ABSTRACTS

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13th European Conference on Tourette Syndrome & tic disorders

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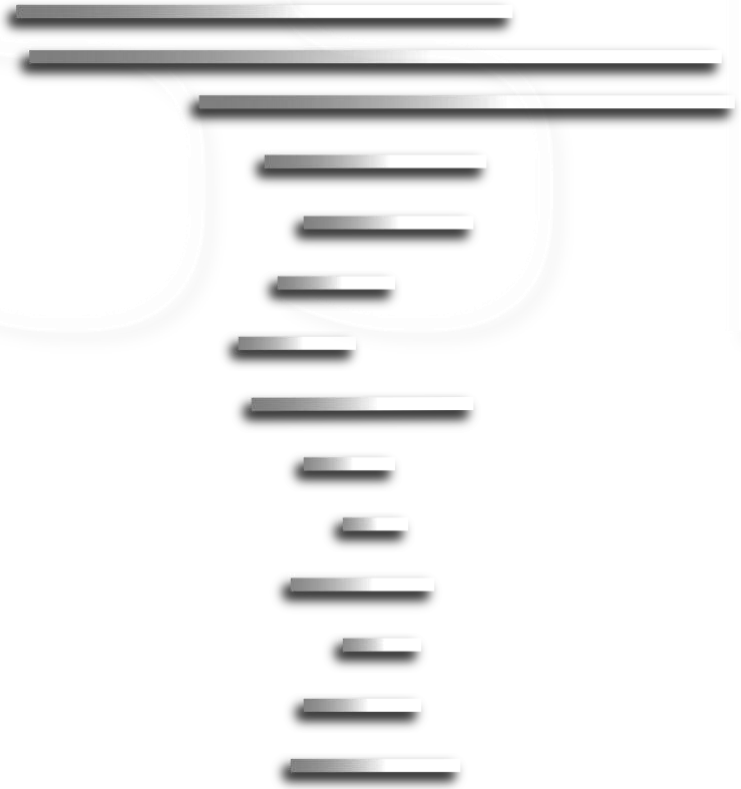

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Oral presentations of selected abstracts

O1. Premonitory urges reconsidered: urge location corresponds to tic location in patients with primary tic disorders

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Background:
One of the main characteristics that distinguishes primary tic disorders (PTD) from other movement disorders is that tics are typically preceded by a premonitory urge (PU). Given the common knowledge that you only scratch were you feel an itch, it would be reasonable to assume that a PU would occur at the body region associated with the tic. In 1993, Leckman and colleagues first investigated PU locations in detail in a sample of 135 patients by using a full body drawing where patients should mark PU locations of their "eight most common motor and phonic tics". While not explicitly comparing locations of individual PUs and tics, the overall result did not suggest a strong association between tic and PU location. Subsequent studies were few and small and none examined corresponding PU and tic locations.
This study was aimed to first replicate Leckman et al.'s study in a larger and more homogenous sample of adult patients with PTD and to investigate whether PUs and tics co-occur in the same body regions, whether PUs depend on specific characteristics of tics and to examine the relationship between PUs and their corresponding tics.

Methods:
This study was conducted as an online survey via the SoSci Survey platform. Participants were recruited through our Tourette outpatient clinic, cooperating study centers, and German Tourette advocacy groups between 11/2017 and 3/2018. Participants needed to be adults and have a diagnosis of PTD. The survey first contained general question on the PU such as if it occurred at all, laterality, and its course over time. Thereafter, participants were asked to indicate all of their current tics. For each tic, participants were shown a full-body drawing and asked to mark the location of the PU by using a cursor. In addition, we collected data regarding relief after tic, perception, consistency, intensity, existence, and lateralization of PU.

Results:
Our survey resulted in 291 adults (>18 years) with PTD (male: n=221 (75.9%), female: n=70 (24.1%)). Overall, 75.9% (n=221) of participants reported experiencing PUs. Significantly more women reported experiencing PUs than men (98.6% (n=69) vs. 73.8% (n=163), $p<0.05$). Of those participants reporting tic-specific PUs, 97% (n=224/232) indicated feeling a momentary relief of the PU after the tic for at least for one of their tics.
We found PUs to be located in the same body area or in direct proximity to the corresponding tic. The vast majority of participants (92.2%, n=214/232) indicated feeling a PU for at least one of their tics in the anatomic location of the tic. The same was true, when we replicated Leckman et al.'s study by specifically looking at the 8 most common tics. Here as well, the PU was to be found at the same location as the tic or at a location in direct proximity.

Most frequently, PUs were located in the face and head (62.1%). Complex (motor and vocal) tics were more often preceded by a PU compared to simple tics with no difference between motor and vocal tics. PUs were more frequently experienced at the front than at the back side of the body (73% vs. 27%), while there was no difference between right and left side (41.6% vs. 41.3%).

Conclusions:
In line with our hypothesis, we found that PUs and their corresponding tics are located in the same body areas. In addition, we demonstrated that the most frequent PU locations are the face and head. The strong association between PU and tic location further supports the hypothesis that PUs represent the core of PTD. Accordingly, future therapies should focus on treating PUs to achieve a larger tic reduction.

O2. The relationship between premonitory urges and tics, comorbidities, quality of life, and treatment

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Background:
Tics have been found to be intimately associated with sensory urges. However, many aspects of the urge-tic relationship remain unclear. This study addressed the following questions: a) is tic frequency and intensity associated with urge frequency and intensity, b) how commonly do patients experience relief, c) which comorbidities are associated with urges, d) what characteristics of urges and tics are associated with lower quality of life, e) how does treatment affect urges.

Methods:
N = 291 patients with Tourette syndrome (age = 18-65, 24% female) filled out an online survey. (Data from this study regarding the distribution of urges in the body has been previously presented and is under consideration for publication). Patients reported each tic they experienced, how frequently they experienced each tic (sometime, multiple times a day, once per hour, all the time), how intense the tic was (1-4), and how frequently they experienced urges (never, sometimes, always) with every tic. Patients could report different types of urges for different tics, i.e. a certain urge quality for each tic. Common comorbidities were also assessed.

Results and Conclusions:
Urge and tic severity were significantly associated, and 85% of urge-related tics were followed by relief. Having a diagnosis of attention deficit hyperactivity disorder (ADHD) or depression, female gender, and older age increased the likelihood of experiencing urges, while more obsessive compulsive disorder (OCD) symptoms and younger age were associated with higher urge intensities. Complex phonic tics, ADHD, OCD, anxiety, and depression were related to lower quality of life. The only treatment that was associated with reduced urges was anti-dopaminergic medication
The results confirm that there is a close relationship between urges and tics and that most patients experience relief after tics. The data also clarify that comorbidities that occur most frequently with tic disorders are associated with an increased likelihood to experience urges. The results shed light on the relationship between quality of life and different aspects of tics and urges, as well as the effect of treatments on urges.

O3. Inter-individual differences in urge-tic associations in Tourette syndrome

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Background:
Premonitory urges are a cardinal feature in Tourette syndrome (GTS) and are commonly viewed as a driving force of tics. However, inter-individual differences in experimentally measured urges, tics and urge-tic associations, as well as possible relations to clinical characteristics and abnormal perception-action processing recently demonstrated in these patients have not been investigated in detail.

Methods:
We analyzed the temporal associations between urges and tics, utilizing a real-time urge-monitoring tool, in 21 adult patients with GTS (mean age ± SD: 30.5 ± 10.6 years; 10 female). The analysis included inter-individual differences and the relation of such associations with clinical measures and experimentally tested perception-action coupling. The association between urge intensity and video-recorded tics (rated by two independent raters) was analyzed using three statistical approaches: logistic regression (predicting tic from urge), linear regression (urge intensity at tics), and correlation (between urge intensity and instantaneous ticcing intensity).
Clinical scores (RUSH video protocol, YGTSS, PUTS, GTS QoL, YBOCS, CAARS) were tested for correlation (Pearson) with these three measures. Additionally, we tested the prediction that a stronger urge-tic relation is associated with stronger stimulus-response binding.

Results and Conclusions:
At the group level, our results confirm known positive associations (all three statistical approaches) between subjective urges and tics, with increased tic frequency and tic intensity during periods of elevated urge. Inter-individual differences in the associations between urges and tics were, however, substantial. While most participants (57 – 66% depending on the specific measure) showed positive associations as expected, several participants did not, and two even had negative associations with tic occurrence and intensity being reduced at times of increased urges. Subjective urge levels and tic occurrence correlated with corresponding clinical scores, providing converging evidence. Measures of the strength of urge-tic associations did not correlate with clinical measures nor the strength of perception-action coupling. Taken together, urge-tic associations in GTS are complex and heterogenous, casting doubt on the notion that tics are primarily driven by urges.

O4. Detecting the functional anatomy of the urge-to-blink

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Background:
Premonitory urge (PU) is thought to be a negative reinforcer of tic expression in Tourette Syndrome. Tic expression during fMRI scanning is required for an overt marker of increased urge-to-tic, however this can lead to a loss of large amounts of data due to head movement. Further, the activity related to PU is difficult to distinguish from that of the motor antecedents associated with tic generation.

Methods:
We examined the urge-to-blink in 20 healthy volunteers, an analogous behaviour that can be expressed overtly in the MRI scanner. The blood-oxygen-level dependent (BOLD) signal during the two conditions, “Okay to blink” and “Suppress”, was compared to identify brain regions involved in blink suppression. We used a novel approach to investigate the BOLD signal correlated with the build-up of urge where participants continuously reported their subjective urge-to-blink using a rollerball device.

