,512 controls and 2,149 cases of European or Ashkenazi Jewish ancestry from the Tourette Syndrome Association International Genetics Consortium (TSAICG), 631 European cases and 544 European controls from the Gilles de la Tourette Syndrome Genome-wide Association Study Replication Initiative (GGRI), 100 trios and 228 cases from the TIC Genetics Consortium, 3,262 controls of mixed ancestry from the Brain Genomics Superstruct Project, 1,008 controls of European or Jewish ancestry from the *National Institute of Neurological Disorders and Stroke and* 1,227 controls of Jewish ancestry from Yeshiva University. Samples were genotyped using genome-wide Illumina OmniExpress Chips. Principal Component Analysis was utilised to match samples and to avoid effect by population substructure. Extensive quality control procedures resulted in a total of 565,395 SNPs. Genome-wide association analysis is being performed using the PLINK software. Our findings provide indications for the implication of several chromosomal regions that warrant further analysis as candidates for TS susceptibility loci.

O2. The Gilles de la Tourette Syndrome GWAS Replication Initiative reveals significant signal of genetic association near the Netrin 4 gene. *Karagiannidis I[1], Yu D[2, 3], GGRI Consortium[4], Paschou P[1], Mathews C[5], Scharf J[2, 3, 6, 7]* - [1] Department of Molecular Biology and Genetics, Democritus University of Thrace, Alexandroupoli, Greece, [2]

Psychiatric and Neurodevelopmental Genetics Unit, Center for Human Genetics Research, Department of Psychiatry, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA, [3] Stanley Center for Psychiatric Research, Broad Institute of Harvard and MIT, Cambridge, Massachusetts, USA, [4] The Gilles de la Tourette Syndrome Genome-wide Association Study Replication Initiative, [5] Department of Psychiatry, University of California at San Francisco, San Francisco, CA, USA, [6] Department of Neurology, Massachusetts General Hospital, Boston, MA, USA, [7] Division of Cognitive and Behavioral Neurology, Brigham and Womens Hospital, Boston, MA, USA.

Tourette syndrome (TS) is a neurodevelopmental, childhood-onset disease characterized by motor and vocal tics. Its high heritability reveals the presence of a strong genetic component, although its genetic etiology is quite complex with many genes interacting with environmental factors in order to lead to the onset of symptoms. The recentlypublished GWAS performed by the Tourette Syndrome Association International Consortium for Genetics (TSAICG) revealed several promising hits of potential association in the studied sample of (1,285 TS patients and 4,964 controls of European ancestry). In the present study, we follow up on 42 of the top GWAS hits, analyzing a sample of a total of 609 individuals with TS and 610 ancestry-matched controls originating from six countries (Hungary, Germany, Austria, Italy, Greece and Canada). Meta-analysis using the joint dataset from the original GWAS and this study was also conducted. Our analysis provides significant evidence for association for one of the studied variants (rs2060546 on 12q22) with TS genetic risk. This variant is located near the Netrin 4 (NTN4) gene, an axon guidance molecule expressed in the developing striatum. Although the functional significance of this variant is unclear it may involve regulation of adjacent histidine catabolism genes.

O3. Genome-Wide Association Study in Obsessive Compulsive Symptoms . *Zilhã N R[1], den Braber A [1], Smit D J A[1], Cath D C[2], Boomsma D I[1]* - [1] Department of Biological Psychology, VU University, Amsterdam, Amsterdam, the Netherlands, [2] Department of Clinical and Health Psychology, Utrecht University and Altrecht Academic Anxiety Disorders Center, Utrecht, the Netherlands.

Obsessive-Compulsive Disorder (OCD) is a neuropsychiatric illness with a complex genetic etiology. It is often associated with comorbid behavioral diseases such as Tourrette's Syndrome, *Attention deficit hyperactivity disorder* (ADHD), and tics disorder. Several studies have seek to report candidate genes for this disorder with, however, inconsistent results. Larger recent collaborative efforts have also indicated that larger sample sizes and/or replications studies are needed to deliver concordant results. This work is part of a larger study that seeks to investigate common susceptibility genetic variants for OC symptoms, and its comorbids. Here we report results from a Genome-Wide Association

Analysis (GWAS), to search for common Single Nucleotide Polymorphisms (SNPs) responsible for predisposition for OC symptoms, and a set-based test (PLINK) for the association between sets of markers (genes) and OC symptoms; this combines the effects of all SNPs in a gene into a test statistic and considers the association between the trait and the genes instead of all markers individually. In a primary analysis we performed a GWAS on 6931 subjects registered at the Netherlands Twin Register; secondly, for the identification of genes associated with OC symptoms, we performed a set-based test based on permutations at the gene level. By complementing GWAS with a gene-based test, a gene centric result is obtained with the relative importance of each gene. Furthermore, confounding factors such as Linkage Disequilibrium (LD) structure and gene size are corrected for. Combining these two approaches is ideally suited for pathway analysis to better interpret the findings from GWAS. We hope with this work to set the ground for a more clear understanding of the genetic susceptibility variants underlying the genetic architecture of OCD.

O4. Targeted re-sequencing approach of TS candidate genes implicates potentially functional variants in TS etiology. *Alexander J[1], Karagiannidis I[1], Potamianou H[1], Georgitsi M[1], Xing J[2,3], Sun N[2,3], Nasello C[2,3], Sandor P[4], Barr C[4], Tischfield J[2,3], Paschou P[1], Heiman G[2,3]* - [1] Department of Molecular Biology and Genetics, Democritus University of Thrace, Greece, [2] Department of Genetics, Rutgers University, Piscataway, NJ, USA, [3] Human Genetics Institute of New Jersey, Piscataway, NJ, USA, [4] Toronto Western Research Institute, University Health Network, Toronto, Ontario, Canada.

Although the genetic basis of Tourette Syndrome remains unclear, several candidate genes have been implicated. Here, using a set of 382 TS individuals we investigate four of the most prominent candidate genes for TS (HDC, SLITRK1, BTBD9 and SLC6A4) and attempt to identify possibly causal variants using a targeted re-sequencing approach and next generation sequencing technology. Identification of possible disease causing variants under different modes of inheritance was performed using the algorithms implemented in VAAST. Furthermore, we propose a novel method to prioritize and rank variants from exome sequencing capture by integrating information from open-source annotation databases. We identified several novel candidate variants that could be implicated in TS etiology and are yet to be further validated using Sanger sequencing. Our method can be used with supplementary bioinformatics filters to prioritize variants in future sequencing projects.

O5. CNV analysis in a large cohort of Tourette syndrome patients from Denmark.

Arumilli M[1, 2], Bertelsen B[1], Jensen L J[2], Paschou P[3], Tümer Z[1] – [1] Applied Human Molecular Genetics, Copenhagen University Hospital,Rigshospitalet, Glostrup, Denmark, [2] Department of Disease Systems Biology, Novo Nordisk Foundation Center for Protein Research, Faculty of Health and Medical Sciences, University of Copenhagen, [3] Department of Molecular Biology and Genetics,Democritus University of Thrace, Alexandroupoli, Greece.

Background: Tourette syndrome (TS) is a neurodevelopmental disorder with a prevalence of 1% in the world population. Copy-number variations (CNVs) have been proved to play a key role in the susceptibility of several complex neurodevelopmental disorders such as autism, schizophrenia and mental retardation. However, CNVs have not been extensively studied in TS and the molecular genetic mechanisms and biological pathways underlying the adverse impacts of TS remain unexplored so far.

Objective: To identify the pathways, protein complexes and genes susceptible to TS using complex bioinformatics methods and perform functional analyses to validate them as the candidate TS genes.

Methods: We have screened 242 TS patients using Affymetrix CytoScanHD chromosome microarray platform and Affymetrix Cytogenetics Whole-Genome 2.7M Array and the CNVs were identified using ChAS software. Inaddition, 2000 controls genotyped on Affymetrix CytoScan HD array platform will be used in this study. In this project the genes within the CNVs found in more than 2 patients along with rare variants will be investigated with pathway analysis tools to identify the significantly enriched biological processes in TS. Protein-interaction data will be used to identify the genes that encode different subunits of the same protein complex that might exhibit similar phenotypes. This study will also focus on meta-analysis of the CNV data, which utilizes the existing linkage and GWAS findings on TS and neurodevelopmental disorders. All the candidate genes identified in TS patients using the bioinformatics analysis will be screened in controls and further investigated through functional studies.

Significance: The novel TS susceptibility genes identified in this project will contribute to understand the genetic mechanisms and the underlying factors in TS that gives insights to develop better diagnosis and treatment strategies.

O6. Intragenic deletions affecting two alternative *IMMP2L* transcripts in patients with Tourette syndrome.

Bertelsen B[1], Melchior L[1], Jensen L R[2], Groth C[3], Glenthøj B Y[4], Rizzo R[5], Mol Debes N[3], Skov L[3], Brøndum-Nielsen K[1,6], Paschou P[7], Silahtaroglu A[6], Tümer Z[1] - [1] Applied Human Molecular Genetics, Kennedy Center, Copenhagen University Hospital, Rigshospitalet, Glostrup, Denmark, [2] Institute for Human Genetics, Ernst-MoritzArndt-University Greifswald, Griefswald, Germany, [3] The Tourette Clinic, Department of Pediatrics, Herlev University Hospital, Herlev, Denmark, [4] Center for

Neuropsychiatric Schizophrenia Research & Center for Clinical Intervention and Neuropsychiatric Schizophrenia Research, Copenhagen University Hospital, Psychiatric Center Glostrup, Denmark, [5] Section of Child Neuropsychiatry, Department of Pediatrics, University of Catania, Catania, Italy, [6] Institute for Cellular and Molecular Medicine, University of Copenhagen, Copenhagen, Denmark, [7] Department of Molecular Biology and Genetics, Democritus University of Thrace, Alexandroupoli, Greece.

Tourette syndrome (TS) is a childhood onset neurodevelopmental disorder characterized by involuntary movements and vocalizations, known as tics. The etiology of TS is complex and largely unknown, but has a strong genetic component. *IMMP2L* (inner mitochondrial membrane peptidase, subunit 2) is one of the few genes that have been suggested to increase susceptibility to TS, after identification of chromosomal rearrangements affecting *IMMP2L* in several families with TS or tics. However, to date only a single study has investigated the role of structural copy number variations (CNVs) of *IMMP2L* in a small cohort of TS patients without finding any deletions/duplications. Through CNV screening of a cohort of 188 unrelated TS patients and 316 controls from Denmark, we identified seven patients (3.7%) and 3 controls (0.9%) with intragenic *IMMP2L* deletions, thus, the frequency of *IMMP2L* deletions was significantly higher in patients than in controls (P= 0.0447). Four of the deletions identified in the patients did not include any known exons of *IMMP2L*, but were within intron 3. These deletions were found to affect a shorter *IMMP2L* mRNA species with two alternative 5'-exons, one of which included the ATG start codon. We showed that this short transcript and the previously published long transcript were expressed in several brain regions, with particularly high expression in cerebellum and hippocampus. The current findings give further evidence for the role of *IMMP2L* as a susceptibility factor in TS and suggest that intronic changes in disease susceptibility genes should be investigated further for presence of alternatively spliced exons.

O7. Tourette's syndrome in a person carrying the Huntington's disease gene.

Piedad J C P[1], Cavanna A E[1, 2, 3], Rickards H[1] – [1] Michael Trimble Neuropsychiatry Research Group, University of Birmingham & BSMHFT, Birmingham, UK, [2] School of Life and Health Sciences, Aston University, Birmingham, UK, [3] Sobell Department of Motor Neuroscience and Movement Disorders; University College London & Institute of Neurology, London, UK.

Background: Tourette's syndrome (TS) is a childhood-onset neuropsychiatric condition characterised by motor and vocal tics, as well as a spectrum of behavioural disorders. Huntington's disease (HD) is also a basal ganglia disorder due to abnormal trinucleotide expansion of the *huntingtin* gene and presents with motor and behavioural disorders as well as cognitive impairment. Although some diagnostic criteria for TS consider HD as the

differential diagnosis, case studies have been reported of TS symptoms in people carrying the HD gene.

Objectives: We set out to examine and present a case of symptomatology consistent with a diagnosis of TS in someone carrying the HD gene.

Methods: Informed consent was obtained for a single-case observational study using clinical interviews, standardised rating scales and video recording (three time points).

Results: We present a male patient with onset of motor and vocal tics at 6 and 7 years old, respectively, and other clinical features suggestive of a TS diagnosis. Molecular analysis confirmed pathological expansion of the *huntingtin* gene, and a family history of HD was reported.

Conclusion: The clinical presentation and history will be discussed, with video clips to illustrate motor phenotypes that may differentiate between TS and HD. We will also discuss the course of the TS symptoms and hypothesise whether carrying the HD gene may impact upon the pattern of its progression. This case highlights potential diagnostic issues in patients with basal ganglia disorders and prompts a discussion about what would be expected from the combination of potentially distinct basal ganglia neuropathological mechanisms such as those seen in TS and HD.

(17:00-17:30) Opening Ceremony

Andreas Hartmann, French National Reference Center for Gilles de la Tourette Syndrome, Department of Neurology, Pitié-Salpêtrière, Paris, France

Peristera Paschou, ESSTS Chair, Democritus University of Thrace, Greece

Ruud Mindera, ESCAP President

Marie Vidailhet, Head of Movement Disorders, Department of Neurology, PitiéSalpêtrière, Paris, France

(17:30-18:30) Keynote Lecture

Chair: *Y. Worbe, Pitié-Salpêtrière, Paris, France*

L14. Brain-Based Vulnerability and Compensation in Tourette Syndrome ? *Peterson B, Columbia University, USA*

The tics of Tourette syndrome (TS) are semi-involuntary movements that can be inhibited voluntarily for brief periods of time. Tics usually decline in severity over adolescence, but can remain highly debilitating in adulthood. Considerable brain imaging evidence suggests that tics arise from a constitutional vulnerability to developing semi-involuntary movements combined with disturbances in the neural circuits that control movements and somatic urges. Anatomical imaging studies, for example, suggest that volumes of the caudate nucleus, a long-surmised site of origin of tic behaviors, and the thickness of

sensorimotor cortices that effect motor commands, are reduced across the life span in persons with TS. These regions seem to represent brain-based vulnerabilities in persons with TS. In contrast, the voluntary suppression of tics powerfully activates prefrontal and parietal cortices, and repeated activation of these regions seems to produce a compensatory, neuroplastic hypertrophy of these cortices that is inversely proportional to the severity of tic symptoms. Activity-dependent, neuroplastic compensation, in other words, likely helps to modulate or control the severity of tic symptoms. Numerous other brain regions, including limbic regions and the corpus callosum, seem to participate in this compensatory response. Failure of this neuroplastic response likely is a major determinant of more severe and more persistent tic symptoms throughout development.

Saturday, April 26

INVITED SESSION IV: The history of Tourette syndrome

Chairs: *A. Hartmann (Pitié-Salpêtrière, France), D. Martino (London, UK)*

L15. George Gilles de la Tourette, The man behind the name: living his writing.

Walusinski O - Family practice, Brou, France.

Georges Gilles de la Tourette (1857-1904) spend less than three years extracting a new pathological entity from the descriptive chaos of chorea. Bearing his name, Gilles de la Tourette syndrome is definitively associated with him. I had the chance to exhume his family archives, stored away for decades in the attic of the Charbonneau Lassay Museum in Loudun, city near his birthplace. It is a small part of these unpublished archives that I will present during the ESSTS 2014 meeting. They help to illuminate ignored aspects of his life. Gilles de la Tourette is also known to be a prolific author who has left us many innovative writings; for instance, I will briefly review his description of restless legs syndrome.

L16. Around Gilles de la Tourette, the 3B: Bourneville, Brissaud, Babinski.

Poirier J, Catala M - Pitié-Salpêtrière, Paris, France).

Georges Gilles de la Tourette learned Neurology in Paris, which was a major centre for the emergence of this medical discipline in the nineteenth century. During his training, he met with several colleagues including Bourneville, Brissaud and Babiński (namely the 3 B 's). These four neurologists were the favourite students of Jean-Martin Charcot at the Hospice de la Vieillesse-Femmes (now known as La Salpêtrière Hospital). Jean-Martin Charcot was undoubtedly both their mentor and father figure. He was the undisputed master of the nascent Neurology at the end of the nineteenth century. He developed the

clinicopathological method that was continuously used by his successors. Georges Gilles de la Tourette had medical or friendly relations with the three members of this school. After analysing the works of the 3 B's, we present the relationships that each B has been able to forge with Georges Gilles de la Tourette. These four neurologists were salient figures of French Neurology in the post-Charcot period.

L17. Armand Trousseau and Georges Gilles de la Tourette: From tics to hysteria.
Cavanna A E - University of Birmingham, UK.

A case series by French neuropsychiatrist Georges Gilles de la Tourette described in 1885 the 'maladie des tics', which earned him eponymous fame. Both his colleagues at La Salpêtrière hospital in Paris and medical historians report that he was a highly intelligent, if irascible, character. Interestingly, the Gilles de la Tourette syndrome was only a very minor contribution of its author, at the time. While Armand Trousseau's description of the 'tic non douloureux' in 1873 had already captured the core features of the tic syndrome, Gilles de la Tourette's main and continued contributions were on hysteria and hypnotism, where he championed the concepts developed by his mentor Jean-Martin Charcot.

(10:00-10:30) Break - POSTERS

(10:30-11:30) Keynote Lecture

Chair: *P.Paschou, Democritus University of Thrace, Greece*

L18. Transcriptome analysis of the human striatum in Tourette syndrome.
Lennington J B[1, 2], Coppola G[1, 2*], Kataoka-Sasaki Y[1, 2*], Fernandez T[1, 3], Palejev D[1, 2*], Li Y[1], Huttner A[2, 4], Pletikos M[6], Šestan N[5, 6], Leckman J F[1], Vaccarino F M[1, 2, 5, 6]* – [1] Child Study Center, [2] Program in Neurodevelopment and Regeneration, [3] Department of Psychiatry, [4] Department of Pathology, [5] Yale Kavli Institute for Neuroscience, [6] Department of Neurobiology, Yale University School of Medicine, New Haven, CT. *equal contribution.

Genome wide association studies have not revealed any risk-conferring common genetic variants in Tourette syndrome (TS), requiring the adoption of alternative approaches to investigate the pathophysiology of this disorder. We obtained the basal ganglia transcriptome by RNA sequencing of TS and normal controls using postmortem brain tissue. We found 309 down-regulated and 822 up-regulated genes in the caudate and putamen (striatum) of TS individuals. Using data-driven gene network analysis, we identified seventeen gene co-expression modules associated with TS. The top-scoring down-regulated module in TS was enriched in neurotransmission-related transcripts, with particular relevance for striatal interneuron, which was confirmed by decreased numbers

of cholinergic and GABAergic interneurons by immunocytochemistry in the caudate and putamen in a parallel set of brains. The top-scoring up-regulated module was enriched in immune-related genes, which was consistent with activation of microglia in patients' striatum. Genes implicated by copy number variants (CNV) in TS were enriched in the interneuron module as well as in a protocadherin module. Module clustering revealed that the interneuron module was correlated with a neuronal metabolism module. Thus, convergence of differential expression, network analyses and module clustering, together with CNVs implicated in TS, strongly implicate disrupted interneuron signaling in the pathophysiology of severe TS, and suggests that metabolic alterations may be linked to their death or dysfunction. The cause for the prominent activation in immune-related genes in patient's striatum remains to be established.

(11:15-12:45) ORAL PRESENTATIONS II: Neuroimaging and Therapies

Chairs: *: I. Bar-Gad (Bar-Ilan University, Israel), M. Vidailhet ((Pitié-Salpêtrière, France)*

O8. Multi-Modal brain imaging in Tourette Syndrome. *Draper A[1], Jackson S[1], Stephenson M[2], Morris P[2], Morgan P[3], Jackson G[4]* - [1] School of Psychology, University of Nottingham, UK, [2] Sir Peter Mansfield Magnetic Resonance Centre, University of Nottingham, UK, [3] School Of Medicine, University of Nottingham, UK, [4] Division of Psychiatry, Institute of Mental Health, University of Nottingham, UK.

Tourette Syndrome (TS) is a developmental neurological disorder characterised by vocal and motor tics and is associated with cortical-striatal-thalamic-cortical circuit dysfunction and hyper-excitability within cortical motor areas. GABA, the main inhibitory neurotransmitter in the brain, is altered in TS, as demonstrated by reduced short-intervalcortical inhibition response and post-mortem findings of reduced GABA-ergic interneurons. This reduction in GABA has been reasoned to accentuate hyper-excitability of cortical motor areas. We used ultra-high-field (7 Tesla) magnetic resonance spectroscopy to investigate in-vivo concentrations of GABA within the supplementary motor area (SMA) of individuals with TS, a region strongly associated with the cortical genesis for motor tics. We demonstrate that GABA concentrations within the SMA are paradoxically elevated in individuals with TS compared to a matched control group. GABA concentrations in the SMA were inversely related to 2 measures of cortical excitability: fMRI BOLD activation, and motor evoked potentials to transcranial magnetic stimulation preceding a volitional movement in the TS group. GABA concentrations were also positively related to the integrity of white matter of the corpus callosum connecting the SMA across hemispheres (as measured by Diffusion Tensor Imaging). By combining

information from different techniques, we can conclude that tonic levels of GABA in the SMA relate to cortical excitability, and inter-hemispheric connectivity in Tourette Syndrome.

O9. Longitudinal MRI analysis of the developmental changes of Tourette Syndrome reveal reduced diffusion in the cortico-striato-thalamo-cortical pathways. *Mol Debes N[1], Jeppesen S S[2], Raghava J M[3], Groth C[1], Rostrup E[2], Skov L[1] – [1]* Paediatric Department, Herlev University Hospital, Denmark, [2] Functional Imaging Unit, Department of Diagnostics, Glostrup University Hospital, Denmark, [3] Center for Clinical Intervention and Neuropsychiatric Schizophrenia Research (CINS), Psychiatric Center, Denmark.

Background: There is evidence that cortico-striato-thalamo-cortical (CSTC) pathways are involved in the pathophysiology of Tourette syndrome (TS). In the present literature, cross-sectional neuroimaging studies are described. We performed a longitudinal imaging study in order to examine the development of tics over time and correlate this with MRI findings. **Methods:** We included 22 patients with TS and 21 healthy controls and performed clinical examinations and MRI scans both at baseline and 3.8-4.4 years later. We divided patients in one group with remission of tics (N=8) and one group with persistent tics (N=14). We performed voxel-based-morphometry (VBM) and tract-based-spatial-statistics (TBSS). **Results:** In the VBM analyses, as expected, a decrease in volume of left putamen was seen in controls, but not in patients. In the TBSS analyses, we found changes in mean diffusivity over time between patients and controls in right caudate nucleus, right thalamus, and right frontal lobe. In contrast to controls, parallel and perpendicular diffusivity decreased over time in most patients with TS, and were most pronounced in the patients with persisting tics compared to those with remission of tics. **Conclusion:** The findings confirm the hypothesis that CSTC pathways are involved in the pathophysiology of TS and suggest that the development of the brain in patients with remission of tics resembles the normal development of the brain more than in patients with persistent tics. This could reflect a change in brain structure or a compensatory mechanism in the brain. These two groups might represent two different phenotypical variants of TS.

O10. Altered synaptic plasticity in Tourette syndrome and its relationship to motor skill leaning. *Brandt V [1], Niessen E [2], Ganos C [1,3], Bäumer T [1], Münchau A [1] - [1]* Department of Paediatric and Adult Movement Disorders and Neuropsychiatry, Institute of Neurogenetics, University of Lübeck, Maria-Goeppert-Str. 1, Lübeck, Germany, [2] Cognitive Neurology Section, Institute of Neuroscience & Medicine (INM-3), Research

Centre Jülich, Jülich, Germany, [3] Sobell Department of Motor Neuroscience and Movement Disorders, UCL Institute of Neurology.

The aim of this study was to investigate whether altered synaptic plasticity is directly linked with impaired motor skill acquisition in Gilles de la Tourette syndrome (GTS). Cortical plasticity was assessed by measuring motor-evoked potentials before and after paired associative stimulation (PAS) in 14 GTS patients (13 male; age 18 – 39) and 15 healthy controls (12 male; age 18 – 33). Motor learning was assessed immediately after PAS and 9 months later, using the rotary pursuit task. Long-term potentiation (LTP)-like effects of PAS were present in healthy controls [$t(14) = -2.41$, $p = .03$] but not in patients [$t(13) = 1.07$, $p = .3$]. In GTS patients, synaptic plasticity was associated with tic severity and urges ($r = .82$, $p = .001$; $r = .56$, $p = .038$). While motor learning did not differ between patients and healthy controls immediately after PAS, motor skill consolidation differed between the groups 9 months later [$t(20) = 2.23$, $p = .037$]. Motor skills in healthy controls but not in GTS patients, correlated with LTP-like effects induced by PAS 9 months earlier [$r = .63$, $p = .03$]. We hypothesise that the relation between synaptic plasticity induced by PAS and symptom severity in GTS patients represents a successful compensatory mechanisms mirroring patients' tendency to de-couple previously learned connections between sensory states and motor events leading to an attenuation of urges and consequently to tic reduction. The rotary pursuit results suggest that this compensatory mechanism may be associated with impaired long-term consolidation of motor learning.

O11. Investigations of voluntary motor control in adult GTS through the lens of motor imagery: a functional MRI study. *Zapparoli L[1], Porta M[2], Gandola M[3], Colajanni V[1], Banfi G[2, 4], Servello D[2], Paulesu E[1, 2]* - [1] Psychology Department, University of MilanoBicocca, Italy, [2] IRCCS Istituto Ortopedico Galeazzi, Milan, Italy, [3] Department of Brain and Behavioural Sciences, University of Pavia, Italy, [4] University of Milano Statale, Italy.

Introduction: In spite of the prominence of motor manifestations in GTS, there are only few neurofunctional studies that investigated voluntary motor control in adult GTS patients. None investigated motor imagery, a *Trojan horse* for the study of motor preparation and rehearsal in the absence of explicit motor outflow. None correlated fMRI motor patterns with clinical scores of tic severity. We investigated (i) the neural correlates of voluntary motor control in adult GTS patients and studied whether imagination and the execution of the same voluntary movement – finger oppositions with the right or with the left hand – are associated with specific patterns of activation and (ii) whether these patterns could be related to the severity of the syndrome as measured by the YGTSS scale for motor tics. We anticipated a reduction of ticking manifestation during the explicit motor task and greater regional activation differences between GTS subjects and normal controls for the motor imagery task.

Materials and Methods: We studied 24 GST patients (5 F, 19 M, mean age 29.6 +/- 12 years; mean educational level: 11 years) and 24 healthy subjects matched for age and gender. The aforementioned fMRI tasks were alternated with resting state time-matched baselines in a block-design paradigm. fMRI data were analysed with SPM8 (Wellcome Department of Imaging Neuroscience).
Results: The SPM8 analyses revealed a significant hyperactivations for GTS patients in the premotor and prefrontal areas as a main effect: this was true for both the explicit movement and the motor imagery task, for both the right and the left hand. However, we also found task specific activation differences with the motor imagery task in more rostral pre-frontal and temporo-parietal regions of the right hemisphere. Regression analyses between the BOLD response for the motor imagery task and the clinical scales showed a positive correlation between the activity of premotor areas (precentral gyrus and supplementary motor area) and the YGTSS scale for the motor imagery task but not for the motor execution task.
Discussion: This evidence supports the hypothesis of a different neurofunctional organization of motor control between adult patients with GTS and healthy controls. We propose that the presence of an explicit motor outflow in GTS mitigates the manifestation of tics, on the one hand, and the need for a compensatory brain activity in the brain region that showed a task dependent hyperactivations in the motor imagery task.

O12. Therapeutic Effects of thalamic Deep Brain Stimulation in Tourette Patients.

Huys D[1], Bartsch C[1], Köster P[1], Lenartz D[2], Visser-Vandewalle V[2], Kuhn J[1] - [1] University of Cologne, Department of Psychiatry and Psychotherapy, Cologne, Germany, [2] University of Cologne, Department of functional Neurosurgery and Stereotaxy, Cologne, Germany.

Background: Since it first application in 1999, the potential benefit of DBS in reducing symptoms of otherwise treatment refractory Tourette Syndrome (TS) has been documented in several publications. Yet, uncertainty regarding the ideal neural targets remains while the eventuality of so far undocumented but possible negative long-term effects on patients' personality fuels the debate about the ethical implications of DBS.
Methods: We present recent publications as well as our own research results. At the University of Cologne we have conducted a prospective open-label trial where eight patients with severe and medically intractable TS were treated with deep brain stimulation of the ventral anterior and ventrolateral motor part of the thalamus. To assess the course of TS, its' clinical comorbidities, personality and self-perceived quality of life, patients underwent repeated psychiatric assessments over twelve months after stimulation onset.
Results: Current study results demonstrate the efficacy of thalamic DBS in treatmentresistant Tourette patients, even when the ideal target point will continue to be the subject of research for the stimulation. Our own results indicated a strongly significant and beneficial effect of DBS on Tourette symptomatology, trait anxiety, quality of life and

global functioning, while the side effect profile appeared to be rather low. Next to this, pre-surgical compulsivity, anxiety, emotional dysregulation and inhibition appeared to be significant predictors of surgery outcome.

O13. Atomoxetine Decreases Vulnerability to Develop Compulsivity in High Impulsive Rats.

Ansquer S[1, 2, 3], Belin-Rauscent A[1, 4, 7, 8], Dugast E[1, 4], Duran T[9, 10], Benatru I[3, 5], Mar A C[6], Houeto J L[1, 3, 4, 5], Belin D[1, 4, 7, 8]* - [1] Institut National de la Santé et de la Recherche Médicale (INSERM) U1084-LNEC Experimental and Clinical Neurosciences Laboratory, Team Psychobiology of Compulsive Disorders, France, [2] University of Poitiers, France, [3] Service de Neurologie de l'Hôpital de Poitiers, Poitiers, France, [4] INSERM European Associated Laboratory Psychobiology of Compulsive Habits, Cambridge, United Kingdom, [5] INSERM CIC-0802, Poitiers, France, [6] Department of Psychology (ACM), Behavioural and Clinical Neuroscience Institute, University of Cambridge, United Kingdom, [7] Department of Pharmacology, University of Cambridge, Cambridge, United Kingdom; CNRS GDR 3557, [8] "Institut de Psychiatrie" , Hôpital Sainte Anne, Paris, France, [9] Institut des Neurosciences de Grenoble-CR Inserm U.836, France, [10] Université Joseph Fourier-Site Santé La Tronche-CHU Grenoble, Grenoble, France. *contributed equally to this study.

Background: The factors contributing to the development and severity of obsessivecompulsive spectrum disorders such as obsessive-compulsive disorder, **Tourette's syndrome**, pathological gambling, and addictions remain poorly understood, limiting the development of therapeutic and preventive strategies. Recent evidence indicates that impulse-control deficits may contribute to the severity of compulsivity in several of these disorders. This suggests that impulsivity may be a transnosological endophenotype of vulnerability to compulsivity. However, the precise nature of the link between impulsivity and compulsivity in anxiety-related compulsive disorders remains unknown.

Methods: We investigated the relationship between impulsivity and the development of a compulsive behavior in rats, which captures the hallmarks of compulsivity as defined in the DSM-IV—namely, that it is maladaptive, excessive, repetitive, and anxiolytic.

Results: We demonstrate that a high-impulsivity trait, as measured in the five-choice serial reaction time task, predicts an increased propensity to develop compulsivity as measured in a schedule-induced polydipsia procedure. Trait impulsivity and compulsivity were nonlinearly related. This impulsivity–compulsivity relationship was lost after the development of compulsivity or under chronic treatment with Atomoxetine, a noradrenergic reuptake inhibitor used to treat attention-deficit/hyperactivity disorder. Atomoxetine treatment both decreased impulsivity and prevented the development of compulsivity in high-impulsive animals.

Conclusions: These observations provide insight into the reciprocal influence of impulsivity and compulsivity in compulsive disorders and suggest that Atomoxetine may be a useful

treatment for patients suffering from compulsive spectrum disorders with high impulsivity.

O14. Medication or behaviour therapy for tics, which works best? *Van de Griendt J* - HSK Group Inc., The Netherlands On behalf of the TRIBET Study Group (van de Griendt, Wertenbroek, Cath, Verdellen, de Bruijn, Becker & Verbraak).

Chronic tic disorders (CTD) and Gilles de la Tourette Syndrome (TS) are ususally treated with medication. Medication has shown positive results in reducing tics in several randomized controlled trials (RCTs) (for an overview, European clinical guidelines part II: pharmacological treatment by Roessner et al., 2011). Behaviour therapy, especially habit reversal training (HRT) and exposure and response prevention (ERP) is developed more recently and has shown its efficacy in RCTs as well. (for an overview, European clinical guidelines part III: behavioural and psychosocial interventions by Verdellen et al., 2011). In both guidelines, behaviour therapy is recommended as first-line intervention for tics if available and also prefered by the patient. However, to date, studies comparing the effectiveness of behavioural and pharmacological treatments in patients with TS are absent. This lecture presents the first scientific data comparing medication with behaviour therapy for tics. Preliminary results of a RCT comparing Risperidon with ERP in 34 patients with TS or CTD are presented. Risperidon was choosen since it has an A level of evidence and is used most in Europe (Roessner et al., 2011). ERP was choosen because of its reported higher effect sizes than HRT (Verdellen et al., 2011). At present, the data are analysed. The outcome of this study is very important in indicating whether behavioural treatment or medication should be tried first.