Results and Conclusions:
We predict that through conventional BOLD analysis we will show that the subjective urge scores are correlated with activity in the right insula and the bilateral mid-cingulate cortex. Furthermore, we predict that blink suppression will be associated with activation of the right ventrolateral frontal cortex. In future, these results will be used to validate a model-free approach where the BOLD response associated with the urge-to-act can be localised without the need for actions to be overtly expressed.

O5. Somatosensory perception-action binding in Tourette syndrome

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Background:
It is a common phenomenon that somatosensory sensations can trigger actions to alleviate experienced tension. Such "urges" are particularly relevant in patients with Gilles de la Tourette (GTS) syndrome since they often precede tics, the cardinal feature of this common neurodevelopmental disorder emphasizing the close connection of premonitory urge sensations and specifc motor actions (i.e. tics) to release this tension. Further underlining the importance of somatosensory processes in the pathophysiology of GTS, there is also hypersensitivity to specific external stimuli in GTS. Furthermore, altered sensorimotor integration processes in GTS as well as evidence for increased binding of stimulus- and response-related features ("hyper-binding") in the visual domain suggest enhanced perception-action binding also in the somatosensory modality. In the current study, the Theory of Event Coding (TEC) was used as an overarching cognitive framework systematically addressing perception–action coupling to examine somatosensory-motor binding.

Methods:
A somatosensory-motor version of a task measuring stimulus-response binding (S-R task) was conducted using electro-tactile stimuli. Stimulation was delivered via eight disposable surface adhesive electrodes attached to the hands. To address stimulus-response binding, behavioral performance in conditions with different degrees of overlap between stimulus and response features was investigated.
To test the "hyper-binding" hypothesis, the data of N = 24 GTS patients (15 males and 9 females, mean age 27.62 years ± 1.82 SEM, range 18–46 years) and N = 20 healthy controls was analyzed (11 males and 9 females, mean age 26.75 years ± 1.63 SEM, range 18–51 years) Furthermore, clinical assessments were conducted.

Results and Conclusions:
Contrary to the main hypothesis, there were no group differences in binding effects between GTS patients and healthy controls in the somatosensory-motor paradigm. Behavioral data did not indicate differences in binding between examined groups. Increased binding of stimulus- and response-related features ("hyper-binding") previously found in the visual domain was not found in the somatosensory modality. Since it has been demonstrated that perceptual thresholds are not altered in GTS, it is suggested that central somatosensory-motor processing might play a role for observed effects. It can be interpreted that, for example, the presence of somatosensory urges and hypersensitivity to external stimuli, leads to a central adaptation or compensatory "downregulation" of somatosensory stimulus saliency. This results in reduced binding with associated motor output, which brings binding to a "normal" level. Therefore, "hyper-binding" in GTS seems to be modality-specific.

O6. Brain mechanisms of cognitive control in youth with Tourette syndrome and attention deficit hyperactivity disorder: an EEG study

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Background:
Tourette syndrome (TS) and attention-deficit/hyperactivity disorder (ADHD) frequently co-occur, especially in children. The co-occurrence of TS and ADHD is associated with increased impairments in adaptive functioning and quality of life. Impaired cognitive control has been suggested as a shared phenotype across both disorders but its neural underpinnings remain unclear. In the current study, we tested the behavioral and electrophysiological correlates of cognitive control in children with TS, ADHD, TS+ADHD, and typically developing controls (TDC). We expected both the ADHD and the TS+ADHD groups to show impaired Go/NoGo task performance, delayed latencies and decreased amplitudes of the N200 and P300 event-related potentials and reduced frontal midline theta power.

Methods:
One hundred and thirty-six children (25 girls), aged 7 to 14 years, participated in the current study. After a clinical assessment, they were allocated to one of the following groups: TS-only (n = 47), TS+ADHD (n = 32), ADHD-only (n = 22), and matched TDC (n = 35). All participants performed a Go/NoGo while EEG was recorded using a dense-array net. Event-related potentials (N200 and P300 latency and amplitude) and frontal midline theta oscillations were assessed time-locked to Go and NoGo stimuli onset and were analyzed using 2 (TS: yes/no) by 2 (ADHD: yes/no) factorial design ANOVAs.

Results:
As expected, children with TS did not differ from TDC in terms of Go/NoGo task performance, frontal midline theta oscillations, and event-related potentials amplitude and latency. Children with ADHD-only had worse behavioral performance during the Go/NoGo task, decreased NoGo frontal midline theta power, and delayed N200 and P300 latencies, compared to typically developing controls. Contrary to our hypotheses, children with TS+ADHD did not differ from children with TS and TDC on behavioral or electrophysiological measures.

Conclusions:
These results pose a question of whether neural underpinnings of ADHD symptoms in children with TS, as least as indexed by event-related potentials and frontal midline theta oscillations, may be different from those in children with ADHD without tics. While both groups share common inattention and hyperactivity symptoms, the neural underpinnings of those symptoms could differ. It is also possible that the Go/NoGo task in our study was not enough cognitively demanding to probe cognitive controls deficits in children with TS+ADHD. However, our findings suggest that children with ADHD-only have a distinct electrophysiological profile during the Go/NoGo task as indexed by reduced frontal midline theta power and delayed N200 and P300 latencies.

O7. Objective quantification of tic expression in Tourette syndrome patients

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Background:
Tourette syndrome (TS) is characterized by the expression of motor and vocal tics and is part of the family of tic disorders. Tics follow a waxing and waning pattern of severity, intensity and frequency and their expression is modulated by behavioral states and environmental factors. The most prevalent measures used for assessing tic expression are subjective qualitative measures based on self-reports and taken periodically during clinical visits, thus lacking objective quantitative assessments of tic expression over prolonged periods of time. Advances in wearable sensors and their application to movement disorders have laid the groundwork for developing measures for motor tics. A major benefit of utilizing smartphones for obtaining objective measurements is their ability to collect visual and kinematic data in a natural environment for prolong periods of time. The goal of the current study is to create an automatic measure for quantifying tic expression modulation TS patients and for characterizing the behavioral modulation factors.

Methods:
Using visual and kinematic sensors of a smartphone, we developed an application to record tics from children and adolescents with chronic motor/vocal tic disorders, TS or other chronic tic disorders. To compare behavioral states, each session included active (playing games, filling questionnaires) and passive (watching videos) tasks on the smartphone, while the patient's facial tics were simultaneously recorded by the frontal camera and kinematic sensors. Trained experts annotated the videos, marking the precise times of tic onset and tic completion, while specifying the type of movement displayed (eye-blink, nose twitch etc.)
To create an automatic measure for facial tic detection, video recordings went through a preprocessing pipeline followed by face detection and extraction of 98-point facial landmarks from each frame for the analysis of local facial movements relating to tics. Videos were segmented to short clips, each labeled "tic" or "non-tic" based on the tic annotations marked by the experts. Advanced machine learning algorithms for pattern recognition were then applied for classifying the segments to match their label, and detecting the tics accordingly.

Results and Conclusions:
We recorded 37 sessions from 11 TS patients (7-18 years old, 1-4 sessions per patient), session duration ranging from 20 to 75 minutes (typically 1-2 seconds per segment). All patients expressed facial motor tics, including eye, nose, head, mouth and lip movements. Our initial task for automatic tic detection included binary classifications, determining whether a video segment contains a tic or not, without differentiating the different types of facial tics. Each binary classification task was applied on video segments taken from a single session. Preliminary experimental results show that our model for the tic detection algorithm achieved about 94.7% accuracy for classifying "tic" and "non-tic" video segments. The model reached recognition precisions of 94.0%

and recalls of 95.6%. Applying the trained model on the whole video, by using a sliding window and then classifying each segment along the video, resulted in detecting about 89.2% of all the tics in the video.

This novel objective measure of tic expression can provide insights to the modulation factors influencing motor tic expression in TS patients. Furthermore, developing an automatic objective tic assessment tool for tic quantification will provide the clinicians a powerful tool for diagnosis and follow-up of their patients, and for evaluating the efficacy of different behavioral and pharmaceutical treatments. Likewise, an objective tool will open a window for future tic disorders research addressing both the underlying mechanism of the disorder and its translation to clinical tools. This in turn may provide tools for reshaping the future structure of clinical trials related to the disorder.

O8. "There is nothing Tourettic about the New York City subways" - representation of tics and Tourette syndrome in literature, cinema, and theatre

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Background:
Tics and Tourette syndrome (TS) have been widely represented in different arts: literature, theatre, and cinema. In some cases, the artistic vision is based on the personal, real-life experience of the authors, or actors / performers, while in the others it derives from the fictional work.

Methods:
We reviewed and analyzed previously released works of art that contained representation of tics and TS.