(13:15-14:30) ORAL PRESENTATIONS III: Clinical Research

Chairs: *: R. Rizzo (University of Catania, Italy), F. Cardona (University of Rome, Italy)*

O15. THERAPIES FOR CHILDREN WITH TS BASED ON THE ADULT'S COGNITIVE PSYCHOPHYSIOLOGICAL MODEL. *Leclerc J[1] , O'Connor K P[2]* - [1] Psychology department, University of Quebec in Montreal and Centre de recherche de l'Institut universitaire de santé mentale de Montréal, P.O. 8888 succ. Centre-ville, Montreal, Canada, H3C 3P8, [2] Centre de recherche de l'Institut universitaire de santé mentale de Montréal (CRIUSMM) 7331 Hochelaga Street, Montreal, Canada, H1N 3V2.

This workshop presents a cognitive behaviour therapy package suitable for managing Tourette syndrome (TS). Although the program draws on existing techniques such as habit reversal and relaxation, it is based on a cognitive-psychophysiological model which

emphasizes regulation of sensori-motor activation, management of emotions linked with frustrated action, and cognitive restructuring of perfectionist style of planning action in high risk tic situations (O'Connor, 2005). The treatment has been adapted for children with TS (targeting tics and explosive outbursts). Different issues related with intervention in children will be addressed as well as the main steps of the therapy. The principal objective of this skills based workshop is to become familiar with the treatment for TS in children based on adult's therapy. Learning objectives are: to understand the psychological characteristics of TS and their impact on tic onset; employing functional analysis to reveal psychological profiles for evaluating triggers in tic disorders; awareness of how negative and positive reinforcement maintain the tic cycle (same issues are presented for explosive outbursts as an emotional tic). Participants will be sensitized to tics assessment strategies, and the main steps of treatment: awareness training, constructing high/low risk profiles, cognitive behavioural restructuring, and relapse prevention. The presenters will offer a formulated therapy model that focuses on an individualized situational assessment that the clinician uses during the intervention.The workshop will have a didactic part to ensure the understanding of the theoretical model. In parallel, examples of exercises, videos and case studies illustrate the application of the program with findings from recent clinical studies.

O16. The effects of co-occurring ADHD symptoms on learning and cognitive control in young people with TS. *Shephard E [1], Groom M J[2], Jackson G[2]* - [1] Institute of Psychiatry, King's College London, UK, [2] Division of Psychiatry, Institute of Mental Health, University of Nottingham, UK.

Current behavioural therapies for tics rely heavily on reinforcement learning (learning new behaviours by positive and negative reinforcements) and cognitive control (voluntary behaviour control) processes. Habit-reversal therapy (HRT) involves withholding tics while executing newly learned non-tic movements and sounds, while exposure and response prevention (ER) therapy consists of learning to suppress tics for increasingly extended periods. HRT and ER have been shown to significantly reduce tic severity in children and adults with TS. However, it is unclear how effective these therapies are for individuals with TS and co-occurring conditions, such as ADHD. ADHD is associated with impaired cognitive control and reinforcement learning, suggesting that behavioural tic therapies will be less successful in young people with co-occurring TS and ADHD (TS+ADHD). To investigate this issue, we compared behavioural performance on two experimental tasks measuring the ability to learn and modify behaviours by reinforcement and voluntarily withhold behaviours between young people with TS, TS+ADHD, ADHD and unaffected controls. We found that young people with ADHD were impaired on both tasks relative to TS and controls. Young people with TS+ADHD showed intact ability to withhold inappropriate responses and learn new behaviours, but impaired ability to modify well-learned

behaviours compared with TS and controls. These findings indicate that co-occurring ADHD symptoms introduce selective impairments in young people with TS that could negatively impact upon the ability to engage in habit-reversal therapy, but not tic suppression or ER therapy. As such, these findings have important implications for the choice of treatments used in TS+ADHD.

O17. Intense Imagination with Movements (IIMs): Neuropsychological case series of children with a newly identified subgroup of motor stereotypies.

Robinson S, Woods M, Hedderly T – Tic and Neurodevelopmental Movement (TANDeM) Clinic, Children's Neurosciences Centre, Evelina London Children's Hospital, Guy's and St Thomas' NHS Foundation Trust, London.

Objectives: We have recently identified a new subgroup of children who present with stereotyped movements in the context of episodes of intense imagination, termed Intense Imagination with Movements (IIMs). Subtypes of stereotypies and neuropsychological characteristics have not previously been reported. The objectives are to report clinical features and preliminary neuropsychological findings for children with IIMs, to inform clinical management and theoretical understanding.

Methods: 10 children (9 boys and 1 girls) were identified via teams with expertise in paediatric movement disorders. Neuropsychological assessments were conducted for four children (3 boys, 1 girl; mean age 9 years 4 months) due to parental concerns regarding the management of IIMs. Children were administered standardized tests of IQ, memory, oral expression, attention and executive functioning. Parents completed of a range of questionnaires.

Results: Stereotypies presented as paroxysmal complex movements. Imagination themes included computer game, cartoons/movies and fantasy. Engagement in acts of imagination preceded the movements, which were not under volitional control. All children exhibited discrepant intellectual profiles, with three functioning predominantly in the superior rage and one in the borderline range. All exhibited clinically significant impairments in processing speed and attention, but strengths in memory or oral expression. Three children had dyspraxic features and all had sensory impairments.

Conclusions: Children with IIMs appear to form a discrete stereotypy subgroup, for whom cognitive skill development is uneven. Good memory or verbal expression skills may underpin imaginary abilities, whilst weaker attention and processing speed skills may contribute to engagement in imaginary acts when bored, with movements likely to serve the function of increasing sensory stimulation. Children with IIMs are of relevance to clinical practice but also raise interesting theoretical questions regarding the association between neural networks underpinning cognition and motor functioning.

O18. Creativity in Tourette Syndrome. *Zanaboni C[1], Mastroianni S[1], D'Adda F[1], Servello D[2], Porta M[1]* - [1]Tourette Syndrome and Comorbid Disorders Center, [2]Functional Neurosurgery -IRCCS Galeazzi, Milan.

Background: Creativity is *"the union of common elements in order to produce new and useful combinations"* (Poincaré H., 1999). As Tourette syndrome does, also creativity activates the dorsolateral prefrontal circuitry and anterior cingulate circuitry of the frontal cortex. Secondly, creative personality is influenced by mesolimbic dopamine, while TS presents an altered dopaminergic synaptogenesis.
Aim: Aim of the study is to demonstrate that TS patients are more creative than not-TS people. The study has been conducted in Italy, then one of the authors (Z.D.C.) has duplicated the study at the Yale Child Study Center, as reported in the 2011 "Yale TS/OCD Research Highlights".
Method: The study involved 41 TS 6-18 year old subjects, and a control group of 41 notTS subjects. Creativity features (flexibility, fluidity, originality, data processing skills) were assessed through Williams' TCD Scale. Together, parents and teachers were assessed on their children's creative features.
Results: Results from TCD flexibility and fluidity subtests confirm the study hypothesis: flexibility is statistically higher (m=8.4) in the TS group than in the control sample (m=7), and fluidity skills are more developed in the clinical sample (m=11.71) than in the controls (m=9).
Conclusion: These data show that TS young subjects are more creative than not-TS young individuals. Many TS patients have a strong creative predisposition that clinicians, school staff and caregivers may know to optimize therapeutic effects.

O19. Prevalence and Comorbidity of Tic Disorder in Israeli Adolescents: Results from a National Mental Health Survey. *Steinberg T, Tamir I, Zimmerman-Brenner S, Friling M, Apter A* - Freund Neuropsychiatry Tourette Clinic, Schneider Children's Medical Center of Israel, Petah Tikva, affiliated with Sackler Faculty of Medicine, Tel Aviv University, Ramat Aviv, Israel.

Background: Tic disorders are common causes of morbidity in Israel but their prevalence in this country needs further study.
Objectives: To assess the prevalence of mental disorders in Israeli youth including tic disorders, as part of the Israel Survey of Mental Health among Adolescents (ISMEHA).
Methods: The ISMEHA was conducted in a representative sample of 957 adolescents aged 14–17 and their mothers during 2004–2005. We interviewed the adolescents and their mothers in their homes and collected demographic information about the use of services. We also administered a psychiatric interview, the Development and Well-Being Assessment inventory (DAWBA), which included a question on tic disorder. The prevalence

of tic disorders was calculated based on the adolescents' and maternal reports. The relationships among demographic data, comorbidity rates, helpseeking behaviors and tic disorder are presented.

Results: The prevalence of tics was 1.3% according to maternal reports and 4.4% according to adolescents' reports. The prevalence correlated with externalizing disorders and learning disabilities. A higher prevalence of tics was found in the I Arab population compared with Jewish adolescents.

Conclusions: The prevalence of tic disorders in Israel, as measured by a direct question in this epidemiological study, and associated comorbidities concurs with previous reports. The complexities of prevalence estimations, comorbidities, demographic correlates, and help-seeking behaviors are discussed.

O20. Employment in Tourette Syndrome. *Palmer E, Stern J S* - St George's University of London.

Introduction: Adults attending specialists for their Tourette syndrome (TS) are a potentially atypical group vulnerable to intrusive disorders that may affect employment prospects.

Methods: Clinical records of 152 patients with TS over the age of 18 were reviewed. Occupation at time of first assessment was categorised according to the UK National Statistic Socio-economic Classification Score (NSSEC) which ranges from 1.1 (higher managers and professions) to 8 (out of employment). Problematic employment histories over more than one time point were assessed including prolonged periods of past unemployment, multiple short employment, disciplinary issues etc. Severity of TS was recorded by YGTSS, MOVES and clinician impression and comorbidities were noted.

Results: Little relationship between tic severity and NSSEC score was seen. However, problematic employment history was assigned in 52% and associated with comorbidities (13% for pure TS v. 57%), clinician-rated severity- (48% for mild/moderate v. 69% for severe, NS), MOVES score (47% score <30, 69% score > 30(69%). Coprophenomena were also associated with employment difficulties.

Discussion: Adults who attend a tertiary specialist centre are employed across the whole spectrum from higher management to unemployment. The presence of more severe tics, comorbidities and coprolalia make a problematic employment history more likely. These comparisons were made within TS patients on the background of rising general unemployment due to economic factors and it should be noted that in this classification students (n=18) are in the same group as jobless people although are likely to have a different future socioeconomic level.

O21. Analysis of the needs of a European Network of clinicians and researchers for Tourette Syndrome: from the online survey to the design of a web based platform. *Seragni G G[1], Anderson S[2], Dobson S[2], Müller-Vahl K[3], Murphy T[4], Murray L[5], Theuws S[6], Van de Griendt J[6], Verdellen C[6]* – [1] Fondazione don Carlo Gnocchi ONLUS, Milano, [2] Tourettes Action, Camberley, [3] Hannover Medical School, [4] Great Ormond Street Hospital, London, [5] Registered Forensic Psychologist. Dumfries, Scotland, [6] HSK Group Inc/HSK Expertise Tics, the Netherlands.

Gilles de la Tourette Syndrome (GTS) is an inherited neuropsychiatric disorder with childhood onset. It is marked by multiple motor and vocal tics and high comorbidity rates with attention deficit hyperactivity disorder and obsessive compulsive disorder. It has only recently become evident that Tourette Syndrome and other tic disorders are not rare at and may negatively impact the quality of life of those affected. Due to lack of education of medical professionals, educators, and the general public, GTS is underdiagnosed and patients are severely discriminated against. To overcome this unsatisfactory situation the European Society for the Study of Tourette Syndrome (ESSTS) has been established since 2000 by Prof. Mary Robertson and others to enhance understanding of the causes of TS, find effective treatments for TS, share good practice, and stimulate European collaboration in research. Until now ESSTS activities have been funded by a COST Action program that is going to expire in the next months. New channels to support and keep connected this pan-European interdisciplinary scientific network are now needed. We are therefore designing an online platform where we could share multimedia files, information and data, discuss cases, spread knowledge and get video connection with other clinicians/researchers and/or patients. To provide the smarter and cheapest solution that could cover all ESSTS needs most we invited all ESSTS members to answer to an online survey about they needs and beliefs about creating an online network. We will discuss the results of the survey and we will outline the main characteristics that this platform should cover.

POSTER PRESENTATIONS (SUBMITTED ABSTRACTS)

P1. Objective vs. Subjective Measures of the Influence of Environmental Factors on Tic Expression. *Barnea M[1], Benaroya-Milshtein N[1], Piacentini J C[2], Woods D W[3], Apter A[1], Steinberg T[1]* – [1] Schneider Children's Medical Center of Israel, [2] University of California, Los-Angeles, [3] Texas A&M University.

Introduction: It is known that expression of tics changes in different environmental situations. However, the specific environmental factors influences on subjective and objective measures of tic expression were not well defined.
Objectives: To examine the influence of environmental factors on tic expression, by using both subjective and objective measures. The subjective measure was a Functional Assessment Interview (FAI) developed for this study, and the objective measure was videorecording covering five common situations: watching television; doing homework; being alone; receiving attention when ticcing; talking to a stranger.
Methods: The research comprised of 41 children aged 6-18 (M=10.15, SD=2.73) with a primary diagnosis of chronic tic disorder. Each child completed the Yale Global Tic Severity Scale (YGTSS); Parent Tic Questionnaire (PTQ); Tourette Syndrome-Clinical Global Impression (TS-CGI); Premonitory Urge for Tics Scale (PUTS); and FAI. Afterwards, each child was filmed in the laboratory under the five research situations, and the videos were scored for the presence of tics.
Results: Analysis of variance revealed the impact of the five research situations on tic expression. The highest number of tics appeared in the "television" situation, and the lowest appeared in the "alone" situation. However, regression analysis revealed a low-moderate ability of the subjective measures to reflect the actual appearance of tics, suggesting low level of awareness to tic expression and environmental influence.
Conclusions: These results could significantlly contribute to the refinement of clinical assessment, research methodology and to the elucidation of the theoretical aspects of tic disorder in order to develop new therapy strategies.

P2. A socio-spatial perspective on Tourette's compulsive behaviour. *Beljaars D N M* – School of Planning and Geography, Cardiff University, Cardiff University.

Recent debates discussing the possibility of environmental or contextual factors influencing Tourette syndrome symptom expressions (e.g. Capriotti et al., 2013) identify such factors in social interactions (Conelea & Woods, 2008) and anxiety-producing events (Hoekstra et al., 2004). However, until now 'place' as potential importance factor has not been studied yet, despite the syndrome's apparent inherently spatial character. Here place is regarded as a site carrying identity, meaning and familiarity to a subject (Relph, 1976). This appears most cogently in the rarely studied behaviours that involve physical interactions with immediate surroundings, such as touch tics and compulsive spatial practices, better known as compulsions or complex motor tics pertaining to the visuospatial component in Tourette induced behaviour. Therefore, this research aims to provide a better understanding on how the composition of places – materially, socially and symbolically – affect people with TS and what strategies they adopt to negotiate certain places and avoid negative impacts on their wellbeing. It intends to take a less conventional, but arguably more suitable, human geographical perspective. Human geography is "concerned with the ways in which place,

space and environment are both the condition and in part the consequence of human activities" (Gregory et al., 2009: 350). This interdisciplinary research both draws on human geographical health and disability studies and on behavioural studies in clinical TS studies. It focusses on the extracorporeal spatial relationships between people with TS and their immediate surroundings that act as external stimuli, and bases its empirical finding on experiential accounts through interviews and ethnography.

P3. Aggressive Symptoms in Children with Tic disorders. *Benaroya-Milshtein N[1], Shmuel-Baruch S[1,2], Apter A[1], Friling M[1], Steinberg T[1]* – [1] The Matta and Harry Freund Neuropsychiatric Tourette Clinic, Schneider Children's Medical Center of Israel, Petach Tikva; affiliated with the Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, [2] Department of Psychology, Bar Ilan University, Ramat Gan, Israel.

Introduction: Sudden and explosive episodes of anger or aggression are a postulated to be a significant source of psychosocial morbidity in children and adolescents with tic disorders but this is controversial

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

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

Results: No significance difference in aggression score was found between tics group and control group. However, boys with tic disorders reported significantly more aggressive behaviors than girls with tic disorders. Verbal aggression was found in 69.6% of the subjects with tic disorders, which was also the most prevalent type of aggression. The level of aggression was not correlated to tic severity. ADHD and OCD enhanced the probability of explosive outbursts in the group with tic disorder. Aggression score was significantly associated with compulsions. Regression analysis showed that the only significant predictor of aggression was ADHD severity score.

Conclusions: Our study suggests that there is no difference in aggressive behavior between children with uncomplicated tics and a control group. Thus aggressive behavior in children with tic disorders is not related to having tics, but rather to the associated co morbidities; ADHD and compulsions.

P4. Self-reported tic reducing effects of music in patients with Tourette

Syndrome. *Bodeck S[1], Lappe C[1], Evers S[2]* – [1] Institute for Biomagnetism and Biosignalanalysis, University of Münster, Germany, [2] Department of Neurology, Krankenhaus Lindenbrunn, Coppenbrügge, Germany.

Objectives: Tourette Syndrome (TS) is characterized by motor and phonic tics. It is assumed that musical activity reduces tic frequency in patients with TS but no studies have investigated this question systematically. In the first part of this study, patients with TS subjectively assessed the impact of musical activity on tic frequency. We hypothesized that a tic reduction is experienced when listening to music or when making music. Furthermore, an exploratory analysis of relevant factors causing tic decrease was conducted.
Methods: A questionnaire was presented to 29 patients with TS. They were asked to assess whether listening to music and making music would lead to "tic frequency reduction", "tic frequency increase", or "constant tic frequency level". Exploratory analysis involved two item batteries, "listening to music" and "making music", relating possible relevant musical and personal factors. Chi-squared tests were applied in all analysis. **Results:** A significant tic reduction ($p < .001$) was found in both conditions. 8 of 20 items of the battery "listening to music" and 15 of 20 items of the battery "making music" were found significant in reducing tics. "Listening to music" resulted in tic frequency reduction when the music fulfilled the following conditions: soft, calming, familiar or favorite, pleasant to the patient, heard relaxed, alone or rested.
Discussion: Generally music has a tic decreasing effect according to the patients' perception. Specific factors seem to be relevant for this effect and should be reflected by music therapy. Further experimental studies have to confirm this observation.

P5. An objective analysis of tic decreasing effects of music in patients with Tourette Syndrome.

Bodeck S[1], Lappe C[1], Evers S[2] – [1] Institute for Biomagnetism and Biosignalanalysis, University of Münster, Germany, [2] Department of Neurology, Krankenhaus Lindenbrunn, Coppenbrügge, Germany.

Objectives: Tics are core symptoms of Tourette Syndrome (TS). In a previous study a subjective self-report assessment of patients with TS revealed that musical activity can significantly reduce tic frequency. In the following study we rated tic frequency to investigate changes during different musical activities.
Methods: A within subject repeated measure design was conducted with eight TS subjects. Five experimental conditions were tested: baseline, instrumental playing/singing, the time after instrumental playing, listening to music, and music imagery. Videotapes were recorded for six minutes for each condition and tic frequency was counted by the modified Rush Video-Based Tic Rating Scale. Friedman's test and Wilcoxon-post-hoc analyses (onetailed) were applied with an alpha level of .0125.

Results: Friedman's test revealed significant difference between baseline and the four conditions, $\chi^2(4, N = 8) = 12.50$, $p < .001$. Wilcoxon post-hoc tests indicated that playing an instrument ($U(8) = -2.31$, $p = .004$), and the time after musical activity ($U(8) = -2.31$, $p = .012$, listening to music ($U(8) = -2.31$, $p = .004$), and musical imagery ($U(8) = -2.31$, $p = .004$), reduced the tic frequency significantly.
Conclusion: Active and passive participation in musical activity reduces tic frequency. There is a short term tic decreasing effect after making music. The data confirm the subjectively perceived tic reduction effect of musical activity. Motor control and focused attention are believed to be relevant factors. The effects can also explained by (neural) entrainment. Further research should be done to investigate which processes lead to tic reduction.

P6. Neural correlates of tactile prepulse inhibition: A combined EEG/fMRI study in children and adolescent with Tourette Syndrome. *Buse J[1], Beste C[1], Herrmann E[1], Bender S[2], Roessner V[1]* – [1] Department of Child and Adolescent Psychiatry, Medizinische Fakultät Carl Gustav Carus, Technische Universität Dresden, Germany, [2] Department of Child and Adolescent Psychiatry, Psychosomatics and Psychotherapy, Johann-WolfgangGoethe University, Deutschordenstraße 50, 60528 Frankfurt am Main, Germany.

Tourette's Syndrome (TS) is associated with reduced prepulse inhibition (PPI) of the startle reflex, which is assumed to reflect abnormal sensorimotor gating. We applied whole-brain functional magnetic resonance imaging (fmri) to investigate the neural correlates of PPI in children and adolescent with TS using a tactile version of the PPI. The tactile startle response was elicited by air bursts delivered to the participant's throat in an event-related fmri-design. The EMG of the startle reflex was recorded inside the scanner simultaneously to the acquisition of the fmri images. PPI-related brain activity was measured as the difference between the cerebral activation to prepulse trials and the cerebral activation to pulse alone trials. The sample consisted of 22 children and adolescents with TS (male, 11-17 years, without comorbidities) and 22 age-matched healthy controls. As expected, PPI of the startle reflex was reduced in patients with TS compared to the healthy control group. TS patients exhibited lower PPI-related brain activity compared to healthy controls in the following regions: Right parietal cortex (subgyral/precuneus, BA 7), right primary somatosensory cortex (BA 3), left precentral gyrus (BA 9), left cingulate gyrus (BA 32) and left caudate body. PPI was correlated to the parietal activation cluster.

P7. The prevalence of tic disorders in primary school children in an electoral district of Mauritius. *Chummun [2], Seetaram V, Rickards H[3]* – [1] Registered Medical officer Mauritus, [2] Northwood Park Hospital, Watford Rd, Harrow, London, HA1 3UJ, United

Kingdom, [3] Psychological Medicine, Great Ormond Street Hospital for Children, Great Ormond Street, London, WC1N 3JH, United Kingdom.

The aim of this project was to ascertain the minimum prevalence of tic disorders including Tourette syndrome, in school children aged 9-11 in all the mainstream schools of an electoral district of Mauritius. So far, there are only 3 studies that have been done in the southern hemisphere countries and they were directed at Tourette syndrome explicitly. This study, first of its kind in the southern hemisphere, consisted of a 2 stage process, screening followed by a face to face clinical interview. Screening questionnaires were sent to all the children in standard 4 to 6 (9-11 years of age– a total of 2003) in the 8 schools of the constituency. The tic positive patients were interviewed and the diagnoses were ascertained in accordance to the DSM IV-TR criteria. Out of the 1287 children screened, 53 (35 males, 18 females) were diagnosed with a tic disorder yielding a prevalence of 4.1%. 8 children (7 males and 1 female) fulfilled the criteria for Tourette Disorder (0.6%). Another 0.8% had chronic tic disorder (6 boys and 4 girls). The majority presented with transient tic disorder at 2.5% with a male to female ratio of 19 to 13 respectively. The distribution of non-specific tic disorder was 0.2% (3 males). Tic disorder estimates were congruent with studies performed in the northern realm of the globe. The study was inaugural in suggesting that Tourette disorder may be common in people of Indian descent but is less frequent in African descent.

P8. Developing Transcranial Direct Current Stimulation as a therapeutic tool for Tourette's syndrome. *Dyke K, Jackson S* – University of Nottingham, UK.

Research suggests that Transcranial Direct Current Stimulation (tDCS) can modulate cortical excitability, both during stimulation and for a period afterwards. Typically these effects are short lived, but it is theoretically possible that tDCS may be able to induce long lasting changes in the brain similar to those induced by repetitive Transcranial Magnetic Stimulation (rTMS). Inducing these changes via the induction of neuroplasticity could be harnessed therapeutically for a number of neuropsychiatric disorders, including Tourette's syndrome. Recently studies have been conducted which suggests that rTMS could be effective in reducing tics. This is an exciting development and highlights the potential therapeutic uses of stimulation techniques. However, for some individuals rTMS may not be an appealing or practical treatment due to its potential side effects. tDCS does not carry the same degree of side effects, and is also cheaper and more portable, making it an attractive alternative. As of yet there is no published research investigating the effects of tDCS on tic scores, this could be an important development in enhancing future treatment options for individuals with Tourette's syndrome. Work investigating the therapeutic uses of tDCS is still in its infancy and there remains large gaps in our current understanding of the technique. In this poster preliminary work done in preparation for a larger trial

investigating the effects of tDCS on tic scores will be examined. It is hoped that further exploration and understanding of the technique will lead to effective therapeutic use.

P9. Jumping to Conclusions: The Beads Task in Tourette Syndrome. *Eddy C M[1], Cavanna A E[1, 2, 3]* – [1] Department of Neuropsychiatry, Birmingham and Solihull Mental Health NHS Foundation Trust and University of Birmingham, UK, [2] Department of Neuropsychiatry, Institute of Neurology and University College London, London, UK, [3] School of Life and Health Sciences, Aston University, Birmingham, UK.

The beads task is a probabilistic reasoning task. Participants are shown two jars, one with a greater proportion of one colour bead (e.g. 60% red beads, 40% blue) and the other jar with opposite proportions (e.g. 60% blue, 40% red). The jars are then obscured from view. The experimenter removes beads one by one, until the participant feels they have seen enough beads to decide which jar the beads are coming from. We compared the amount of beads needed before a decision was made for patients with Tourette syndrome (TS) and matched healthy controls. Beads task performance may be linked to executive functions, so measures of inhibition, verbal fluency and working memory were also used. Standard TS symptom scales, including measures of attention deficit hyperactivity disorder (ADHD) and obsessive compulsive disorder (OCD) were taken for patients. When compared to controls, patients tended to need fewer beads before making a decision, suggestive of a 'jumping to conclusions bias' in TS. There were limited differences between the groups for executive functions, and executive performance was not correlated with beads task performance. However, significant relationships were apparent between beads task performance and symptoms of OCD and ADHD. Our findings imply that a tendency to jump to conclusions in TS is likely to be related to impulsivity and/or compulsivity. Taking together the beads task performance of patients with TS and the finding that patients with schizophrenia exhibit a similar bias, a link between dopamine dysregulation and jumping to conclusions seems all the more likely.

P10. Primary Care prescribing problems for Tourette syndrome in the UK.
Emberton J S, Stern J S, Simmons H – St. George's University of London, St George's Hospital.

Introduction: Drugs given for Tourette syndrome (TS) are frequently unlicensed or offlabel for the condition and in some cases not licensed for use in children at all. Pharmaceutical companies have not yet applied for marketing licences for the condition. This can cause problems in the transfer of prescribing from specialist to primary care (family medicine, general practice) due to unfamiliarity of non-specialists with the drugs even where continued usage appears safe and unproblematic. The two most relevant drugs in the UK

were felt to be aripiprazole and melatonin. We reviewed the experience of a large cohort of children and adults who had been prescribed drug treatment.
Methods: 500 patients records were reviewed, of these 177 had been prescribed aripiprazole or melatonin or had experienced problems with other drugs in primary care prescribing. Results were quantified in terms of primary care location, patient age and year of prescription.
Results: We concluded that GPs in the UK refuse to continue prescribing aripiprazole far more than any other drug prescribed by the clinic: 8.6% of all aripiprazole prescriptions. The refusal rate was higher in adult patients (11%) than in children (6.3%). There was no change over time for prescriptions made between 2005 and 2013.
Discussion: Transfer of prescribing to primary care of a currently widely used drug for tics in the UK has been problematic in a small minority of cases.

P11. Studying glutamatergic function in the frontal-straital circuitry in TS and OCD: an MRS study.

Fan S, Schols K, de Wit S, Pouwels P J, Ven der Werf Y D, Veltman D J, Van den Heuvel O A, Cath D C. University of Utrecht, VUMC Amsterdam.

The aim of this research project is to investigate how the glutamatergic function in the frontal-straital circuitry affects patients with Tourette Syndrome (TS) and Obsessive Compulsive Disorder (OCD) in comparisons to healthy individuals. Functional magnetic resonance imaging (fMRI), magnetic resonance spectroscopy (MRS) from the dorsal anterior cingulate cortex (dACC), bilateral thalamus and bilateral caudate, as well as the behavioral (from series of neuropsychological assessments) data are currently being collected. We have selected 20 OCD patients, 20 TS patients and 20 healthy control participants. The OCD patients as well as the control participants are chosen from the baseline OCD research study conducted by my colleagues Wit et al. three years ago. We have carefully matched age, gender and education across three groups. Up to date, 12 control subjects and 2 OCD patients' data have been successfully collected. On the other hand, a Diffusion Tensor Imaging (DTI) study of 45 OCD patients is also on-going. We thank our colleague Stella de Wit for her generosities of sharing the use of this dataset with us. DTI data analysis is currently being planned and will be carried out in the very near future. We truly wish to have some intriguing results to share at the Paris meeting at the end of April combined with a poster presentation.

P12. Neural Structure and Function in Tourette syndrome: distinguishing neural structure and function in Tourette syndrome from healthy controls and ADHD.

Forde N J[1], Buitelaar J K[2], Dietrich A[1], Hoekstra P J[1] - [1] University Medical Centre Groningen, Department of Psychiatry, Groningen, the Netherlands, [2] Radboud University Nijmegen

Medical Centre, Donders Institute for Brain, Cognition and Behaviour, Nijmegen, the Netherlands.

Rationale: Attention-Deficit/Hyperactivity Disorder (ADHD) is often found comorbid with Tourette syndrome (TS), similarly tic disorders often comprise secondary diagnoses in ADHD, making it difficult to eliminate the potential confounds of comorbidity on research findings in TS. Although the frontostriatal circuits and its main regions, the prefrontal cortex and the basal ganglia have been implicated in TS, there are multiple inconsistent findings in imaging measures and executive functioning in TS. Furthermore glutamate is a major neurotransmitter modulating the activity of the frontostriatal circuits, but its role in TS in unclear.
Objectives: The aim of the study is to identify brain (1) structural, (2) functional and (3) connectivity abnormality differences, and (4) neuropsychological differences between TS and ADHD, to elucidate which neural correlates correspond to each condition, which are common and which unique. Similarly (5) glutamate concentrations from the frontostriatal region, acquired with magnetic resonance spectroscopy (MRS), will be compared between groups.
Methods: 180 children (n=60 per group, 8-12 years old); (1) TS, (2) ADHD and (3) healthy controls will be recruited and undergo imaging and neuropsychological assessment. Structural, diffusion and functional (resting state and task specific) magnetic resonance images will be obtained as well as MRS glutamate and neuropsychological data. Advanced neuroimaging analysis techniques will be applied, including the use of FreeSurfer. Results from the three groups will be analysed in a multiple regression model.
Outcome: This will be the first study to explicitly investigate the neural correlates of TS and ADHD in children.

P13. Premonitory Urges: Are they closer to OCD or to ADHD?

Garcia-Delgar B, Ortiz A, Pérez A, Lázaro L, Morer A – Hospital Clínic Barcelona.

Introduction: Although premonitory urges are a main feature of Tourette Syndrome, its nature is still unclear. Whereas some studies relate these sensory phenomena to "justright" perceptions, others associate them to attention abnormalities.
Objective: The aim of this study is to examine the relationship between premonitory urges and Obsessive Compulsive Disorder (OCD) or Attention Deficit Hyperactivity Disorder (ADHD).
Methods: 27 subjects with Tourette Syndrome from the Outpatient Child and Adolescent Psychiatric Unit at Hospital Clinic were assessed with the Premonitory Urge for Tics Scale (PUTS); the Childhood Version of the Yale Brown Obsessive Compulsive Scale (CYBOCS) and the Swanson, Nolan and Pelham-IV (SNAP-IV). Non-parametric tests were used to

analyse differences and correlations between premonitory urges and OCD and ADHD symptoms.

Results: From the 27 subjects with Tourette Syndrome (mean age = 12.04, SD= 3.01), 5 (18.5%) met DSM-IV-TR diagnostic criteria for OCD and 17 (63%) for ADHD. The mean PUTS score was 17.30 (SD= 5.05), being significantly higher in subjects > 10 years (p=0.02). No significant differences in age were found in the groups of analyses.

PUTS score was significantly higher in subjects with OCD compared to those without OCD (p =0.024). Correlation between PUTS and CYBOCS scores was moderate for the obsessions subscale (ρ = 0.351; p > 0.05).

No significant difference was found in PUTS score between subjects with or without ADHD. Correlations were weak between PUTS score and SNAP-IV subscales and total score (p >0.05).

Conclusions: Premonitory urges appear to be closer to OCD than to ADHD symptoms.

- The relationship between premonitory urge and obsessional thoughts may help improving behavioural treatments for tics.

P14. A comparison of medication-naive patients exhibiting uncomplicated complex and simple tics : an ERP study. *Sauvé G[1, 2], Morand-Beaulieu S[1, 2], O'Connor K P [1, 2], Blanchet P[1, 3], Lavoie M E[1, 2]* - [1] Research Center of the Institut Universitaire en Santé Mentale de Montréal, Qc, Canada, [2] Department of psychiatry, Faculty of medicine, University of Montreal, Qc, Canada, [3] Department of stomatology, Faculty of dental medicine, University of Montreal, Qc, Canada.