Results and Conclusions:
We were able to identify variety of pieces of art, mainly from the areas of literature, cinema, and theatre. As for the literature, the first reports date back to the 19th century and could be attributed to Charles Dickens and his novel *Little Dorrit,* in which one of the protagonists, Mr. Pancks, experienced diverse motor and vocal tics as well as obsessive-compulsive symptoms. Similarly, famous 19th century Spanish writer, Benito Perez Galdos, depicted tics in his novel *Angel Guerra.* Another book regarding this topic is *Salka Valka* by Islandic writer and Nobel Prize laureate, Halldor Laxnesss. *Salka Valka* is a story of a young lively girl from a small village in Island who overcomes diverse adversities in spite of being bullied for her hyperactivity and tics. More recent example constitutes *Motherless Brooklyn,* recently adapted as an excellent movie by prominent actor and director, Edward Norton. TS could be treated as one of the most performative disorders and in the recent years there have been many examples of performances/theatre plays based on the experience of patients with tics. *Theatre of disgraceful people* is a fruit of cooperation between theatre director, Hans-Jörg Kapp, a neurologist, Alexander Münchau, a philosopher, Timo Ogrzal and a performer with TS, Daniel Weber, the latter being the key figure for the play as his tics are directing and structuring the play.
Theatre of disgraceful people is based on the *Lettres de cachet,* a collection of 17th century letters of French citizens addressed to French officials with the purpose to denounce their relatives and friends. In the play, the fragments of the *Lettres* are recited by the actors and combined with real-life situations that TS patients have to face on daily basis. Similarly, tics play a crucial role for the construction of another play, *Backstage in Biscuit Land* by a British performer with TS, Jess Thom. In this play, Thom is the main character, and she uses her tics, such as vocalizations, "biscuit" and "hedgehog", to create a moving vision of her disease. Finally, there are many outstanding examples of movies exploring the topic of tics, mainly documentaries and dramas. The most recent ones are *Free-Tic Zone,* directed by Thomas Oswald and previously mentioned *Motherless Brooklyn* by Edward Norton. *Free-Tic Zone* is a documentary in which three patients with TS are travelling across Europe to the North

Cape. They first travel to TS research centers in France in Germany and then across Finland and Lapland.
Contemplation of patients' worries and doubts regarding their life with the disease and current treatment options are the main focus of the film. *Motherless Brooklyn*, on the other hand, is a detective story intercepted by the disease narrative, the narrative of a detective affected by TS. Other films that present problem of TS are *Young and Innocent*, *Alive and Ticking*, *The Tic Code*, *Matchstick Men* or *Vincent Wants to Sea*.

It can therefore be concluded that the artistic representation of TS and tics is not that uncommon. They constitute an important avenue for the patients to represent and inform others about their emotional and psychological realities that they face. Moreover, in the context of disability narratives, these works of art serve can provide a cathartic and psychotherapeutic experience that enables achievement of mind/body integration. At the same time, they open possibilities to spread social awareness about tics and, more widely, initiate discussion about the boundaries of normality. On the other hand, dramatic representations of tics and tic-like behaviors in social media may lead to popularization of misconceptions, and sadly lead vulnerable individuals to mimic tic-like movements and sounds on internet sites.

O9. Sex Differences In Tourette Syndrome

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Background:
Tourette Syndrome (TS) is a chronic neuropsychiatric disorder defined by multiple motor tics and at least one vocal tic for longer than a year, often accompanied by the comorbidities Attention Deficit Hyperactivity Disorder (ADHD) and/or Obsessive-Compulsive Disorder (OCD). For unknown reasons, predominantly boys are diagnosed with the sex ratio being 3-4:1. In this study we want to examine possible differences in the course of the disorder between males and females in a large longitudinal clinical cohort.

Methods:
The data was collected at the Danish National Tourette Clinic in two separate phases; 2005-2007 (T1) and 2011-2013 (T2), with N = 314 included at T1 and N = 227 reexamined at T2, respectively. Tic severity was assessed by Yale Global Tourette Severity Scale; OCD was assessed by Children's Yale-Brown Obsessive-Compulsive Scale and Yale-Brown Obsessive-Compulsive Scale; and ADHD was assessed by ADHD Rating Scale and Adult ADHD Self Report Scale.

Results and Conclusions:
No statistically significant differences in age at onset of tics or age at diagnosis between the sexes were found. Likewise, no statistically significant differences between sexes were obtained regarding the total tic score, the total motor tic score, the tic impairment score or the tic severity score. At T1, there was a statistically significant difference in total vocal tic score between the sexes (mean males: 7.79, mean females: 5.85, P-value=0.032), but not at T2. Relatively more females shifted from having zero points in total vocal tic score at T1 to experiencing vocal tics at T2. No statistically significant correlation between remission of tics and sex was found (P-value = 0.575).
ADHD was more prevalent amongst males than females at T1, but not at T2. We found no statistically significant difference between sexes in OCD score, obsessions or compulsions.
Regarding phenotypes, there were no statistically significant differences between sexes. There was not found any statistically significant difference in severity of tics or comorbidities between the sexes, except a significant higher total vocal tic score in males at T1 and higher prevalence of ADHD amongst males at T1. Furthermore, we found a tendency towards an increased number of females with vocal tics at T2. Further analyses are ongoing and will be presented at the conference. Future studies are needed to examine possible differences in the course of TS between the sexes.

O10. An online survey investigating experiences of pain and use of pain management techniques in tics and Tourette syndrome

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Background:
Tic disorders (TDs) are complex neurological conditions characterised by involuntary vocal and motor movements called tics. Adults with TDs, such as Tourette Syndrome (TS), have reported a reduced quality of life. Pain resulting from tics is often considered an invisible aspect of TDs, and there has been limited investigation into this area. Understanding individual's experiences of this pain and how they manage it is required in order to sufficiently help and support them. The aim of this study was to investigate the experiences of pain and use of pain management techniques in people with TDs.

Methods:
Participants completed a mixed-methods survey, which was open from June to July 2021. Participants were recruited from online advertisements shared through the websites and social media pages of four Tourette patient support associations, and one online Tourette forum. The survey contained six parts regarding questions on participants' tics and tic-related pain; the Brief Resilience Scale (BRS); questions concerning pain management and relief techniques; and the Adult Tic Questionnaire (ATQ). The study was open to anyone with tics who experienced tic-related pain, participants were required to be 16 years and older and proficient in English. Descriptive statistics were used to analyse the quantitative questions and ATQ. Qualitative responses were analysed using thematic analysis.

Results and Conclusions:
The data are currently being analysed (July-August 2021). 181 respondents from 18 countries (57.5% female) completed the survey, with ages ranging from 16-71 years old (M = 29.4 years). The most common type of tic related pain was caused by the physical effort of the tics (97.8%), followed by the repetitiveness of tics (77.9%) and the consequences of tics (72.4%). Three interrelating themes were extracted from the qualitative data: 'the tic-pain cycle'; the impacts of pain; and importance of support. Almost a third (64.6%) reported seeking out help for their pain, of which 60.7% had received it. Participants utilized a variety of different pain relief methods, with distraction techniques being the most commonly reported. The results confirm that pain from tics is a frequent and chronic problem, highlighting the need for research into how pain can affect the quality of life of patients. There is still a requirement for healthcare professionals to be better educated regarding TDs. The aim of this research is to stimulate discussion into the treatment of pain for tic disorders as well as promote pain research and improve patient care.

O11. Tics and sleep: Qualitative insights from parents of children with Tourette syndrome

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Background:
Sleep disturbances in children with Tourette syndrome (TS) are common. There have been increased efforts in recent years to elucidate sleep in this population through systematic reviews and empirical studies with clinical scales and objective measures. Co-occurring disorders seem to play a role in explaining sleep disturbances, but research exploring how tics impact and are impacted by sleep is limited. We could not identify any qualitative research exploring this phenomenon. Given the relative infancy of research on sleep in TS, it is important to gather qualitative data from patients and caregivers to guide future research and allow for a more holistic understanding of sleep in this population.

Methods:
Parents of children with TS (aged between 7 and 17 years) completed an online questionnaire between October 2020 and March 2021. It comprised of validated child sleep and behaviour scales, concluding with a set of open-ended questions aimed at gathering qualitative data. The present study reports the qualitative analyses of parents' textual responses from this larger questionnaire study exploring sleep in children with TS. 112 parents of the 136 total sample answered the question "have you noticed that tics affect your child's sleep?" and 113 responded to "have you noticed that how well your child sleeps at night affects his/her tics the next day?" Responses were collated and a content analysis was conducted for each question to identify common themes and sub-themes.

Results:
78% of parents felt that tics impact their child's sleep. Over half of all responses noted that tics can prevent children from falling asleep at night, often due to being unable to "lay still to settle" (P35) or severe tics that cause pain "to lay on parts of the body" (P38). Many parents reported that tics tend to increase in severity at night and that their child continues to tic during sleep, with some noting that "bad tics wake [the child]" (P5). 74% of parents felt that poor sleep impacted children's tics the next day, with most describing how disrupted or insufficient sleep leads to tics being "more frequent and intense the next day" (P78). Some felt that this was due to having less ability to "suppress tics if [the child] chooses to do so" (P42).

Conclusions:
The present study supports the clinical observation that tics can directly impact and be impacted by sleep in children with TS. While these findings may be of no surprise to TS families and clinicians, this study appears to be the first to provide empirical qualitative data on the bidirectional impact of tics and sleep in a large sample of parents. Findings also highlight the prevalence of sleep disturbances in children with TS and the need to consider the role of tics in causing or exacerbating issues with sleep. Previous sleep studies have used tic severity scales with wide timeframes (e.g., tic severity over the past week), but our findings suggest a more direct impact of tics and sleep. Future

studies should therefore consider tic severity in the hours before and after sleep. Supplementing objective sleep studies with qualitative elements is also recommended.

O12. An innovative person-centred research approach for Tourette's

Diana Beljaars[1] and Jo Bervoets[2]

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Background:
Tourette Syndrome is almost exclusively seen through the lens of disruptive tics. The most relevant question seems to be: how to combat tics? This is the focus of the classical 'lack of inhibition' model of Tourette's that is dominant in current-day Tourette's research. To include a broader set of phenomena that people with Tourette's often suffer from in addition to disruptive tics (e.g. cognitive tics, compulsive-like rituals, physical discomfort, and ability to concentrate) in the analysis of Tourette syndrome, we explore the possibilities for a more person-centred approach. Such an approach centres holistically on the lived experience of a Tourettic person instead of only looking at the disruptions caused by their tics. This shift is ethically motivated in line with the tenets of the neurodiversity movement, but may have important theoretical and clinical implications, as has already been the case in autism research.

Methods:
In exploring this shift in centre, we perform a critical analysis of the consequences of the 'lack of inhibition' model and in what ways it cannot account for the lived experience of Tourette's. This analysis is combined with the insights provided by Beljaars' in-depth multi-method qualitative research with 15 people with Tourette's and interviews in Bervoets' participatory research project with 4 Tourettic individuals (all adults with a formal diagnosis from the Netherlands and Belgium). These insights are then reanalysed according to the recent 4E (Embodied, Embedded, Enactive, Extended) trend in the cognitive sciences to account for the as yet largely neglected situational and relational aspects of the Tourettic lived experience.

Results and Conclusions:
The 'lack of inhibition' model reveals a constant pressure to inhibit actions that strongly compels one to do. This inhibition is dependent on what is overwhelmingly signalled as disruptive by others and is therefore suppressed for their sake. The Tourettic person's distress or felt impairment thus seems more tied to an onlooker's focus on their tics than on the severity, frequency, and kind of tics. Rather, disruptive tics are only the tips of icebergs that consist of spontaneous interactions with the environment beyond onlookers' focus and they work in relation to other phenomena. Our person-centred approach thus produces a more nuanced view of Tourette's that suggests that problems experienced by those diagnosed should not only be regarded as located in individual brains, but that these require comprehensive study of how tics and other phenomena develop situationally. Following the 4E trend in the cognitive sciences we propose that Tourette's needs to be understood from this holistic view of its lived experience without only centring on disruptive tics. This holistic attitude towards Tourette's is worth considering, both clinically and theoretically. Clinically, we believe this aligns with the findings that felt impairment and tic severity come drastically apart and that the overall good prognosis as felt impairment correlates with finding trusted environments where one does not feel they live under constant scrutiny. Theoretically, this approach can shed a light on how tics are related to the social and physical environment, how related phenomena play a part in Tourette syndrome, how the COVID-19 pandemic impacts Tourette's, and how gender becomes important in when what tics are performed.

O13. Self-Injurious Behavior in Patients with Chronic Tic Disorders – new Insights and preliminary Validation of the Self-injurious Behaviour Scale (SIBS)

Natalia Szejko[1,2], Heike Lampe-Goessling[3], Anna Pisarenko[3], Martina Haas[3], Ewgeni Jakubovski [3] and Kirsten R. Müller-Vahl[3]

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Background:

Self-injurious behavior (SIB) is a well-known symptom in patients with chronic tic disorders (CTD) and Tourette syndrome (TS). However, the database on SIB in TS is scarce and systematic studies in larger samples are missing. This is also due to the fact that no standardized instrument is available measuring specifically SIB in TS.

Methods:
To investigate for the first time prospectively the clinical spectrum and severity of SIB in adults with CTD/TS, we initially formulated 6 items to assess severity of SIB covering number, frequency, intensity, resistance, control over SIB and impairment (each rated on a scale from 0 to 5). Using the internet platform SoSci-Survey, we performed an online survey and asked patients with CTD/TS to complete the SIB items and in addition a variety of further assessments for tics and comorbidities. Moreover, we investigated internal consistency when combining all items to a draft scale and carried out an exploratory factor analysis (EFA).

Results and conclusions:
We enrolled 123 adult patients (n=82 males (66.7%), mean age 36.5 (SD 14.18)) with TS (n=102. 82.9%), CTD (n=13, 10.6%) and unspecified tic disorder (n=8, 6.8%). SIB was reported by 103 patients (83.7%) with a mean age at onset of 15.2 years (SD 8.46). On average, patients reported 2.9 (SD 1.26, range 1-5) different types of SIB with the most frequent types being self hitting/head banging (79.6 %), pinching (67.9%), and biting/licking (67.9%) with no difference between males and females. A large number of patients reported suffering from SIB several times a day (n=28, 27.2%) or several times a week (n=25, 24.3%). However, the majority of patients rated SIB intensity as mild (49.5%) or moderate (22.8%). Nearly all patients tried to resist against SIB (94%), but about half of the patients reported having only little (22.8%) or moderate (26.0%) control over SIB. Due to a comparatively low corrected item-total correlation and low loading in the EFA, the item "resistance" was excluded from the draft scale. For the resulting scale – the Self-Injurious Behaviour Scale (SIBS, range, 0-24, higher values indicate greater severity) – an internal consistency of Cronbachs $\alpha = 0.88$ was found. The EFA supports a one-factor model which accounted for 61.6% of the variance across the items.
Exploratory several analyses were conducted to examine correlations between the SIBS and further assessment: self-assessed tic severity (according to Adult Tic Questionnaire, ATQ) correlated positively with SIB severity ($p=0.002$), in particular severity of vocal tics ($p<0.001$) and complex tics ($p=0.001$), while we found no correlation between SIB severity and copropraxia. In contrast to previous reports, we did not find a correlation between SIB and OCD ($p=0.177$). However, we found a positive correlation between SIB severity and depression (according to Beck Depression Inventory, BDI), $p=0.005$)

and ADHD (according to ADHD Self-Rating Scale p=0.008). Importantly, higher SIBS scores were associated with greater impairment of quality of measured with the Gilles de la Tourette Quality of Life Scale (GTS-QoL) ($p<0.001$).

Since we assume a selection bias, we think a true prevalence rate of SIB in TS cannot be calculated based on our data. Anyhow, SIB can be regarded as a common comorbidity in patients with TS. From our results, it is strongly suggested that SIB can be regarded as a specific type of a complex tic rather than a compulsive behavior. This finding has major implications with respect to treatment of SIB. Finally, we were able to demonstrate that SIB significantly impairs patients' quality of life, which even results in increased rates of depression.

Oral presentations of selected abstracts for Plenary session on functional "Tourette-like" behaviours exacerbated by COVID-19 pandemic

O14. Rapid onset of functional tic like behaviours in adults during the COVID-19 pandemic

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Background:
Clinicians have reported an increase in functional tic-like behaviours in children and youth during the COVID-19 pandemic. We describe adults developing rapid onset of functional tic-like behaviours in the last 12 months.

Methods:
Data were analyzed from participants in the Adult Tic Disorders Registry, a single-site,12-month prospective cohort study which began enrolment in January 2021. Clinical features present at the registration visit in adults with rapid onset functional tic-like behaviours were contrasted with adults with Tourette syndrome (TS), Persistent Motor Tic Disorder (PMTD) or Persistent Vocal Tic Disorder (PVTD). Participants completed several self-report questionnaires, including the Obsessive-Compulsive Inventory (OCI), the Adult Self-Report Scale for ADHD (ASRS), the Patient Health Questionnaire for depression (PHQ9), the GAD7 anxiety scale, the Tobacco, Alcohol, Prescription Medications and Other Substance Tool (TAPS), the Premonitory Urge for Tics Scale (PUTS), and the Gilles de la Tourette Quality of Life Scale (GTSQOL). The clinician collected demographic and clinical information from the patient through clinical interview, confirmed diagnoses and performed the Yale Global Tic Severity Scale (YGTSS). Continuous variables were compared between groups using a two-sample t-test; categorical variables were compared using the Fisher's exact test.

Results:
29 participants registered between January and May 2021; 9 had Rapid Onset Functional Tic-Like Behaviours, and 20 had Tourette syndrome or Persistent Motor Tic Disorder. Of the individuals with rapid onset functional tic-like behaviours, 7 presented with the first ever onset of tic-like movements, and 2 had a history of mild simple motor or vocal tics in childhood with sudden and dramatic onset of complex tic-like behaviours in the past 12 months. All participants with rapid onset functional tic-like behaviours reported symptom onset over a period of hours to days, with many able to give a precise date of onset. All endorsed the presence of premonitory urges prior to tics, suggestibility and distractibility, while suppressibility was present in 6 of 9 cases. Participants with Rapid Onset Functional Tic-Like Behaviours were younger (19.9 vs 38.3, $p=0.004$), had older age of onset (15.3 vs 10.6, $p=0.003$), and were more likely female ($p<0.0001$). They had higher motor and vocal tic severity and impairment scores (all $p<0.01$) and were more likely to have complex arm/hand motor tics ($p=0.0003$) complex vocal tics ($p<0.0001$) and coprolalia ($p<0.03$). Participants with rapid onset functional tic-like behaviours had significantly higher scores on the ASRS ($p=0.04$), OCI ($p=0.03$), PHQ9 ($p=0.0006$), and GTSQOL ($p=0.005$).

Conclusions:
The most suggestive clinical features for the diagnosis of functional tic-like behaviours was their phenomenology, gender, onset age and clinical course.

O15. Pandemic tic-like behaviours following social media consumption

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Background:
Over the last few years, new-onset tic-like behaviors have created a lot of interest worldwide. There is a marked increase of children/adolescents and young adults presenting with new and sudden onset of severe functional tic-like movements and vocalizations after consumption of videos on platforms such as TikTok or Youtube showing influencers allegedly having Tourette syndrome, who, in fact, are staging it. These patients are often misdiagnosed with a primary tic disorder, particularly Tourette syndrome, but on clinical grounds, it has been suggested that there are a number of characteristics that set the former apart from the latter.

Methods:
We directly compared demographic and clinical variables between 13 patients with tic-like behaviors following social media consumption [8 males, 5 females, mean age 16.54 years ± 3.13 standard deviation, range 12-24 years] and 13 age- and gender-related patients with Tourette syndrome [8 males, 5 females, mean age 16.85 years ± 3.76 SD, range 10-22 years] using quantitative statistics.