Introduction: Patients with Tourette Syndrome and chronic tic disorders daily struggle with simple and/or complex tics. However, patients with body-focused-repetitivedisorders (BFRD; e.g. trichotillomania, excoriation) also show behaviours similar to tics. Historically, BFRD have been moved from one DSM category to another suggesting that we really do not grasp their essence. In this study, we argue that BFRD can be a manifestation of very complex tics. Thus, we aimed at comparing the EEG recordings of medication-naive patients exhibiting uncomplicated simple motor (SM) vs complex motor (CM) tics. According to previous data in a classical *Oddball* paradigm, the amplitude of the EEG P300 component can discriminate between participants presenting distinctive symptoms.

Methodology: Groups of patients exhibiting SM (n=12) or CM (n=12) tics were paired (age, sex, intelligence) to neurologically/psychiatrically healthy control participants (n=15). The amplitude of the P300 component has been extracted from EEG by an averaging procedure synchronized to the stimulus within a classical *Oddball* paradigm requiring a motor response; subsequently topographical maps of cortical activations were built.

Results/Conclusions: The TSGS scores of CM patients suggest that they struggle with motor conditions comparable to tics. Furthermore, the CM group showed a significantly reduced P300 amplitude compared to the control group in the left central region. From

these, we can infer that very complex tics might be related to anomalies in the working memory's context update processes. As well, it is possible that the P300 generators (frontal, parietal, limbic and cingulate areas) also show abnormal functioning for CM patients.

P15. Suicidality in patients with Tourette's syndrome (TS). *Gharatya A, Stern J S, Man C H A, Williams D, Simmons H, Robertson M M* - St George's University of London.

Aims: To investigate the clinical characteristics of suicide attempts and ideation in a cohort of TS patients
Methods: We reviewed the clinical notes of 524 patients diagnosed with TS attending the St. George's Tic Disorder Clinic. The control group used an existing database of 309 patients, according to availability of relevant items.
Results: Of the total cohort of 524 patients, suicide attempts (SA) were recorded in 25, mean age 26.9, M:F 1.8:1 and suicidal ideation (SI) in 30, mean age 21.4, M:F 2.3:1. * $p<0.05$
SA patients had more severe tics compared to SI and control group with an average Yale Tic Severity Score of 30.4 vs. 28.3 vs. 24.6. SA patients also had higher comorbidity rates including depression (75%* vs. 81.48%* vs. 12.30%), anxiety (80%* vs. 70.83%* vs. 12.94%), SIB (20% vs. 26.67% vs. 16.42%), ADHD (81.82%* vs. 68.97% vs. 53.92%,), OCD (73.91%* vs. 51.72%* vs. 28.20%).
Family history of suicide attempts (36.84%* vs. 26.67%* vs. 4.69%,) and depression (60.87%* vs. 66.67%* vs. 28.16%) were increased, as were unemployment, drug and alcohol abuse and criminality.
Conclusion: This is the first study to examine suicidality in a clinical TS cohort. These 55 patients had severe disease and other medical/psychosocial problems. Study limitations include referral bias and an age-unmatched control population, hence we have not yet given a prevalence for suicide attempts as it is important for this to be valid.

P16. Profiles of comorbidity in children and adolescents with Chronic Tic Disorders. *Giannini V, Salvi M, Valente F, Panunzi S, Santoro F, Molica G, Cardona F* – Department of Pediatrics and Child Neuropsychiatry Sapienza - University of Rome – Italy.

Aim: The study aims to evaluate the influence of different comorbidities on tic severity and quality of life of patients with Chronic Tic Disorder (CTD).
Subjects and methods: The sample consisted of 56 patients (F=8, M=48), aged between 6 and 16 years (mean=10.97) with clinical diagnosis of CTD (YGTSS score mean=33, median=30) and normal IQ (mean=107,05). All patients were at their first evaluation and were all drug-naïve. The instruments included measures of assessment (YGTSS, CY-BOCS,

K-SADS), questionnaires both for children (MASC, STAI, CDI, PSS, GTS-QOL) and parents (PSS-10, CBCL).

Results: Although only in very scattered CTD patients a comorbid diagnosis was suggested by K-SADS (with the exception of OCD, n=23), in several subjects the test results were positive for depressive (n=10), overall anxiety (n= 9) or separation panic (n=17) symptoms. The main self-reported anxiety or depression measures (scores of MASC, STAI 1-2 and CDI) were significantly correlated each other and showed a strong and significant correlation with measures of quality of life (GTS-QOL). A moderate but significant correlation was found between measures of anxiety or depression and both total and subtotal scores of CYBOCS. There was a good agreement between these measures and the parent reported instruments (CBCL Total and Internalization, Anxious/Depressive, Thought Problems, Social Problems subscales). No correlation was found between anxiety or depression measures and tic severity.

Conclusions: Comorbidities in CTD patients seem to be strongly interconnected and affect significantly the quality of life of patients, considerably more than tic severity.

P17. Executive function in children and adolescents with Tourette Syndrome.

Groth C, Kristjansen K, Mol Debes N, Skov L - Department of Psychology University of Copenhagen and Pediatric Department Herlev Hospital, Denmark.

Background and aim: Tourette Syndrome (TS) is a neurodevelopmental disorder assumed to involve the basal ganglia and the frontostriatal circuits which are also expected to be related to executive dysfunctions. Previous studies have shown some impairment of the executive functions but often blurred by few corrections for the very frequent comorbidity such as obsessive compulsive disorder (OCD) and attention deficit hyperactivity disorder (ADHD).

Most studies have used performance-based test in structured clinical and research settings. To increase the ecologic validity with a subjective view of executive functioning, we aim to examine the executive function in a clinically well characterized cohort of children and adolescent with TS using self-rapporting scales from everyday setting and its correlation to comorbidity, age, severity of tics and IQ.

Methods: We included 180 children and adolescents with TS aged 11-25 years and 44 controls aged 15-24 years. We used validated structured interviews to assess comorbidity and the Yale Global Tic Severity Scale Score to assess the severity of tics. The Behavior Rating Inventory of Executive Function (BRIEF) with self-rated, parents/informant-rated and teacher-rated scores was used for the executive functions. Participants had their IQ tested with subtests from Wechslers Intelligence Scale.

Results: Participants are divided in subgroups according to comorbidity. The effect of comorbidity, age, severity of tics, and IQ will be correlated with BRIEF scales. Analyses are still ongoing and the final results will be presented at the meeting.

Discussion: We expect to find executive difficulties in all patients-groups with more impairment in the TS+ADHD group.

P18. Premonitory urges in youngster affected by TS: long term follow-up.

Gulisano M[1], Robertson M M[2], Calì P V[1], Rizzo R[1] - [1] Department of Medical and Pediatric Sciences, Child and Adolescent Neuropsichiatry, Catania University, Via Santa Sofia 78, 95123, Catania, Italy, [2] Department of Neurology, St Georges Hospital & Department of Mental Health Sciences St Georges Medical School, & Department of Mental Health Sciences, University College London, UK.

Tourette Syndrome is characterised by involuntary motor/vocal tics. Although there is a substantial evidence that tics arise from neurobiological dysfunction, tic expression can be influenced by enviromental influences including both internal and external stimuli. One internal stimulus is the premonitory urge (PU). Many individuals report experiencing "urges" which are described as unpleasant somatic phenomena that build up prior the tic (Leckman et al. 1993). In some instances PU are more bothersome than the tics themselves (Kane 1994). Premonitory urges were found by Kwak and Jankovic (2003) in 92% of individuals affected by TS. The aims of the study were to examine in a longitudinal fashion the premonitory urges in children and adolescents suffering from TS, as well as to examine the correlations of the urge with clinical aspects of TS and evaluate the premonitory urge phenomena in a long term follow-up perspective. Ninety five patients (83 male, 12 female), aged 4-10 years at the onset (mean 7.3, SD 1.5) and 10-16 year at the follow up (mean 13.1, SD 3.7), participated in the study. They were assessed at diagnosis and then after 7 years follow-up with the following scales/schedules: PUTS, YGTSS, CY-BOCS, CADS. Our results suggested that although both younger (<10) and older children (>10) reported the PU. The value at the onset is statistically significant lower than at the follow up; moreover, in children older than 10 years the premonitory urge did correlate with obsession and compulsions, as opposed to in younger patients.

P19. Tic Related Neuronal Activity in Freely Moving Rats.

Israelashvili M, Bar-Gad I* - Gonda Multidisciplinary Brain Research Center, Bar Ilan University, Ramat Gan, Israel. *Corresponding author

Motor tics are repetitive, involuntary brief muscle contractions which interfere with ongoing behavior and appear as a symptom in several disorders, such as Tourette syndrome (TS). Tics have been associated with abnormalities in the cortico-basal ganglia system, and specifically to abnormal inhibition within the striatum. Motor tics can be induced in rodents and primates by local micro-injection of bicuculline (GABAA antagonist) into the dorso-lateral striatum. In the current study we utilized this model to study the

behavioral manifestation and the neuronal correlates of motor tics in freely moving rats. Chronic multi-electrode recordings following the injection revealed tic related activity in the striatum which was accompanied with local field potential (LFP) spikes. In light of the fact that the role of the motor cortex and the cortico-striatal pathway in tic formation is still unknown, following the injection we performed electrical stimulation in the primary motor cortex (M1). M1 stimulation facilitated the formation of motor tics and caused changes in neuronal activity corresponding to the related tics' activity. Thus, our current findings provide new insights into the role of the cortico-striatal pathway in tics manifestation and the underlying mechanisms of tic formation.

P20. Health-related quality of life of adolescents with Tourette Syndrome: A controlled study. *Jalenques I[1, 2], Auclair C[3, 4], Hartmann A[5, 6], Angonin C[1, 7], Morand D[8], Derost P[2, 9], Durif F[2, 9], Gerbaud L[3, 4, 10], Et le Groupe d'Etude SYNDROME DE GILLES DE LA TOURETTE: Deniau E, Legrand G, Marcheix M, Müllner J, Ramanoël C, May R* – [1] CHU Clermont-Ferrand, Service de Psychiatrie de l'Adulte A et Psychologie médicale, F-63003 Clermont-Ferrand, France, [2] Clermont Université, Université d'Auvergne Clermont 1, UFR Médecine, Equipe d'Accueil 7280, F 63001 Clermont-Ferrand, France, [3] CHU ClermontFerrand, Service de Santé Publique, F-63003 Clermont-Ferrand, France, [4] Clermont Université, Université d'Auvergne, EA 4681, PEPRADE, F 63000 Clermont Ferrand, France, [5] Centre de Référence National Maladie Rare : 'Syndrome Gilles de la Tourette'
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Objective: Our aim was to investigate Health-Related Quality of Life (HRQoL) in clinicreferred adolescents with Gilles de la Tourette syndrome (GTS).
Method: After neuropsychiatric hetero-evaluations using Yale Global Tic Severity Scale (YGTSS) and Children's Yale Brown Obsessive Compulsive Scale (CY-BOCS), clinic adolescents' HRQOL was assessed using self-administered instruments, Short-Form-36 (SF-36), Vécu et Santé Perçue des Adolescents (VSP-A) and Childhood Health Questionnaire Assessment (CHAQ). Matched healthy controls (MHC), depending on gender and age, completed the same HRQoL instruments. The parents of patients and controls completed socio demographic and medical questionnaires, the Child Behaviour Check-List (CBCL) to measure behaviour and emotional problems their adolescents

suffered from, and two hetero-evaluations of their adolescent's HRQoL, Vécu et Santé Perçue des Adolescents parental version (VSP-P) and CHAQ parental version. All patients, MHC and their parents gave written informed consent.

Results: Were included 75 adolescents with GTS and 75 controls. The mean age of adolescents was 14.8 years (SD=1.8); 80% were male; first symptoms began 8.1 years ago (SD=3.5). The mean YGTSS score of adolescents with GTS was 33.9 (SD=20). Their HRQoL was significantly impaired compared to controls for all SF-36 dimensions, for Vitality, Relationship with Friends and Leisure activities dimensions of VSP-A, and for total score of CHAQ.

Conclusion: Physical, psychological and social HRQOL dimensions are impaired in adolescents with GTS. Thus it is important to advocate a multidisciplinary approach including the assessment of these different dimensions in their care.

Key words: Gilles de la Tourette syndrome, Health-Related Quality of Life, Adolescents

P21. Clinical determinants of health-related quality of life among adolescents with Tourette Syndrome: A controlled study.

Jalenques I[1, 2], Auclair C[3, 4], Hartmann A[5, 6], Angonin C[1, 7], Morand D[8], Derost P[2, 9],Durif F[2, 9], Gerbaud L[3, 4, 10], Et le Groupe d'Etude SYNDROME DE GILLES DE LA TOURETTE: Deniau E, Legrand G, Marcheix M, Müllner J, Ramanoël C, May R - [1] CHU Clermont-Ferrand, Service de Psychiatrie de l'Adulte A et Psychologie médicale, F-63003 Clermont-Ferrand, France, [2] Clermont Université, Université d'Auvergne Clermont 1, UFR Médecine, Equipe d'Accueil 7280, F 63001 Clermont-Ferrand, France, [3] CHU Clermont-Ferrand, Service de Santé Publique, F-63003 Clermont-Ferrand, France, [4] Clermont Université, Université d'Auvergne, EA 4681, PEPRADE, F 63000 Clermont Ferrand, France, [5] Centre de Référence National Maladie Rare : 'Syndrome Gilles de la Tourette' Département de Neurologie Pôle des Maladies du Système Nerveux, Groupe Hospitalier Pitié-Salpêtrière 47-83 Boulevard de l'Hôpital 75651 Paris Cedex 13, [6] Centre de Recherche de l'Institut du Cerveau et de la Moelle Epinière UPMC/INSERM UMR_S1127; CNRS UMR 7225 Groupe Hospitalier Pitié-Salpêtrière 47-83 Boulevard de l'Hôpital 75651 Paris Cedex 13, [7] CHU Clermont-Ferrand, Service de Psychiatrie de l'Enfant et de l'Adolescent, F-63003 Clermont-Ferrand, France, [8] CHU - CIC - Clermont-Ferrand, [9] CHU Clermont-Ferrand, Service de Neurologie, F-63003 ClermontFerrand, France, [10] Clermont Université, Université d'Auvergne, UFR Médecine, F-63001 Clermont Ferrand, France.

Objective: Our aim was to investigate in clinic-referred adolescents with Gilles de la Tourette syndrome (GTS) the association between their Health-Related Quality of Life (HRQoL) and severity of GTS and tics, behaviour and emotional problems, socio demographic characteristics.

Method: After neuropsychiatric hetero-evaluations using Yale Global Tic Severity Scale (YGTSS) and Children's Yale Brown Obsessive Compulsive Scale (CY-BOCS), adolescents'

HRQOL was assessed using self-administered instruments, Short-Form-36 (SF-36), Vécu et Santé Perçue des Adolescents (VSP-A) and Childhood Health Questionnaire Assessment (CHAQ). The parents of patients completed socio demographic questionnaires and the Child Behaviour Check-List (CBCL) to measure behaviour and emotional problems their adolescents suffered from.

Results: Were included 75 adolescents with GTS, their 75 mothers and 63 fathers. The mean age of adolescents was 14.8 years (SD=1.8); 80% were male; first symptoms began 8.1 years ago (SD=3.5). The adolescents' mean YGTSS Global Severity score was 33.9 (SD=20). Using CBCL total score, Internalizing and Externalizing Scales scores, respectively 39.4%, 52.1% and 33.3% of adolescents were considered to be pathological range. There were significant negative correlations between YGTSS Motor Tic and Global Severity scores and SF-36 psychological and social dimensions. Positive correlation between YGTSS Phonic Tic score and total CHAQ score of adolescents was also found.

Adolescents with borderline or pathological CBCL Internalizing Scale and total scores had significantly lower scores in several dimensions of HRQoL.

Conclusion: Both severity of tics, behaviour and emotional difficulties have a widespread negative impact on physical, psychological and social dimensions of HRQoL in adolescents with GTS.

Key words: Gilles de la Tourette syndrome, Health-Related Quality of Life, Adolescents, Behaviour, Emotion

P22. Association of the BTBD9 gene polymorphisms with Gilles de la Tourette syndrome in Polish population of patients. *Janik P[1], Berdyński M[2], Safranow K[3], Żekanowski C[2]* - [1] Department of Neurology, Medical University of Warsaw, Banacha 1a 02-097 Warszawa, [2] Laboratory of Neurogenetics, Mossakowski Medical Research Center, Polish Academy of Sciences, Pawińskiego 5, 02-106 Warszawa, [3] Department of Biochemistry and Medical Chemistry, Pomeranian Medical University, Al. Powstańców Wielkopolskich 72, 70-111 Szczecin, Poland.