Results
Patients with tic-like behaviors following social media consumption had several characteristics allowing to distinguish them from patients with Tourette syndrome, some of which discriminated perfectly, i.e. abrupt symptom onset, lack of spontaneous symptom fluctuations, symptom deterioration in the presence of others, and some nearly perfectly, i.e. predominantly complex, slow and tonic movements involving trunk/extremities rather than rapid and phasic movements involving head/face. In addition, symptom onset was significantly later [15.31 years ± 2.96 SD in patients with tic-like behaviors vs. 5.15 years ± 2.79 SD in patients with Tourette syndrome ($t(24)=-9.0$; $p<0.001$)].
Premonitory sensations, ability to suppress symptoms, the presence of complex vocalizations including repetition of random words and coprolalia, and the presence of comorbidities did not significantly differ between groups.

Conclusions:
In this sample, tic-like behaviors after social media consumption clearly differ from tics in Tourette syndrome. Furthermore, there are some highly distinguishing features that have yet not consistently been associated with functional tic-like movements, i.e. symptom continuation during neurological examination, goal-direction of extra movements, which can be particularly offensive and aversive, and clear symptom deterioration when patients meet others, indicating that tic-like behaviors following social media consumption represent a novel phenomenon.
Given the occurrence of similar cases in many countries and the increasing number of adolescents and young adults staging symptoms resembling Tourette syndrome on

platforms such as TikTok or Youtube, this phenomenon might be referred to as “pandemic Pseudo-Tourette”.

O16. Tics on TV - Tourette syndrome and the media: lived experiences

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Background:
In recent years, there have been a number of television programmes in the UK which have centred on Tourette syndrome (TS), a neurological condition characterised by motor and vocal tics. TS has a prevalence of around 1% in school-aged children (Scharf et al., 2015) and is associated with high levels of mental health difficulties such as anxiety and depression (Anderson & van de Griendt, 2021). The first programmes featuring TS were documentaries *'John's Not Mad'* made by the BBC in 1989 with a follow-up in 2002, *'The Boy Can't Help It'*. These documentaries shone a light on what life was like for an adult with severe TS and coprolalia. While only 10% the TS population experiences coprolalia (a vocal tic characterised by obscene language or swearing), the majority of television programmes appear to feature individuals with this particular tic.

There seems an appetite by the general public to watch programmes involving people with tic disorders such as TS. This leads to a discussion of how TS is discussed and portrayed by the media, which is important to investigate given the potential effects on both the TS community and public knowledge and awareness of TS. Media representations of TS come through a variety of types of programme ranging from 'reality' entertainment (e.g. dating programmes) to fly-on-the-wall documentaries. To our knowledge, research has not yet considered the impact of media portrayals of TS in a UK context. It is important to investigate this question and explore whether certain types of programme may potentially reinforce myths surrounding TS.

Methods:
To gather qualitative data on the experiences of adults who have been on TV programmes in the UK, 24 people with TS were contacted via email or social media. Participants were invited to answer questions anonymously about their experiences of being involved in media. Of the 24 approached, 21 participants responded positively and were emailed a set of questions. This took place between September and November 2020.

Results and Conclusions:
The participants reported having been involved programmes ranging from reality shows to health-related medical programmes and documentaries. From their responses, common themes emerged which provided more detailed insight into their experiences. Although people were in general driven by a desire to educate the public about TS through their involvement in the TV programme, many expressed concerns about being misrepresented and reported experiencing an invasive element to this involvement. This sometimes brought negative attention either during the TV programme or afterwards, leaving them feeling exposed and vulnerable. Some reported that being involved in TV was different to what they expected and many reported that it was more physically and emotionally tiring that they had anticipated. Participants felt they lacked editorial or format control, with one saying they put themselves 'in the hands of these strangers to cut, edit and manipulate what they think makes/tells the best story'. While some reported very positive experiences overall, the common issues noted by a number of participants highlight the need for caution and guidance.

With collaboration from the participants and drawing on the themes from the interview questions, guidelines were produced based on what advice they would give to other people with TS who may be approached to be on a TV programme. These guidelines can be accessed here https://www.neuro-diverse.org/blog/guidelines-for-engaging-with-the-media

References:

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O17. Mixed methods follow-up of children and young people following a diagnosis of functional tics: a prospective study

Dr Morvwen Duncan[1], Dr Tara Murphy[1], Dr Sara Shavel-Jessop[1,2], Dr Holan Liang[1], Professor Isobel Heyman[1,2], Sophie Allen[1], Dr Nimmi Parikh[1], Dr Eve McAllister[1]

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Background:
Commentary papers are emerging from clinical centres noting an unexpected increase in what appear to be functional tic disorders and other functional neurological symptoms – seemingly related in timing to the Covid-19 pandemic of 2020-21 (Heyman, Liang, Hedderly, 2021; Hull, Parnes, Jankovic, 2021). There are also reports of worsening of tics in individuals with pre-existing tic disorders (Robertson et al., 2020). The only study in children and young people with tics was a survey conducted in Italy with parent respondents. The survey demonstrated that 67% of parents reported worsening of their child's clinical symptoms since COVID-19, with 20.5% reporting an improvement and 6.7% reporting no change. The findings were not influenced by parental health or their economic situation (Conte et al., 2020).

Emerging findings indicate that lockdown has been associated with poor mental health for children and young people (Newlove-Delgado et al., 2021). It is likely that young people with an existing mental health condition and/or neurodevelopmental difficulties may be particularly vulnerable to the negative mental health impact of COVID-19. This might be related to biological, psychological and social factors including infection itself, and illness/bereavement in family members, school closures, loss of routine and activities, and practicing social distancing.

Preliminary studies characterising the case details of young people presenting with functional tics, suggest that many present with co-morbid anxiety and depression, and undiagnosed co-morbid neurodevelopmental disorders (Buts et al., under peer review). Preliminary studies have linked the increase in functional tics to social media use, describing it as a mass sociogenic illness (Olvera et al., 2021). Previous research suggests that psychological therapy that included cognitive and behavioural techniques with metacognitive and attention training was effective in reducing tic severity and anxiety, and improving mood and quality of life in children with 'tic attacks' in Tourette syndrome (Robinson, & Hedderly, 2016). However, there have been no studies to date characterising the course and prognosis of children and young people presenting with functional tics.

Therefore, this proposed mixed-methods study aims to quantitatively follow up on the symptoms and outcomes for children and young people that received a diagnosis of functional tic disorder and to qualitatively explore their experience of diagnosis and treatment.

Methods:
A consecutive series of children, aged 8-18 years old who are diagnosed with functional tics in the National Tourette's clinic at Great Ormond Street Hospital will be followed up 12 months after their initial assessment. All young people diagnosed with functional tics at assessment are invited to a one-off psychoeducation group within 6 months. A power analysis using the Gpower computer programme (Faul & Erdfelder, 1998)

indicated that a total sample size of 24 would be required to detect a medium effect size (d=.25, probability=.5%, power=80%) using repeated measures ANOVA with four measurements. Braun & Clarke's (2013) recommendation of a sample size of 10-20 participants for a mixed-methods and UK professional doctorate will be considered appropriate for the qualitative analysis.

The measures at baseline will include tic severity (YGTSS; Leckman et al., 1989), and psychiatric and wellbeing measures, including the Development and Well-Being Assessment (DAWBA; Goodman et al., 2000), Strengths and Difficulties Questionnaire (SDQ; Goodman, 2001) and Children's Global Assessment Scale (CGAS; Shaffer et al., 1983). Before and after the one-off psychoeducation group goal based outcomes will be collected (GBO; Law & Wolpert, 2014). The measures will be repeated at the 12-month follow up, and include a further questionnaire developed by the study team, which will determine whether the recommendations from assessment were carried out by local services and whether the young person received any further treatment. We plan to involve service users in the development of the interview schedule. The semi-structured interview will be conducted via zoom for one-hour and include questions on how the young person and families experienced diagnosis, how their symptoms may have changed and their experience of support locally.

Results and Conclusions:
Data will be imported and analysed using IBM SPSS Statistics 26. Descriptive statistics of all participants at assessment will be calculated. To determine the distribution of the data we will assess the histograms and Kurtosis statistics, and if necessary non-parametric tests will be used. A repeated measures t-test will evaluate the effectiveness of the psychoeducation group. Correlational analysis will be used to identify any potential co-variates to control for in subsequent analysis. A repeated measures ANOVA will be conducted to determine whether the young people's symptoms changed from assessment to 12-month follow up (DAWBA, SDQ, CGAS, YGTTSS). Hierarchical linear multiple regression will be used to predict what factors at assessment predict the outcomes at follow up.

Following the completion of interviews, thematic analysis will be used to explore the young people's experience of functional tics and treatment. This will follow an iterative method for identifying and analysis patterns within the data. The analysis will follow the six steps of thematic analysis, which includes familiarisation with the data, coding, searching for themes, reviewing themes, defining themes and to develop a contextual narrative. The qualitative analysis will complement the quantitative findings.

The findings of the proposed study will be vital in determing the longer-term outcomes for children and young people diagnosed with functional tics, and help us to begin to understand their treatment journey from assessment. The findings will have important clinical implications for services receiving an increase in referrals of young people with functional tics in 2021.

O18. Functional Presentations in a Tic Disorder Clinic

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Background:
Discussion amongst clinicians and an evolving recent literature suggests that the COVID-19 pandemic has been associated with an increased incidence of new onset functional tic-like movements, affecting adolescent females more than males. Whilst primary tic disorders present in children, adult-onset tics are also reported. An increasing focus on functional symptoms in clinical neurology has led to a reappraisal of abrupt later presentations of tics and phenomena such as tic attacks. The aim of this clinical notes analysis was to investigate the characteristics of 57 patients over 17 years old presenting to a tic disorder clinic felt to have a predominantly functional syndrome.

Methods:
Typed clinical reports of all patients over 17 years from 2014 to May 2021 were analysed using text search, to identify those with functional symptoms at their first consultation for tic disorders. Patients who were only felt to have functional symptoms at later visits were excluded. Search terms examined were "functional", "overlay" and "dissociative". Each record was analysed to record age, gender, comorbidities, the presence of acute florid presentations, tic attacks, dissociative seizure-like episodes and family history of tic disorders. Co-morbidities were either already established from referring clinicians or from clinical interview.

Results and Conclusions:
57 patients were identified. 42% (24) of these patients were felt to have a definite functional component, the remainder had a "likely" functional element. Assessment was clinical, there is no current practical biomarker to distinguish underlying causes of tic-like movements. Functional interpretations may have increased over the period studied. 63% (36) of patients were female. Ages ranged from 17 to 69. 37% (21) of patients had a history of a milder tic disorder in childhood. 39% (22) patients had a family history of tic disorders. 16% (9) had obsessionality of any severity, 11% (6) of these had OCD. 7% (4) had ADHD. 16% (9) had ASD which anecdotally may be an underestimate, especially for patients seen since the pandemic. Depression was present in 40% (23) and anxiety in 33% (19). 70% (40) of patients experienced premonitory urge to tic, and 67% (38) had a degree of suppressibility. Previous commentary suggests the absence of these features supports a functional nature for tic-like symptoms. Coprolalia was present in 37% (21), echolalia 19% (11) and copropraxia 12% (7). In Tourette Syndrome coprolalia is said to affect around 10% so these symptoms may be more common in those with functional symptoms, referral bias must also be considered. 49% (28) of this cohort presented acutely with tic attacks or seizure-like episodes.

The most common demographic of patients presenting to the Tic Disorder Clinic with predominant functional symptoms is female, often with an adult-onset of their symptoms, or a late exacerbation of a mild tic disorder and common family history of tics. This suggests that there is a group of patients more vulnerable to expressing functional tic-like symptoms which may in some cases be related to a genetic diathesis.

O19. Psychological treatment of Functional Tics

Marleen Tibben

Content:

Movements resembling tics are observed in a small proportion of patients with functional movement disorders (FMD). Functional tics resemble organic tics. Clinical features can help to differentiate the two movement disorders. Functional tics usually occur in adulthood with an abrupt onset of immediately severe symptoms. Functional tics are usually not accompanied with premonitory urges and tend to increase with voluntary tic suppression. In addition, functional tics do not respond well to anti-tic medication and evidence based behavioural treatments for tics, ie habit reversal and exposure and response prevention, usually do not work well. This talk will introduce you to the treatment of functional tics using behavioural therapy consisting of hypnosis and katalepsy (Hoogduin, 2017). These techniques have shown their efficacy in FMD. Clinical practice shows they are promising in the treatment of functional tics as well. Techniques will be illustrated with videomaterial, excersises, and case discussion.

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Oral presentations of selected abstracts for Plenary session on behavioural interventions in tics

O20. ONLINE-TICS: internet-delivered behavioral treatment for patients with chronic tic disorders

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Background:
According to the comprehensive systematic review of the American Association of Neurology (AAN), Comprehensive Behavioral Intervention for Tics (CBIT) is the only treatment for tics that reduces tics with "high confidence". Accordingly, in the recently published ESSTS guidelines, CBIT is recommended as first-line therapy for children and adults with tics. However, due to a lack of qualified therapists, the availability of CBIT is extremely limited. The present study is the first study providing data on efficacy and safety of an internet-delivered CBIT intervention (iCBIT Minddistrict®) for adult patients with Tourette syndrome (TS) or chronic tic disorder (CTD) completely independent from a therapist.

Methods:
We conducted a three-arm, multicenter, randomized, controlled, observer-blind trial including 161 patients with TS/CTD that were randomized to iCBIT (*n*=67), placebo (internet-delivered psychoeducation) (*n*=70) or face to face (F2F) CBIT (*n*=24). In the primary analysis, superiority of iCBIT over placebo was analyzed in a linear mixed model with the change to baseline of tic severity (as assessed by Yale Global Tic Severity Scale-Total Tic Score, YGTSS-TTS) as dependent variable. The key secondary analysis was embedded into a hierarchical testing strategy and included non-inferiority testing of iCBIT to F2F-CBIT. Further secondary analyses included the course after end of treatment.

Results:
The sample included 112 (69.6%) male and 49 (30.4%) female patients with a mean (*SD*) age of 35.7 (12.5) years (range: 18-62 years). Statistical significance for superiority of iCBIT over placebo at a significance level of 5% was narrowly missed (1.28 [-2.58; 0.01]; *p*=0.053). However, secondary analyses showed that during follow-up, the difference in tic reduction between iCBIT and placebo increased resulting in a significant difference 6 months after end of treatment (-2.71 [-4.27; -1.16]; *p*<.001). Although the key secondary analysis was tested exploratory, a significant non-inferiority of iCBIT to F2F-CBIT could be shown in the intended-to-treat population (0.98 [-1.01; 2.96]) as the upper limit of the 95% confidence interval was below the non-inferiority margin of 3.00. Results were limited by a higher than expected drop-out rate. However, as missing values are assumed to be missing-at-random (in the mixed

model) or were replaced conservatively, no bias in favour of iCBIT is assumed. Overall, no safety signal of iCBIT were detected.

Conclusions:
Our data indicate that treatment with iCBIT results in a clinically relevant tic reduction in adults with TS/CTD. Although the primary endpoint was narrowly missed since the null hypothesis could not be rejected, several secondary endpoints showed that iCBIT is superior compared to placebo and nearly as effective as F2F-CBIT. Remarkably, treatment effects of iCBIT even increased over time up to 6 months after end of treatment, while effects of F2F-CBIT diminished at the same time.

O21. Applying an established Exposure Response Prevention protocol for Young People with Tourette's syndrome in an intensive, group format: a UK feasibility study.

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Background:
Tourette syndrome (TS) is a childhood-onset neuropsychiatric disorder characterized by motor and vocal tics (sudden, recurrent, and involuntary movements or sounds; Bloch & Leckman, 2009). TS and persistent tic disorders can have a negative impact on children's daily functioning (Storch et al., 2007) and affect well-being and quality of life (Cutler et al., 2009). Behavioural treatments are the first line in the treatment of tic disorders (Andrén et al., 2021). These interventions are typically carried out with patients individually over 12 weeks with a therapist. The lack of behavioural therapists specialising in treatment of tics is often a barrier to children receiving the correct treatment in a timely manner (Cuenca et al., 2015). Tics are 'suggestable' in social settings which may explain existing caution about offering TS group interventions. Preliminary data suggest group therapy could be implemented usefully but these are combination CBITs/ERP approaches (Nissen et al., 2019; Nissen et al., 2021) or clinically derived protocols (Heijerman-Holtgrefe et al., 2021). This study is the first to explore the acceptability, feasibility and impact of an established manualised ERP treatment protocol, developed for individual therapy, but here uniquely delivered intensively, to a group.

Methods:
A consecutive series of children (N=20), aged 8 to 16 years (M= 12, SD= 2.17) were offered ERP in one of two groups, delivered in series. The treatment consisted of 12 sessions of evidence-based exposure and response prevention (ERP) treatment, delivered intensely over 3 days with a booster session 4 weeks post the intensive group treatment. Session content closely mirrored the evidence based individual treatment protocol described by Verdellen et al. (2011). Parallel parent sessions focused on psychoeducation and introducing parents to skills to support their child's treatment. Assessments were performed pre-treatment as well as at the 4 week booster session. The measures explored tic severity (YGTSS; Leckman et al., 1989), quality of life (C&A-GTS-QOL; Su et al., 2017) and goal based outcomes (GBO; Law & Wolpert, 2014). Measures of feasibility included number of dropouts and percent completion of the Yale Global Tic Severity Scale (YGTSS) at both time points. Treatment satisfaction was measured using a 10-item questionnaire developed by the study team. Characteristics and co-morbidities were typical of the UK TS population. Pre-treatment tic severity fell into the 'moderate range' according to the YGTSS.

Results and Conclusions:
There were no patient dropouts or missing data on the primary outcome measure. Responses from the feedback questionnaire suggested high levels of self-reported and parent-reported acceptability. The YGTSS and the Giles de la Tourette Syndrome Quality of Life Scale for Children and Adolescents (Satisfaction Scale) showed significant improvement following treatment with moderate to large effect sizes. Thirty

five percent of children demonstrated a reliable improvement on the YGTSS Global Tic Severity score.

These results suggest that an established ERP protocol can be delivered in an intensive, group setting with a positive clinical outcome. The study's low attrition and high attendance rates also suggest acceptability and feasibility of the group intervention for families.
Replication in a randomized controlled trial is an important next step.

O22. Development of a Self-help Digital Intervention for Young People with Tourette Syndrome

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Background:
Young people with Tourette Syndrome and Tic Disorders experience difficulties with psychological wellbeing and reduced quality of life. Nonetheless, accessing healthcare support for these young people is difficult due to barriers including a lack of healthcare professionals, low healthcare coverage and reduced help-seeking behaviour of young people. Current psychological interventions for people with tics do not show cost-savings or effectiveness to substantiate large-scale implementation. Interventions delivered digitally, utilising a self-help approach may overcome these limitations and have been shown to be effective in young people with mental health difficulties. Furthermore, the development of a wellbeing intervention using person, evidence and theory-based approaches could promote adherence and engagement.