Background: Gilles de la Tourette syndrome (GTS) is a neurodevelopmental disorder characterized by motor and vocal tics. The etiology of the disorder is unknown, although the predominant role of genetic factors has been established. Variants of the *BTBD9* gene (rs4714156, rs9296249 and rs9357271) have been reported to be associated with GTS in French Canadian and Chinese Han populations.

Aim: To test the association between GTS and polymorphisms of the *BTBD9* gene in Polish patients. **Material and methods**: Our cohort of GTS cases comprised 162 patients aged 454 years (mean age: 19.9 ± 8.7 years; 131 males, 80.9%)**.** The control group consisted of 180 healthy persons aged 14-55 years (mean age: 23.1 ± 2.1 years; 149 males, 82.8%). The rs4714156, rs9296249 and rs9357271 variants of the *BTBD9* gene were genotyped using a polymerase chain reaction system (TaqMan SNP genotyping assay).

Results: No significant differences were found in minor allele frequencies (MAFs) of the SNPs tested between the two groups. The frequency of MAFs of the genotyped SNPs was significantly lower in GTS patients with Attention Deficit Hyperactivity Disorder and higher in patients without comorbidities. There was a trend toward an association between the minor allele of the SNPs and mild tics (p=0.089 for rs9357271 and rs9296249, p=0.057 for rs4714156).
Conlusion: Examined *BTBD9* variants are not associated with GTS risk but may be associated with comorbidity and tic severity in the Polish population.

P23. Neurochemical and network based analysis of the pathophysiological mechanisms of Gilles de la Tourette Syndrome. *Kanaan A S[1, 2], Margulies D[2], Moller H[2], Müller-Vahl K[1]* – [1] Department of Psychiatry, Social Psychiatry and Psychotherpay, Hannover Medical School, Hannover, Germany, [2] Max-Planck-Institut fur Kognitions- und Neurowissenschaften StephanstraRe, Leipzig, Germany.

Gilles de la Tourette syndrome (GTS) is a neurodevelopmental movement disorder whose cardinal features are the presence of fluctuating motor and phonic tics. Approximately 90% of GTS patients exhibit comorbidities that most commonly include Attention Deficit Hyperactivity Disorder (60%) and Obsessive Compulsive Disorder (20-60%). Currently, there is an ongoing effort to further characterize the pathophysiology of GTS and to identify new tic-suppressing therapies. Extensive evidence supports a role for the dopaminergic system within cortico-striatal-thalamo-cortical (CSTC) circuitry as a primary abnormality in GTS. However, given the heterogeneity of clinical symptoms associated with GTS, it has been postulated that other neurotransmitter systems and networks might be involved. In this study, we will focus on the role of the glutamatergic system, iron content and cognitive control networks, and use a procedure that is commonly used in the neuropsychiatric literature in which clinical and MRI data is acquired both off- and ontreatment. We aim to acquire (i) MR spectroscopy data to investigate alterations in glutamate metabolite levels; (ii) quantitative susceptibility maps (MP2RAGE-Multiecho) to quantify iron deficiency; (iii) resting state fMRI data to interrogate the functional decoupling between cognitive control and basal ganglia motor networks; and (iv) diffusion weighted imaging data for exploratory analysis of structural networks. This work will have implications on future glutamatergic modulatory therapies for tic-suppression and could potentially extend the current pathophysiological model of GTS beyond CSTC circuitry.

P24. Dissociable response inhibition in children with Tourette's Syndrome compared with children with Attention-Deficit/Hyperactivity Disorder. *Hovik K*

T[1,2], Plessen K J[3,4], Skogli E W[1,2], Andersen P N[1,2], Øie M[1,2] - [1] Innlandet Hospital Trust, Division Mental Health Care, Lillehammer, Norway, [2] Department of Psychology, University of Oslo, Norway, [3] Centre for Child and Adolescent Psychiatry Capital Region Psychiatry & Institute for Clinical Medicine, University of Copenhagen, Denmark, [4] Institute for Clinical Medicine, Faculty for Medicine and Odontology, University of Bergen, Norway.

The study investigates whether performance in a verbal response task (Color-Word Interference Test) and a motor response task (Conners' Continuous Performance Test) discriminates children with Tourette's Syndrome (TS), Attention-Deficit/Hyperactivity Disorder (ADHD) and typically developing children (TDC).
Method: Nineteen children with TS, 79 with ADHD, and 50 TDC participated (8-17 years).
Results: Children with TS committed significantly fewer errors in the verbal response task than those with ADHD. Moreover, the TS children without ADHD performed better than TDC. Errors in motor task and speed of response did not differentiate groups. A cautious tendency of response correlated with rates of tics in children with TS.
Conclusion: Children with TS were superior in inhibiting a prepotent verbal response; however, the presence of ADHD in those children negatively influenced performance**.** Results support the hypothesis that levels of inhibitory control distinguish children with TS, ADHD and TDC, but differ between motor and verbal response tasks.

P25. Distinct Patterns of Executive Dysregulation Distinguish Children with Tourette Syndrome from Children with ADHD or Autism Spectrum Disorders.

Hovik K T[1, 2], Egeland J[2, 3], Isquith P K[4], Gioia G[5], Skogli E W[1, 2], Andersen P N[1,2], Øie M[1, 2] – [1] Innlandet Hospital Trust Lillehammer, Division Mental Health Care, Norway, [2] Department of Psychology, University of Oslo, Norway, [3] Vestfold Hospital Trust, Norway, [4] Department of Psychiatry, Geisel School of Medicine at Dartmouth, New Hampshire, [5] Division of Neuropsychology, Children's National Medical Center, Washington, D.C.

Everyday executive regulation was investigated in children with Tourette Syndrome (TS) compared with children with Inattentive or Combined subtypes of Attention-Deficit/ Hyperactivity Disorder (ADHD-I, ADHD-C), children with Autism Spectrum Disorders (ASD) and Typically Developing Children (TDC). Method: Nineteen children with TS, 33 with ADHD-C, 43 with ADHD-I, 34 with ASD, and 50 TDC participated (8-17 yrs.). Parents completed the Behavior Rating Inventory of Executive Function (BRIEF). Results: Children with either TS, ADHD-C, ADHD-I or ASD had significantly greater executive function problems on all BRIEF scales compared with TDC. Children with TS or ADHD-C were more impaired than those with ADHD-I or ASD on the Inhibit scale, and children with ASD were more impaired than those with ADHD-I or ADHD-C on the Shift scale. Scale configurations dissociated children with TS from children with ASD on the Emotional Control (EC) and

Shift scales, children with TS from children with ADHD-C on the EC and Inhibit scales, and children with TS from children with ADHD-I on the EC and Plan/Organize scales. Conclusion: Paired BRIEF scales successfully dissociated executive function problems in children with TS from children with other common neurodevelopmental disorders. Identifying the specific deficit in executive function for individual children may guide treatment toward more targeted interventions versus a global omnibus executive function rating or intervention.

P26. Music, tics, Tourette. *Gersdorff Korsgaard A (Specialist in neurology)* - Skt. Anne Plads 2-4, 5th floor, DK-5000 Odense C, Denmark.

It is proved that the prefrontal activity can suppress tics. There is scientific proof that exposure to musical training shapes the brain, and that musician's brains in some areas are larger than non-musician's brains. It has been proved that music especially beyond stimulation the primary acustic center also stimulates many other areas, primarily the prefrontal area, the limbic system, especially hippocampus, and brain stemm as well as cerebellum. Music is a strong activator for several neurotransmittors, especially dopamine, oxytocine, serotonine, endorphines, endocannabinoids, immunoglobulin A, opioid receptors. Also, it reduces the stress hormone cortisol. Music especially stimulates the prefrontal area. This is involving creation and suppression of tics.
My hypothesis was that tics must be able to be reduced by music therapy. Even if there – until now – is no scientific material, which confirm music therapy acting in tics, there are a lot of case stories referring to suppressing tics by playing an instrument or by singing/dancing or listening to music. Also, there is a previous documentation that music can improve arousal and thereby concentration as well as social adaptation. In our clinic we have performed 1 project with professional music therapy for 20 Tourette patients aged 8 to 16 years. They received different types of individual music therapy, depending on the interest of the person. They were informed to practise for 20 minutes at home and count their tics. The result from this project is that almost all, except from 1, could suppress their tics, as long as they listened to the music, an as long as they were in close contact with the music therapist. But the end result was very dependent on the person's ability to train at a daily basis. The project shows that age and maturity had a large influence on the end point. When a patient completed the project and training, there was a very positive results. We are now performing a new project with 10 Tourette patients aged 12 to 30 years. All will receive professional music therapy (modified GIM therapy – Guided Imaginary Music therapy). Some patientes have started, and all patients except 1 suppress their tic at the music therapy seance. Until now there is 9 patients practising daily. All of these experience very good tic suppression and have their self confidence and social adaptation is improved. This will be presented at the congress. I will show a short video

about Tourette patients suppressing their tic by singing and/or playing music + a clip from a music therapy seance with GIM therapy.

P27. A neurocognitive approach for the evaluation and treatment outcome of the Gilles de la Tourette syndrome and chronic tic disorders. *Lavoie M E[1,2,3], Sauvé G[1,2], Morand-Beaulieu S[1,2], O'Connor K P[1,2,3]* - [1] Centre de Recherche de l'Institut universitaire en santé Mentale de Montréal, Montréal, Québec, Canada, [2] Laboratoire de Psychophysiologie Cognitive et Sociale, [3] Département de Psychiatrie, Université de Montréal, Montréal, Québec, Canada.

Background: Research from cognitive neuroscience and psychology revealed that the adult brain has an intrinsic plasticity following stimulation, constantly reshaping his synaptic connections. It is the basis of new learning, but similar mechanism applies to changes following a cognitive-behavioural therapy (CBT). To date, very few studies have sought to relate cerebral activity and clinical improvement following CBT in patients with the Gilles de la Tourette Syndrome (GTS) and chronic motor tics. It has been shown that the activity of the supplementary motor area (SMA) is correlated with symptom expression and this could represent a sensitive marker of change following CBT.
Goal: This presentation will present the outline of our research program, integrating neuropsychological and electrophysiological methods to evaluate symptoms related to GTS and related disorders such as chronic tics disorder.
Method: Electroencephalogram (EEG) was recorded in 15 un-medicated GTS patients, matched with 15 control participants on the basis of laterality, age and intelligence. Derived from the raw EEG, the brain Event-Related Potentials (ERP) and the lateralized Readiness Potentials were computed to isolate the SMA activity related to response activation during a stimulus-response compatibility task. The traffic light task was also administered to elicit motor ERPs related to error processing flexibility generated by the anterior cingulate cortex.
Results: A repeated measures ANOVA (pre-post CBT) revealed a normalization of motor ERPs, positively correlated to an improvement of chronic tics symptoms.
Discussion: Motor activation ERPs represents a sensitive marker of cerebral plasticity and to clinical change following CBT, in patients with the GTS.

P28. Is there an association between Tourette syndrome and maternal smoking during pregnancy? - A nationwide register-study. *Leivonen S[1, 2], Chudal R[1], Suominen A[1], Joelsson P[1], Voutilainen A[2], Brown A[3], Sourander A[1, 4]* – [1] Department of Child Psychiatry, University of Turku, Finland, [2] Children´s hospital, Child neurology, University of Helsinki and Helsinki University Central Hospital, Finland, [3] Department of Psychiatry, New York

State Psychiatric Institute, College of Physicians and Surgeons, Columbia University, New York, NY, USA, [4] Department of Child Psychiatry, Turku University Central Hospital, Finland.

The study aimed to examine if there is an association between maternal smoking during pregnancy (MSDP) and Tourette syndrome (TS), and whether the association is different for the cases diagnosed with only TS or both TS and hyperkinetic disorder. This is a nationwide register-study based on a nested case-control study design. The sampling frame is all 1,199,112 children born in Finland between 1.1.1991-31.12.2010. All children diagnosed with TS in Finnish Hospital Discharge Register (FHDR) were identified. Each case (n=747) was matched to four controls on sex, date and place of birth. The mothers of the cases and controls were identified from the Finnish Medical Birth Register (FMBR). The FMBR includes also data on MSDP collected in maternal health clinics. Conditional logistic regression was used for analysis. The unadjusted analyses showed a 1.3 (CI 95% 1.05-1.6, p=0.018) fold increased risk of TS if the offspring was exposed to maternal smoking after 1st trimester. No association was found if the exposure occurred only during the first trimester. When the cases were stratified into groups of TS (n=537) and TS + hyperkinetic disorder (n=210), no association between MSDP and TS only was found. TS and hyperkinetic disorder was associated with smoking during the first trimester (OR 4.3, CI95% 1.7-10.6) and during the entire pregnancy (OR 2.1 CI 95% 1.4-3.1). No association between only TS and MSDP was found. The association between TS+ hyperkinetic disorder and MSDP may be explained by the hyperkinetic disorder. In future analyses the potential confounding factors will be included.

P29. The concept of refractoriness to a given anti-tic medication: preliminary results from a multicenter European survey. *Macerollo A[1,2], Cardona F[3], Cavanna A E[4], Gulisano M[5], Hartmann A[6], Hoekstra P J[7], Hedderly T[8], Mol Debes N[9], Müller-Vahl K[10], Neuner I[11], Rickards H[4], Rizzo R[5], Roessner V[12], Martino D[13]* – [1] Sobell Department of Motor Neuroscience and Movement Disorders, The National Hospital of Neurology and Neurosurgery, Institute of Neurology , University College London, London, United Kingdom, [2] Department of Neuroscience and Sense Organs, Aldo Moro University of Bari, Bari, Italy, [3] Department of Psychology, University of Rome, La Sapienza, Rome, [4] Department of Neuropsychiatry, BSMHFT and University of Birmingham, United Kingdom, [5] Section of Child Neuropsichiatry, Dipartimento di Scienze Mediche e Pediatriche, Catania University, Catania, Italy, [6] Centre de Référence National Maladie Rare: Syndrome Gilles de la Tourette, Département de Neurologie, Pôle des Maladies du Système Nerveux, France, [7] Department of Child and Adolescent Psychiatry, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands, [8] Tourettes ClinicEvelina Childrens Hospital at Guys and St. Thomas', Kings Health Partners AHSC, London, UK, [9] Pediatric Department, Glostrup University Hospital, Glostrup, Denmark, [10] Clinic of Psychiatry, Socialpsychiatry and Psychotherapy, Hannover Medical School, Carl-

NeubergStreet 1, D-30625 Hannover, Germany, [11] Institute of Neuroscience and Medicine 4, INM 4, Forschungszentrum Jülich, Jülich, Germany, [12] Klinik und Poliklinik für Kinder- und Jugendpsychiatrie und -psychotherapie, Technische Universität Dresden, [13] Centre for Neuroscience and Trauma, Queen Mary University of London, London, UK.

Background: Refractoriness of tics to pharmacological therapy lacks a standardized definition. The degree of consistency across clinicians in formulating this judgment is uncertain.
Objective: To examine the concept of refractoriness to a single anti-tic medication across European expert clinicians.
Methods: Information on patients' refractoriness to a single anti-tic medication was obtained from 7 Tourette syndrome clinicians from 4 European countries. A refractoriness in tic treatment rating scale (RTTRS) was developed on relevant items identified by consensus of 6 experts not involved in the survey, comprising effect on tic severity, dosage, tolerability and adherence to treatment. Refractoriness judgment implied the clinician's decision to discontinue the medication.
Results: 44 patients (39 male, 15±7 years) were deemed refractory to one among the following drugs: aripiprazole, clonidine, risperidone, haloperidol, pimozide, tiapride, sulpiride. No tic severity reduction was reported in 15 patients from 4 centers, based on non-standardized clinical assessment (patients' subjective report). In 29 patients, tic severity was reduced using YGTSS severity score despite the refractoriness judgment (median reduction 20%, range 1-60%). Median treatment duration was 44 weeks (range 10-150 weeks). The last dose used was the minimal dose that reached the highest efficacy (19/44) or the highest tolerated dose (25/44). All participants showed good treatment adherence, with less than 1 dose missed over a period of 10 days.
Conclusion: Refractoriness to single anti-tic medication is not judged homogeneously across expert clinicians, due to differences in ascertainment of tic severity change, treatment duration and dosing. Additional collaborative work is needed to identify a more systematic definition of this clinical concept.

P30. Students with Tourette Syndrome in Greece: the teachers' perspective.