Methods:
This research gives the findings from a doctoral thesis, which aimed to develop a digital self-help intervention to support and promote psychological wellbeing in young people with Tic Disorders. A person-based approach was applied throughout. The research included a systematic review to assess similar interventions that were available for young people with Tic Disorders and young people with reduced psychological wellbeing. Qualitative research methods were used to interview young people with Tic Disorders, professionals who work with young people with Tic Disorders, and focus groups with parents and young people with Tic Disorders to explore what would be needed from such an intervention. Thematic analysis was used to code data inductively and a hybrid thematic analytical approach was used to apply deductive analysis to the data. The findings from across the methods were integrated to develop guiding principles and a logic model to support the future development of the intervention.

Results and Conclusions:
The systematic review identified 985 studies, leaving 11 to be included in the review. Across the qualitative methods, 16 professionals, 51 young people and 35 parents or caregivers were recruited for interviews or focus groups. A digital health intervention that would be suitably applied to young people with tics was not identified in the literature, and it was concluded that such an intervention would be desired by young people and thought useful by professionals. Many features and functions of the intervention were highlighted across participant groups, and the most important features were prioritised. These were combined with theory to develop guiding principles and a logic model. The research outputs include the development of guiding principles and a logic model, informed using the person based approach, behaviour change theory and evidence. These findings will support future developers in creating an engaging and effective intervention for YP with tics, to promote and support their wellbeing.

Poster presentations of selected abstracts

P1. A question of information mismatch in the SPC and PIL on the effect of ADHD stimulant medications on tourette's syndrome

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Background:
Estimates suggest that between 35% to 90% of TS patients also have ADHD. However, there remains a pervasive belief that the use of stimulants to treat ADHD symptoms in children with comorbid tic disorders is contraindicated because of concerns about possible tic exacerbation. Recent studies has disproved this, which is reflected in United Kingdom(UK) and European ADHD and TS guidelines. Pharmaceutical companies are legally required to provide a Summary of Product Characteristic (SPC) and Patient Information Leaflet (PIL) for each medicine as it is an integral part of the marketing authorisation approval. The SPC contains vital information for the usage and prescription of a drug for use by healthcare professionals. The PIL included in the medication packaging is a patient-friendly version of the SPC.

Methods:
The available stimulant medications licenced for use in paediatric patients with ADHD in the UK were identified through the Medicines & Healthcare products regulatory Agency (MHRA) website. The SPC and PIL were then accessed from the Electronic Medicines Compendium (EMC) website. Those not on the site were obtained directly from the marketing authorisation holder. Any direct mention of tics or Tourette's in the contraindication, warning and caution, or side effect section were documented. The information was then tabulated and compared.

Results and Conclusions:
Of the three stimulant drug types, 17 variations are currently available for use in the UK. There were inconsistencies found between the SPC and PIC in reference to the impact of these drugs on tics and TS in all 17 licensed medication. Most discrepancy was found in regard to TS as a side effect (16/17) and also tics (15/17). TS is also listed as a contraindication in the SPC and PIL for all available variety of Dexamphetamine class drugs. This is inconsistent with current clinical evidence and guidelines.

The disparities in information regarding the impact of stimulant medications on tics and TS can have wide ranging effects. Outcomes could include poor patient adherence, or prevention of initiation of potentially beneficial treatment. It would benefit to standardize the information between these two documents to minimize inconsistencies in understanding between doctor and patient.

P2. Abnormal EEG in Gilles de la Tourette Syndrome

Cecylia Rajczewska-Oleszkiewicz[1] , Justyna Kaczyńska[1] and Piotr Janik[1]

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Background:
Patient with Gilles de la Tourette Syndrome (GTS) have an 18-fold increased risk of epilepsy. On the other hand, first presentation of tic disorder may mimic seizures, especially focal epilepsy. Epileptiform discharge found on EEG in patients with tic disorders may lead to the unnecessary introduction of antiepileptic medications.
The aim of this work was to show the incidence and characteristics of EEG abnormalities in patients with GTS who do not have epilepsy as a comorbidity.

Methods:
We analyzed retrospectively the database of 386 patients (292 males, mean age was 16, range 5-66, SD 9,5 years) with GTS who were treated in outpatient clinic in years 2017-2021. Four patients who had been diagnosed with epilepsy were excluded from the analysis. EEG was performed in different outpatient clinics and analyzed by different clinicians who were licensed in EEG. Four groups of EEG results were distinguished: i) normal; ii) generalized epileptiform discharge (sharp waves, polyspikes, sharp-and-slow wave complex); iii) focal epileptiform discharge; iv) abnormal result without epileptiform discharge (slow waves e.g. theta and delta waves). The statistical analysis was made in MS Excel.

Results and Conclusions:
EEG results were available at evaluation in 33% of patients (122 of 386, 86 males). Age groups were as follows: 74 children (up to 11 years old), 22 adolescents (aged 12 to 17) and 26 adults. Mean age was 13, range 5-43, SD 7,2 years. The abnormal findings were recorded in 43% of individuals (n=53). In 16% (n=20) we observed generalized epileptiform discharge, in 11% (n=13) focal epileptiform discharge, and in 16% (n=20) abnormal EEG without epileptiform discharge. Nearly half of the GTS patients with no evidence of epilepsy had abnormal EEG and one third showed typical EEG changes for epileptic seizures. Clinicians should be aware of these abnormalities in differentiating tic disorders from epilepsy.

P3. CANNA-TICS: Efficacy and Safety of Nabiximols in the Treatment of Adults with Chronic Tic Disorders

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Background:
New treatment strategies are urgently needed for patients with Tourette Syndrome (TS) and chronic tic disorders (CTD), since current first-line therapies have several limitations. Based on case studies and two small randomized controlled trials (RCT), it has been suggested that cannabis-based medicines might be a promising new treatment option resulting not only in a reduction of tics, but also an improvement in a variety of comorbidities such as attention deficit/hyperactivity disorder (ADHD). This study aimed to examine for the first time efficacy and safety of the cannabis extract nabiximols (a complex botanical mixture containing THC, CBD (at a 2.7:2.5 ratio) and other cannabinoid and non-cannabinoid components that was provided by GW Pharmaceuticals Ltd.) in an investigator-initiated, multicenter, placebo-controlled, parallel-group, phase IIIb RCT funded by the German Research Foundation (DFG).

Methods:
A total of 98 adult patients with TS/CTD were randomized across 6 study sites with a 2:1 ratio into a nabiximols and a placebo arm. The primary efficacy endpoint was defined as tic reduction of at least 25% according to the Total Tic Score of the Yale Global Tic Severity Scale (YGTSS-TTS, range: 0-50) after a 4-week up-titration period and 9 weeks of stable treatment. As a key secondary endpoint, in 2 study sites fitness to drive was investigated with respect to a non-inferiority margin of -32%. The primary as well as the key secondary analyses were performed with a center-stratified Mantel-Haenszel estimate for the risk difference (nabiximols – placebo). To examine effects on tics (as assessed by YGTSS-TTS) in specific subgroups, mixed linear models were used. (Severe) adverse events were analyzed.

Results:
A total of 97 patients (75.3% males, mean age=36.6 years (*SD*=13.3)) received treatment and were analyzed. In the primary analysis, 14/64 (21.9%) patients in the nabiximols, but only 3/33 (9.1%) in the placebo group met the responder criterion. However, in the intention-to-treat population, we failed to demonstrate superiority of nabiximols over placebo with respect to tic reduction according to YGTSS-TTS (-0.13 [-0.28; 0.01], *p*=0.07). Further subgroup analyses, however, showed differences depending on patients' sex and comorbidities with larger tic reduction in males (-1.9 [-3.7; -0.1], p=0.04) compared to females (1.9 [-1.3; 5.1], p=0.24) and patients with

comorbid ADHD (-6.1 [-12.0;-0.2], *p*=0.04) compared to those without (-0.33 [-2.0; 1.3], *p*=0.69).
25/35 (71.4%) patients in the nabiximols and 9/16 (56.3%) in the placebo group met the criterion for fitness to drive in the per-protocol population. Thus, non-inferiority of the nabiximols group (vs. the placebo group) could be demonstrated (risk difference 0.14 [-0.15; 0.42]). Safety analyses did not show any substantial differences between nabiximols and placebo. However, after treatment with nabiximols, a higher number of distinct adverse events (e.g. dry mouth) was reported.

Conclusions:
Although a larger number of patients responded to treatment with nabiximols compared to placebo, we failed to demonstrate superiority of nabiximols over placebo. Subgroup analyses showed that male patients and patients with comorbid ADHD responded better to treatment with nabiximols compared to females and patients without ADHD. Fitness to drive was not impaired after use of nabiximols and even improved. Based on our data, nabiximols can be regarded as a safe treatment in patients with TS/CTD.

P4. Candidate Genes and Pathways Associated with Gilles de la Tourette syndrome — Where are we?

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Background:
Gilles de la Tourette syndrome (GTS) is a childhood-onset neurodevelopmental and -psychiatric tic-disorder of complex etiology which is often comorbid with obsessive-compulsive disorder (OCD) and/or attention deficit hyperactivity disorder (ADHD). Twin and family studies of GTS individuals have shown a high level of heritability suggesting that genetic risk factors play an important role in disease etiology. However, identification of major GTS susceptibility genes has been challenging, presumably due to the complex interplay between several genetic factors and environmental influences, low penetrance of each individual factor, genetic diversity in populations and presence of comorbid disorders.