Malli M – University of Kent, UK

The main aim of the current research is to critically evaluate and appraise the teachers' perspective on secondary students with Tourette Syndrome (TS) in Greece. Taking into account that the subject has been scarcely examined, grounded theory has been utilised and through in depth interviews with ten Greek teachers who have had children with TS in their classroom their point of view was sought. The study suggests that the insufficient information the teachers have on the syndrome allows them to accept the stereotypical images that have been linked to the portrait of children with TS. Thus, the image that is

depicted in the media which is fraught with comical elements including coprolalia has not been utterly rejected by them. Furthermore, the overwhelming sympathy that the tics create may hinder the educators from unveiling the students real academic potentials. More specifically, they had lesser expectations of them as far as scholastic attainment is concerned in comparison to other children that age. Moreover, due to the unsatisfactory understanding on the subject the educators are ill prepared to help ameliorate the social isolation the students with TS endure. Lastly, teachers are obliged to base their interventions on their observations and limited understanding of Tourette Syndrome, due to the lack of books and articles that are published in their native language. Overall, the essential need to raise awareness within the educational community in Greece about TS should be pointed out.

P31. Psychosocial characteristics of Tourette syndrome in older adults attending a specialist clinic. *Man C H A[1], Stern J S[1, 2], Gharatya A[1], Williams D[1], Simmons H[2], Robertson M M[1, 2, 3]* – [1] St George's, University of London, [2] Department of Neurology, St George's Hospital, [3] University College London.

Aims: Tourette syndrome (TS) is associated with impaired social functioning and a lowered quality of life. The aim of this study is to investigate the psychosocial health of older adults attending a specialist clinic.

Method: Clinical records of adults over the age of 25 attending a specialist TS clinic were reviewed. Younger adult patients (aged 25-39) were compared with three older subgroups: ages 40-49, 50-59, and over 60. Yale Global Tic Severity Score (YGTSS) and clinician-rated severity impression were recorded with rates of comorbid psychopathology, coprophenomena, forensic history, alcohol abuse, employment and marital status, and highest level of education.

Results: Of 524 patients, 46 were younger adults. 48 older adults were identified in total: 35 aged 40-49, 8 aged 50-59 and 5 aged >60. Older adults present with greater tic severity compared to younger adults (mean YGTSS of 28.05 vs. 24.95 and a "severe" clinician-rated severity in 22.0% vs. 12.2%). Rates of anxiety (10.4% vs. 4.5%) and depression (29.2% vs. 16.4%) were greater in older adults than younger adults. At 50-59 there were higher rates of unemployment (50%), incomplete education, and divorce/single status. At 40-49 divorce/single status, alcohol abuse and criminality were more common.

Conclusion: Older adults attending a specialist TS clinic are subject to referral bias and a potentially atypical evolution with ageing. In this clinical cohort, the older group have more severe tics and are often in poor psychological health, with a history of past and current social impairment.

P32. Selection of treatment targets for patients with Tourette Syndrome. *McNulty R K F, Stern J S, Simmons H, Robertson M M* - St George's University of London.

Introduction: Most patients with Tourette syndrome (TS) seen in specialist clinics are also diagnosed with various comorbidities including OCD and ADHD. We aimed to identify the primary therapeutic targets that were selected in a large cohort of consecutively examined patients.
Methods: Clinical records of 446 patients seen between 2004-2013 were reviewed. Features including clinician-rated global severity and treatment outcome at first visit were collated.
Results: In 18% of adults and 30% of children immediate management did not include new drug or behavioural intervention with the main outcome being psychoeducation and reassurance. Tics were an initial target for treatment in 45% (adults: 57%, children 36%) and comorbidities in 55% (multiple target in 48% of these). Patients with more severe tics were more likely to have tics selected as the target.
Discussion: These findings emphasise clinicians' impression of the importance of identification of comorbidities and of even mild tics not requiring management as a marker of these disorders. Children were less likely than adults to have an active management target chosen at first visit, reasons could include a higher threshold for drug prescription, fewer severe cases and the lack of availability of specialised psychology therapies.

P33. Behavioural therapy in a tertiary clinic for Tourette syndrome in Denmark. *Mol Debes N, Grejsen J, Aaslet L, Skov L* - Paediatric Department, Herlev University Hospital, Denmark.

Background: Behavioural therapy has shown to be the first choice of treatment for tics in patients with Tourette syndrome (TS). We have introduced Exposure and Response Prevention and Habit Reversal in our tertiairy clinic for TS in Denmark.
Methods: In order to evaluate the effect of behavioural therapy, we administer Yale Global Tic Severity Scale Score (YGTSS), Premonitory Urge for Tic Scale (PUTS) and quality of life questionnaire (PedsQL) before the start of training, after 4 sessions, after 8 sessions, and after 12 sessions.
Results: We have included 10 patients and the patients and their parents are very satisfied. The analyses are still ongoing og we will present the final results at the meeting. We expect to find decreased YGTSS and PUTS, and increased quality of life after 12 sessions.

P34. Normalization of pre-motor processes following cognitive behavioural therapy in Tourette syndrome and chronic tic disorder patients. *Morand-Beaulieu S[1, 2, 3], Sauvé G[1, 2, 3], O'Connor K P [2, 3], Blanchet P [2, 4], Lavoie M E[1, 2, 3]* - [1] Laboratoire de psychophysiologie cognitive et sociale, Montreal, Canada, [2] Centre de recherche de

l'Institut universitaire en santé mentale de Montréal, Montreal, Canada, [3] Département de psychiatrie, Université de Montréal, Montreal, Canada, [4] Département de stomatologie, Université de Montréal, Montreal, Canada.

Introduction: Tourette syndrome (TS) is a neuropsychiatric disorder involving motor and phonic tics. Studies have shown that a therapy based on regulating the chronically heightened sensorimotor activation and elevated muscle tension could improve motor performance and general condition in TS patients. Still, physiological and behavioural mechanisms behind the therapy are not fully understood.
Objectives: This project aims to study the activation and inhibition of motor processes in TS patients, and the psychophysiological modifications induced by the therapy.
Method: Twenty participants with motor tics were matched on age, sex and intelligence with 20 healthy controls. EEG activity was recorded at 500 Hz, at electrodes C3 and C4, during a Stimulus-Response Compatibility task. EEG data was averaged into stimuluslocked event-related potentials. Lateralized readiness potentials (LRP) were then obtained through a double subtraction, to eliminate any electrical activity unrelated to motor processes. Measures were taken before and after the therapy for the TS group, while the control group was only tested once.
Results: Before the therapy, the LRP onset was significantly slower for TS patients, compared to controls [$F(1,38)=4.243$, $p<0.05$]. After the therapy, this difference disappeared. In the TS group, the LRP onset was significantly faster after the therapy [$F(1,19)=7.782$, $p<0.05$].
Conclusion: The group difference on the LRP onset latency disappears after the therapy, suggesting that the therapy induces a normalization of pre-motor processes. It could lead TS patients to have a greater control of movement preparation. These results could also indicate a modification of the cerebral activity in the supplementary motor area.

P35. Improving CNV calling methods for Genome-wide association Studies.

Nawaz M S - deCODE Genetics, Reykjavik, Iceland.

Tourette's syndrome (TS) which a complex neuropsychatric developmental disorder has strong genetic pattern. Scientific studies are still trying to ascertain genetic architecture of TS. In this study we improved copy number variations calling algorithm and searched for genome-wide association studies of CNVs affecting TS in 676 cases and 100114 controls for which genealogy and long range phased haplotype (LRPH) data was available from Icelandic population. PennCNV was used to call CNVs from 111515 genotyped Icelanders, which generated 7861540 CNV calls. To remove false positive CNV calls we used quality control steps from cnv-pipeline developed during this study. Later, each CNV call was confirmed through haplotypes derived from LRPH data which validated 67426 CNV bins having 9865 unique CNVs. These unique CNVs bins were tested for association with TS. In

next phase, we further expect to confirm these findings and quite hopeful that current results may be replicated in our cohort(s).

P36. Finding developmental aspects and possible drug targets of TS and OCD: metabotropic glutamatergic mechanisms in a neurodevelopmental rat model of repetitive behaviors. *Nespoli E[1, 2], Rizzo F[1], Ludolph A G[1], Ferger B[2], Hengerer B[2],*– [1] Department of Child and Adolescent Psychiatry, University of Ulm, Steinhoevelstrasse 5, 89075 Ulm, Germany, [2] Boehringer-Ingelheim Pharma, GmbH & Co. KG Div. Research, Germany.

Tourette syndrome (TS) is a neurodevelopmental disorder affecting 0.4-1% of the general population. Symptoms become evident during childhood and involve several motor tics and at least one vocal tic. Unfortunately, the etiology of the disease is still unclear, but a broad range of findings support the idea that tics in TS occur as a consequence of a deregulated activity of the corticostriatal-thalamocortical circuit, which leads to an increased sensitivity to dopamine in the striatum. (Buse et al., 2013). Up to now, numerous animal models of TS have been published, but all in adult animals. The unilaterally lesioned 6-hydroxidopamine (6-OHDA) rat is a well-established model used in Parkinson´s Disease research. In this model a degeneration of nigrostriatal neurons is chemically induced by the intrastriatal or intranigral administration of 6-OHDA, which selectively targets monoaminergic neurons. Chronic application of L-dopa to 6-OHDA lesioned rats leads to the development of repetitive involuntary movements, mainly involving the forepaw, the neck and the mouth. This appears as a consequence of the striatal super sensitivity to DA, caused by higher surface expression of dopamine receptors, which is a putative pathological mechanism of TS and is induced in this model via previous DA deprivation. We propose to translate this model to juvenile rats, inducing the lesion in postnatal days and monitoring its neurodevelopmental consequences. This could provide a new insight about TS pathological mechanism, and a new tool to test therapeutic option for this disease.

P37. Motor versus vocal tics. *Omar A Y, Stern J S, Simmons H, Robertson M M* - St George's University of London.

Introduction: Some patients with Tourette syndrome present with predominant motor or vocal tics rather than a more balanced combination. We looked at the distribution of the two tic types in a large cohort and also at the clinical characteristics of outliers.
Methods: The Yale Global Tic Severity Scale (YGTSS) scores of 315 patients taken at first visit were reviewed and motor and vocal tic scores plotted graphically. A visual cut-off for outliers with unbalanced tic severities was selected as a difference of 9 or more points.

Results: 31 patients had predominantly motor tics with a range of severity, 2 had more vocal tics and the remaining 282 were considered "balanced". There was a trend to reduced rate of ADHD in the predominant motor group (p=0.054). Values for the YGTSS impairment component were equally spread in the unbalanced group.
Discussion: Most patients have fairly balanced motor and vocal tics, unbalanced presentations seem far more likely to be motor than vocal and the trend to less ADHD in this situation may relate to the gradient of comorbidity rates in TS compared to chronic vocal and chronic motor tics seen in epidemiological samples which are lower for motor tics.

P38. Gene expression studies in TS. *Padmanbhuni S S[1], Ander B P[2], Sharp F[3], Drineas P[4], Paschou P[1]* - [1] Department of Molecular Biology and Genetics, Democritus University of Thrace, Alexandroupoli, Greece, [2] Medical Investigation of Neurodevelopmental Disorders (MIND) Institute, University of California Davis, Sacramento, California, United States of America, [3] Department of Neurology, University of California at Davis, Davis, California, [4] Department of Computer Science, Rensselaer Polytechnic Institute, Troy, New York 12180, USA.

The aetiology Tourette Syndrome (TS) is complex with multiple genes interacting with environmental factors. Given this complexity, the investigation of gene expression patterns in TS may provide useful insights on gene and environment interactions. Changes in gene expression in the brain can be observed in peripheral blood as expected through its interaction with the brain. Studies have shown distinct gene expression profiles in peripheral blood for many neuropsychiatric disorders. Here, we are performing metaanalyses of gene expression datasets for TS (made available to us by our collaborators at the University of California Davis). The gene expressions arrays that were used are the Affymetrix U133 Plus 2.0 arrays and the Affymetrix HuExon arrays for 26 TS cases and 23 Healthy Control samples. We are exploring various algorithms for clustering and classification of the gene expression data, ranging from Principal Component Analysis (PCA) and other dimensionality reduction techniques to clustering and classification tools such as k-means and Support Vector Machines to predict tic severity (which is scored through standard measures) using gene expression profiles. The algorithmic methods and pipeline established here will be transferred to the study of a much larger dataset that is currently being collected under the auspices of the EU-funded EMTICS project.

P39. Excitability of the motor cortex in Tourette syndrome in the period preceding volitional movement. *Pépés S, Draper A, Jackson S* – (University of Birmingham, UK)

Tourette syndrome (TS) is a neurodevelopmental disorder characterised by the frequent occurrence of motor and phonic tics. It has been suggested that the disorder has arisen from a dysfunctional cortical-striatal-thalamocortical (CSTC) pathway. This suggests that as well as dysfunction in deeper brain structures there is impaired function at the level of the cortex. Transcranial magnetic stimulation (TMS) allows us to examine corticospinal excitability (CSE) in the motor cortex and thus allows us to explore and understand dysfunction that occurs in this region in TS. Here, we explore the responsiveness of the motor cortex to TMS stimulation by using different intensities of resting motor threshold (RMT) and measuring MEP responses to plot an input-output curve (IO curve) in a group of adolescents with TS and matched controls. Secondly, we investigate alterations in CSE during the preparation of a volitional movement by recording TMS-induced motor-evoked potentials (MEPS) at different percentages of reaction time during a simple Go/NoGo task in the same group. We look at differences in MEP amplitude and variability during different periods of movement preparation. Finally we look at diffusion tensor imaging (DTI) data collected for the TS group to determine if there is a relationship between tic severity, CSE measures and the white matter connectivity.

P40. Deep Brain Stimulation (DBS) in TS: comments and recommendations for an international clinical trial. *Porta M[1], Zekaj E[1], Broggi G[1], Servello D[1]* - Tourette Center and Functional Neurosurgery, Hospital IRCCS Galeazzi, Milano – Italy.

The evidence from a Literature review on the “minimum” surgical approach (DBS) for the treatment of Tourette syndrome (TS) shows many aspects still to be clarified. At the present time DBS in severe, refractory TS patients remains used, as investigational procedure. Many Authors consider this procedure in TS as belonging to the domain of the psychosurgery. TS is an organic medical condition including in the clinical picture, as part of the syndrome, not only sound and motor tics but also OCD (obsessive compulsive disorder), reduced impulse control, addicted behavior, which significantly alter the quality of the life, and increase the social impairment of TS patients. Unfortunately, DBS data in TS are mostly anecdotal experiences for the time being, obtained in different centers following the so called “compassionate use” procedure. The interpretation of such data therefore exposes to many methodological bias. DBS devices are not yet approved by the Authorities for TS. CE mark is not yet obtained, and FDA (USA) has not approved DBS for this indication. The targets stimulated by different Authors are too many, often without a precise explanation of the rationale used, and without considering adequately the mood spectrum presented by TS patients. No predictive tests (pre-DBS) are available for TS patients candidates to the procedure: in Parkinson disease the CAPSIT evaluation has a tremendous impact in the determining the outcome of the procedure. Evaluation of the results obtained isin the majority of the cases done without a prospective protocol. Moreover, degree of severity of TS that allows evaluation of eligibility for DBS, the

minimum age for candidates to the procedure and the definition of refractoriness of the subjects are not well established. Last but not least, the majority of the drugs used in TS are “off label”; they are not available in many countries. Specifically regarding DBS, drugs consumption after surgery is not described in details in reported cases, and the role of DBS in TS therapeutical algorithm in terms of cost/quality is not studied. These considerations point out very clearly the need for a multicenter, prospectic, and well-designed controlled clinical trials in TS patients candidates to DBS.

P41. Culpability of patients with Tourette Syndrome. *Porta M[1], Mastroianni S[1], Zanaboni C[1], Servello D[2], Saleh C[1], Marconi S[2], Raugna M[1]* – [1] Tourette Center and Functional Neurosurgery, Hospital IRCCS Galeazzi, Milano – Italy, [2] Penal Lawyer, Milano – Italy.

- Tourette syndrome (TS) is now recognized as one of the most common genetic neurological disorders of childhood onset.
- Ignorance of the organic basis of TS often results in inadequate therapy, inappropriate hospitalization, social ostracism, and possible culpability in justice. Jankovic and colleagues (2006) pointed out very clearly that the “organic” medical condition in evaluating causality of committing crimes has to be carefully considered in TS subjects.
- TS includes in the clinical picture, as part of the syndrome, not only motor and sonor tics, but also (a) obsessive compulsive symptoms (OCB) (b) addicted behavior (c) reduced impulse control (d) conduct disorders (e) disinhibition (f) rage attacks • Inappropriate and often incomplete diagnosis are frequent
- Epidemiological data are scanty; TS is still considered a rare disease
- Reduced capacity in TS patients is not adequately taken into consideration in the criminal justice system
- Frequency of unlawful or criminal activity in TS is unknown
- Following consideration of all the above, it becomes more and more important to define:

- responsibility of the medical community in making correct diagnosis
- role of the family and the school in taking care of TS subjects
- importance of prevention
- role of mass media in improving the knowledge of TS
- well-defined treatment strategies
- controlled studies to investigate behavioral consequences of TS
- guidance to the legal system and in general to the Law

- “Actus reus” and “Mens rea” have to be carefully evaluated in determining culpability in TS patients

- TS patients are young “per definition” at the onset of the disease: according to the Italian Law, a younger than 14 years old (at the time of the event) child is not imputable. Despite that, if the child is plead dangerous for himself or for the others, a number of safety measures are considered, such as probation or the intervention of social services.
- A 14-till-18-year-old young person is imputable just if at the moment of the event he/she was able to understand and take action. Therefore, the Judge decides case by case and with the necessary medical and/or psychological assessment culpability.

P42. Investigation of the molecular effects of Aripiprazole and Riluzole in a TS rat model – An MR Spectroscopy Study. *Rizzo F[1], Nespoli E[1,4], Udvardi P[1], Hengerer B[4], Ferger B[4], Rasche V[3], Abei A[3], Ludolph A G[1]* – [1] Department of Child and Adolescent Psychiatry, University of Ulm, Steinhoevelstrasse 5, 89075 Ulm, Germany, [2] Institute of Anatomy and Cell Biology, University of Ulm, Albert Einstein Allee 11, 89081 Ulm, Germany, [3] Department of Inner Medicine II, University of Ulm, Albert Einstein Allee 23, 89081 Ulm, Germany, [4] Boehringer-Ingelheim Pharma, GmbH & Co. KG Div. Research, Germany.

Introduction: Dysfunctions in the dopamine metabolism in Tourette Syndrome (TS) are well documented, especially since the efficacy of dopamine antagonists in tic suppression has got a reasonable effect size. Aripiprazole, a partial dopamine agonist, and tiapried, a dopamine antagonist, are the drugs most often used in Germany for TS treatment. Research data from imaging and genetic studies give definite hints that other neurotransmitter systems are involved: histamine, serotonin, norepinephrine (also alpha 2A agonists are used as treatment in TS) and glutamine. The glutamine and dopamine metabolism are closely connected. More than 60% of the neuronal synapses are glutamatergic. Clinical trials with glutamatergic compounds are ongoing. In this study we want to investigate aripiprazole´s and riluzole´s effect on the cerebral glutamatergic metabolism in rats by MR spectroscopy.
Methods: Wistar rats and spontaneous hypertensive rats (SHR), an ADHD animal model, will stereotactically undergo intrastriatel microinjections of bicuculline, a GABA antagonist (Bronfeld et al., 2013). Control animals will be sham-operated. Animals will be treated with either aripiprazole or riluzole, a glutamatergic modulator. MR spectroscopy will be conducted.
Results: This study is ongoing. Data about set up, surgery, anaesthesia etc will be presented.

P43. Modified Atkins diet for treatment of tics in Tourette syndrome (TS).
Sørensen C B, Aaslet L, Mol Debes N, Skov L, Miranda M J - Tourette Clinic, Department of Pediatrics, Herlev University Hospital, Copenhagen University, Denmark.

Background and aim: The Modified Atkins Diet (MAD) is a variant of the classic ketogenic diet (KD). The diet consists of high fat, adequate protein and minimal carbohydrates, which forces the body (and brain) to use ketone bodies as energy source instead of glucose. KD is an effective non-pharmacological treatment for pharmacoresistant childhood epilepsy. KD might be neuroprotective and has shown to affect several systems in the brain, as the dopamine system. Since a disturbance in dopamine is a pathophysiological factor in TS, MAD might be effective in reducing tics.

Hypotheses:

MAD may

- Reduce frequency and severity of tics assessed by YGTSS (Yale global tics severity scale).
- Reduce severity of Attention Deficit Hyperactivity Disorder (ADHD) and obsessivecompulsive disorder (OCD) assessed by ADHD-RS and CYBOCS respectively.
- Improve the quality of life, assessed by PedsQl.

Methods: A prospective study with intention-to-treat design. We will examine a clinical cohort of children, aged five to seventeen years, with TS and severe tics. After an observation period of two months, the patients will be randomized blindly into two groups. The first group will start MAD immediately and the other group will start after three-six months. Flowchart and outline of the investigation are illustrated in illustration 1.

Discussion and results: We expect primarily to see a reduction in tics severity and frequency. Furthermore, the presence of co-morbidities frequently seen in patients with TS will be evaluated. This is the first study where a KD is tried in a randomized prospective way in children with TS.

P44. Psychogenic tics: how to differentiate them from organic tics. *Szejko N, Milanowski Ł, Janik P* - Department of Neurology, Medical University of Warsaw.

Introduction: Psychogenic tics are considered rare and often it is difficult to differentiate them from organic tics.

Objectives: The aim of the work was to find features that may be useful for differentiating PT from organic tics.

Methods: Medical documentation of 268 consecutive patients (221 males, 82.5%, 134 adults, 50%), aged 4-54 years (mean: 18.4±8.4), presenting with different phenotypes of tics, was analyzed.

Results: PT were found in 5 patients, aged 17 to 51 years, four men and one woman. The phenotype included vocalizations (both meaningless sounds and linguistically meaningful utterances) and complex movements (such as kicking, bouncing, bending the body in an arc, throwing of the head to the back etc). In none of the patients simple motor facial tics, inability to tic suppress, unchanging clinical pattern, peak tic severity from the beginning

of the disease, lack of concern about the disease were present. The absence of premonitory urges, disappearance in unexpected positions, and the presence of atypical for GTS mental disorders (paranoid syndrome, oligophrenia) were found in two persons. PT occurred in three persons in whom organic tics were present in childhood. Pharmacological treatment and psychotherapy were unsuccessful. In two persons spontaneous resolution occurred, in two patients the tics persist, in one person the course of PT is unknown.

Conclusions: PT may occur in patients with organic tics. The most typical features of PT are: early onset in adulthood, lack of simple motor tics, inability to tic suppress. The diagnosis is established if a few atypical symptoms for organic tics occur.

P45. Do prenatal and perinatal complications influence tic severity in patients with Gilles de la Tourette syndrome? *Taylor K, Stern J S, Simmons H, Robertson M M* – St George's University of London.

Aim: Evidence for the role of genetics in the clinical expression of Gilles de la Tourette (GTS) is widespread, but studies on environmental factors are inconclusive. The aim of this project was to investigate whether perinatal complications are associated with increased tic severity in patients who develop GTS.

Method: 193 GTS patients attending St George's Hospital between 2004-2011 were retrospectively reviewed for exposure to perinatal complications (Mean age 20.3 ± 13.55; age range 3-76; 145 males: 48 females) The Yale Global Tic Severity Score (YGTSS) was used to assess current tic severity, giving each patient a score out of 25 for phonic and motor tics, and 50 for total tic severity. An additional impairment score was given between 0 (no impairment) to 50 (severe impairment). Records were reviewed for the presence of co-morbidity associated with GTS (ADHD/OCB/OCD); and any family history of GTS, tics, ADHD, OCD or OCB.

The mean tic severity and impairment scores for complications v. no complications were compared.

Results: Perinatal complications were reported in 101 out of 193 (52%) of patients. The mean total tic severity score compared to patients with a history of complications was 25.94 v. 24.88 and the mean impairment scores were 29.01 v. 25.24 respectively.

Conclusions: In this cohort, perinatal complications were not associated with increased tic severity or impairment and there was no increase in comorbidity or family history. Limitations include recall bias, a univariate approach, and YGTSS- which only records severity of a fluctuating condition at one point in time.

P46. Neuropsychological functioning in young people with Tourette Syndrome: the impact of Attention deficit/hyperactivity disorder. *Selvini C[1], Luoni C[1], Fontolan*

S[1], Perego L[1], Rossi G[2], Cavanna A E[3,4,5], Termine C[1,2] – [1] Child Neuropsychiatry Unit, Department of Experimental Medicine, University of Insubria, Varese, Italy, [2] Child Neuropsychiatry Unit, Ospedale di Circolo & Macchi Foundation, Varese, Italy, [3] School of Life and Health Sciences, Aston University, Birmingham, UK, [4] Department of Neuropsychiatry, BSMHFT and University of Birmingham, UK, [5] Sobell Department of Motor Neuroscience and Movement Disorders, UCL and Institute of Neurology, London, UK.

Aims: Tourette Syndrome (TS) is a neurodevelopmental disorder characterized by motor/phonic tics, frequently associated with co-morbidity such as Attention Deficit/Hyperactivity Disorder (ADHD). Several studies report low executive functioning in TS, but it is difficult to distinguish whether neuropsychological deficits are due to TS or to comorbidities. We assessed cognition, memory, attention and executive functions in children with TS, TS+ADHD, ADHD and unaffected controls.
Methods: Thirteen TS patients, 8 TS patients with ADHD (TS+ADHD), 39 ADHD patients and 66 age and gender-matched healthy controls participated in this study. All recruited participants completed a standardized neuropsychological battery, including vocabulary and block design from Wechsler Intelligence Scale for Children III, Tower of London, Italian ADHD Battery, short-term memory tests (Corsi, digit span) and graphomotor fluency test. Results were compared with similar data obtained from controls.
Results: Scores on most of neuropsychological tests showed significant differences between patients and controls ($p<0,001$). ADHD subgroup showed higher impairment on memory, attention and fluency tests compares with TS+ADHD and TS groups. Moreover, executive tasks turned out to be most impaired in TS+ADHD group.
Conclusions: Both TS and ADHD patients show lower executive functioning compared with controls. ADHD seems to be responsible of poor neuropsychological functioning in TS children.

P47. Personality profile of adolescents with Tourette syndrome: A controlled study.

Balottin L[1], Selvini C[2], Luoni C[2], Mannarini S[1], Chiappedi M[3], Seri S[4], Termine C[2,5], Cavanna A E[4,6,7] – [1] Department of Philosophy, Sociology, Education and Applied Psychology, Section of Applied Psychology, University of Padova, Italy, [2] Child Neuropsychiatry Unit, Department of Experimental Medicine, University of Insubria, Varese, Italy, [3] Department of Child Neurology and Psychiatry, "C. Mondino" National Neurological Institute, Italy, [4] School of Life and Health Sciences, Aston University, Birmingham, UK, [5]Child Neuropsychiatry Unit, Ospedale di Circolo & Macchi Foundation, Varese, Italy, [6] Department of Neuropsychiatry, BSMHFT and University of Birmingham, UK, [7] Sobell Department of Motor Neuroscience and Movement Disorders, UCL and Institute of Neurology, London, UK.

Background: Tourette syndrome (TS) is a neurodevelopmental disorder characterized by multiple tics and commonly associated with behavioural problems, especially obsessivecompulsive disorder and attention-deficit hyperactivity disorder. The presence of specific personality traits has been documented in adult clinical populations with TS but has been under-researched in younger patients.
Methods: We assessed the personality profile of 22 adolescents with TS and 66 age and gender-matched healthy controls using the Minnesota Multiphasic Personality Inventory – Adolescent version (MMPI-A), along with a standardized battery of psychometric instruments.
Results: All participants scored within the normal range across all MMPI-A scales. Patients with TS scored significantly higher than healthy controls on the Obsessiveness Content Scale only (p=.037).
Conclusions: Our findings indicate that contrary to what has been reported for adults, younger patients with TS do not report abnormal personality traits and have similar personality profiles to healthy peers, with the exception of obsessionality traits, which are likely to be related to the presence of co-morbid obsessive compulsive symptoms rather than tics. This study prompts further research on the developmental trajectories of personality disorders in TS across the lifespan.

P48. Sleep disturbances in children with Tourette syndrome. *Robinson S, Woods M, Grose C, Brennan H, Hedderly T* - Tic and Neurodevelopmental Movement (TANDeM) Clinic, Children's Neurosciences Centre, Evelina London Children's Hospital, Guy's and St Thomas' NHS Foundation Trust, London.
Objectives: Sleep difficulties have been reported for individuals with Tourette syndrome (TS), with sleep efficiency affected by tic severity and co-morbid neurodevelopmental problems (Kirov, et al., 2007). The aim of the current study was to explore the behavioural characteristics of sleep-related problems for children with TS.
Methods: The parents/carers of 27 children (23 boys and 4 girls; mean age=10years) with TS were administered the TANDeM Sleep Disturbance Questionnaire. 13 questions addressed sleep onset, duration and rising, as well as the relationship between sleep and tics, and parent/carer satisfaction. The Yale Global Tic Severity Scale (YGTSS) was used to assess tic severity and attention problems were recorded.
Results: Most reported a worsening of tics at night (77%), with **s**leep onset problems (66%) and night time waking (52%). For half the sample tics affected sleep onset, occurred during sleep and worsened following a bad night sleep. 60%were not satisfied with their child's sleep, with satisfaction inversely related to sleep onset (r=0.63). Attention and sleep onset problems were related (r=.49), though satisfaction did not differ between those with/without attention problems. Tic severity was related to the occurrence of tics in sleep (r=.71).

Conclusions: Sleep problems are common in TS and characterized by poor sleep onset and duration, with a relationship between tic severity, tiredness and the occurrence of tics in sleep. Interestingly, parental satisfaction was not related to attention difficulties, which suggests that tic specific factors contribute to sleep difficulties. This highlights the importance of effective sleep management strategies for children with TS.

P49. A Comparison of Clinician and Self-Report Measures of Tics, Co-morbid Difficulties and Quality of Life. *Woods M, Robinson S, Brennan H, Bunton P, Hedderly T* - Tic and Neurodevelopmental Movement (TANDeM) Clinic, Children's Neurosciences Centre, Evelina London Children's Hospital, Guy's and St Thomas' NHS Foundation Trust, London.

Objectives: Research on children with chronic tic disorders indicates a high frequency of co-morbid emotional and behavioural problems. The relationship between tics and comorbid difficulties is of importance to guide clinical assessment and treatment. The aim was to explore the relationship between clinician and patient ratings of tics and co-morbid difficulties and quality of life.
Methods: 85 children (67 male, 18 female; mean age=11years old) with a chronic tic disorder participated. To assess tics, clinicians completed the YGTSS-C and patients the MOVES questionnaire. Other self-report measures included the CY-BOCS, Paediatric Index of Emotional Distress (PI-ED) and GTS Quality-of-Life (GTS-QoL).
Results: There was a significant positive relationship between motor and phonic tics for both the YGTSS-C (r=.38) and MOVES (r=.65), but patients rated motor tics as occurring more frequently than clinicians. YGTSS-C tic severity and MOVES scores were both significantly related to PI-ED scores (r=.55). There was no significant relationship between YGTSS-C and GTS-QoL scores, but GTS-QoL was significantly related to CY-BOCS (r=.75), PIED (r=.46), and MOVES total tic (r=.86) scores.
Conclusions: Clinician and self-report measures consistently scored the frequency of phonic tics, but not motor tics. This appeared to reflect objective clinical ratings underestimating subjective tic experiences. Tic severity was related to emotional wellbeing, whilst quality of life was related to self-reported levels of tic frequency, emotional distress and obsessive compulsive behaviours. This highlights the importance of monitoring emotional well-being and subjective tic experiences, with the child's perceptions of tics and co-morbid difficulties informing quality of life and treatment needs.

P50. Evaluation of international guidelines on the pharmacological treatment of patients with Tourette syndrome. *Zenonos K[1], Kyprianou K[1], Cavanna A E[1,2,3*]* - [1] Department of Neuropsychiatry, University of Birmingham and BSMHFT, Birmingham, UK, [2] School of Life and Health Sciences, Aston University, Birmingham, UK, [3] Sobell

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Two sets of guidelines (European Society for the Study of Tourette Syndrome, 2011; Canadian Tourette Syndrome Association, 2012) have recently been developed to assist treating clinicians in the choice of pharmacological options. We retrospectively assessed the use of pharmacotherapy in adult patients attending the specialist TS clinic in Birmingham, UK. Clinical outcomes rated by the treating clinician using the Clinical Global Impression - Improvement scale (CGI-I) were available for 22 patients treated according to the European Guidelines and 17 patients treated according to the Canadian Guidelines. Although comparison of demographic and clinical characteristics between the European Guidelines group and the Canadian Guidelines group did not reveal statistically significant differences, a higher proportion of patients in the European Guidelines Group had a CGI-I score of 1 ('very much improved': 8/22 or 36.4% versus 4/17 or 23.5%) and 3 ('minimally improved': 3/22 or 13.7% versus 1/17 or 5.9%) at the routine follow-up assessment (average: 6 months). The most frequent outcome in the Canadian Guidelines Group was a CGI-I score of 4 ('no improvement': 7/17 or 41.2%), however this group of patients had a lower frequency in the CGI-I score of 5 ('minimally worse': 1/17 or 5.9% versus 3/22 or 13.7%). In addition to contributing to the standardisation of prescribing practices across specialist TS services, each of the two sets of guidelines appear to have specific advantages, with higher rates of efficacy in the European Guidelines, and better tolerability in the Canadian Guidelines.

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