Methods:
To understand the genetic components of GTS etiopathology, we carried out an extensive review of 150 publications compiling the candidate susceptibility genes identified through various genetic approaches.

Results and Conclusions:
We reviewed recent and notable studies aiming to identify candidate GTS susceptibility genes, as well as studies of historical significance. Furthermore, we described the associations made between GTS etiology and the dopaminergic and serotonergic neurotransmission pathways. Strong candidate genes, such as *FLT3*, *CELSR3*, *WWC1*, and *ASH1L* have hitherto been identified through exome sequencing and large genome wide association studies (GWAS). However, none of these genes are likely to be major susceptibility genes, suggesting that several rare genetic risk factors contribute to disease etiology in addition, application of different diagnostic criteria, genetic diversity in populations, and presence of comorbid disorders may add to the complexity of GTS etiology.

P5. Characteristics of tics in follow-up study of community-based high risk cohort of 2511 children

Natalia Szejko[1,2], Pedro Macul Ferreira de Barros[3], Mariusz Pańczyk[4], Pedro Gomes de Alvarenga[3], Marcelo Queiroz Hoextra[3], Kiara Timpano[5], James Leckman[6], Euripides Constantino Miguel[3], Pedro Mario Pan[7]

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Background:
Although several studies have aimed to investigate risk factors for occurrence of tics as well as determinants of tic remission or exacerbation, previous findings regarding this research questions were conflicting. Moreover, all of these studies were done in cohort of patients examined in centers specialized in tics and, therefore, in patients with more severe phenotype. To the best of our knowledge this is the first study analyzing the data from a community-based cohort.

Methods:
Our analysis was based on the High-Risk Cohort Study for the Development of Childhood Psychiatric Disorders (HRC). It is an ongoing multicentric follow up study of 2511 children and adolescents who were born between the years of 1998 and 2004, and who live in the cities of Porto Alegre and São Paulo (Brazil). Up to this date, assessments have already been made in three different phases: screening (2010), baseline (wave 0; 2010/2011), 3-year-follow up (wave 1; 2013/2014) and the 6-year (wave 2) follow-up (2017/2018). An extensive demographic, clinical evaluation and battery of psychological test was conducted in all participants. To define the presence of tics and phenomenology we have used data from the Development and Well-Being Assessment designed to generate ICD-10 and DSM-IV psychiatric diagnoses on 5-16-year-olds. Variety of perinatal, prenatal and psychological factors were taken into consideration in comparative and longitudinal analysis. We disponed only with the baseline data and the data from the first follow up and therefore only these were included in the analysis.

Results and Conclusions:
Our baseline cohort included 2511 participants (1375 males, 54.8%). Lifetime history of tics was reported by 289 participants (11.5%). The mean age of tic onset was 6.83 (3.01 SD). When comparing baseline and follow up data, the incidence of tics decreased from 23.2% to 10.4% ($p=0.08$), this trend was significant for motor tics ($p<0.001$). When analyzing variety of prenatal and perinatal factors and their influence on tic persistence lack of parent's support during their offspring's childhood ($p=0.012$) influenced tic perseverance. Other factors influencing tic persistence when comparing baseline and follow up assessments were the history of bullying ($p=0.035$), smoking at very young age ($p=0.034$), history of behavioral treatment ($p=0.038$), history of school suspension ($p=0.024$) and referral to custody council ($p=0.040$) and higher score in the Dimensional Yale-Brown Obsessive-Compulsive Scale ($p=0.025$). To summarize, as expected, the incidence of tics decreased with age. Importantly, several sociopsychological risk factors, such as lack of parent's support, history of bullying or behavioral problems, were found to have impact on tic persistence. Detailed history taking should be considered not only in children with tics consulted at the specialized Tic Outpatient

Clinics, but also by pediatricians in order to identify these individuals that are at greater risk of developing more severe phenotypes. A number of interventions targeting to reduce risk factors found in this study would help to diminish tic persistence over time.

P6. Contextualising Compulsive Acts: The value of studying lived experiences in everyday spaces.

Diana Beljaars

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Background:
In the neuropsychiatric and clinical psychological study of compulsivity in the diagnostic context of Tourette syndrome, compulsive acts have been conceptualised as 'compulsions' (e.g. Robertson and Cavanna 2007; Shapiro and Shapiro 1992; Shapiro et al. 1988). 'obsessive/compulsive symptoms' (e.g. Cavanna et al. 2009, Eapen et al. 1994), 'repetitive behaviour' (e.g. Leckman et al. 1994, Miguel et al. 2000, Neal and Cavanna 2013), 'repetitive phenomena' (e.g. Cath et al. 2001), 'Complex motor tics' (e.g. Verdellen et al. 2008) and 'compulsive-like tics' (e.g. Robertson et al. 2008). Whilst phenotype studies provide a good idea as to what urge-driven compulsions entail; for instance touching, ordering, aligning, balancing, and counting (Worbe et al. 2014), not much is known about the circumstances under which such tics have to be performed, nor what their effects are and what coping mechanisms may work to diminish negative consequences.

Methods:
A qualitative study based on in-depth interviews, observations, and mobile eye-tracking sessions with 15 adults (8 men, 7 women) with Tourette syndrome can change this. The interviews, conducted in the homes and other everyday spaces of the participants, allowed for a detailed and context-specific analysis of lived experience of performing tics. The observations revealed the relations between the body and objects with which compulsions took place (e.g. pressing one's thumb into a ridge of a mug when carrying it to the kitchen) and what kind of activities would increase their frequency. The mobile eye-tracking sessions, using a Tobii Glasses 2 eyetracker, helped to pinpoint how perceptions of the bodily surroundings may help identify the way in which such compulsions take place.

Results and Conclusions:
The results of this study about the occurrence of compulsions in the everyday lives of Tourettic people demonstrate how the social and physical context are related to what compulsions are performed. The organization of certain spaces, for instance items on the windowsill, colour combinations of furniture, or carpeted stairs, evoke certain kind of compulsions and with relative higher frequency. It also demonstrates how compulsions are tied to daily activities; cooking, cleaning, or doing groceries tend to evoke many particular compulsions. Also, the study shows how compulsive acts can be avoided to a certain extent by adapting one's bodily environment. In addition to producing valuable new insights into this fringe phenomenon of Tourette syndrome, the paper concludes that these results reveal helpful coping mechanisms that people with Tourette's already employ, and how renewed attention needs to be paid to the home environment as part of formal clinical treatment. Ultimately, it suggests how paying attention to the contexts of compulsions produces more knowledge about why this compulsive act happens here under these circumstances.

P7. Contribution of rare and non-coding genetic variants to Gilles de la Tourette syndrome

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Background:
Gilles de la Tourette syndrome (GTS) is a neurodevelopmental disorder from the spectrum of tic disorders (TDs). GTS and other TDs have a substantial genetic component with the heritability estimated at between 60 and 80%.

Methods:
Here we propose an oligogenic risk model of GTS and other TDs using whole-genome sequencing (WGS) data from a group of Polish GTS patients and their families (n=185). The model is based on the overrepresentation of putatively pathogenic coding and non-coding genetic variants in genes selected from a set of 86 genes previously suggested to be associated with GTS. Based on the variant overrepresentation (SKAT test results) between unrelated GTS patients and controls based on gnomAD database allele frequencies five genes (HDC, CHADL, MAOA, NAA11, and PCDH10) were selected for the risk model. Putatively pathogenic variants (n = 98) with the median allele frequency of ~0.04 in and near these genes were used to build an additive classifier which was then validated on the GTS patients and their families.

Results and Conclusions:
This risk model successfully assigned individuals from 22 families to either healthy or GTS groups (AUC-ROC = 0.6, $p < 0.00001$). These results were additionally validated using the GTS GWAS data from the Psychiatric Genomic Consortium. To investigate the GTS genetics further we identified 32 genes from the list of 86 genes as candidate genes in 14 multiplex families, including NEGR1 and NRXN, with variants overrepresented in multiple families. WGS data allowed construction of an interpretable oligogenic risk model of GTS based on possibly pathogenic variants likely contributing to the risk of GTS and TDs. The model includes putatively deleterious rare and non-coding variants in and near GTS candidate genes that may cooperatively contribute to GTS etiology and provides a novel approach to the analysis of clinical WGS data.

P8. EWAS of monozygotic twins implicate a role of mTOR pathway in pathogenesis of tic spectrum disorder

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Background:
Tic spectrum disorder (TSD) is an umbrella term which includes the childhood-onset Gilles de la Tourette syndrome (GTS) and chronic tic disorder (CTD). They are considered highly heritable, yet the genetic components remain largely unknown, and epigenetic changes brought on by environmental factors are hypothesized to contribute to the phenotype.

Methods:
We performed an exploratory analysis of the genome-wide DNA methylation patterns in whole blood samples of 16 monozygotic twin pairs, of which eight were discordant and six concordant for TSD, while two pairs were asymptomatic.

Results and Conclusions:
Although no sites reached genome-wide significance, we identified several sites and regions with a suggestive significance, which were located within or in the vicinity of genes with a biological function associated with neuropsychiatric disorders. The top genes identified in the site-specific analysis (*TSC1*), the region-based analysis (*CRYZ/TYW3*) and the enriched pathways and components (phosphoinosides and PTEN pathways, and insulin receptor substrate binding) are all related to, or have been associated with, the PI3K/AKT/mTOR pathway and mTOR signalling. Genes in this pathway have on several occasions been associated with GTS, and mTOR signalling has been implicated in a broad range of neuropsychiatric disorders including autism. It is thus possible that disturbances in the mTOR signalling could play a role in the complex pathogenesis of TSD.

P9. Elevated Expression of *SLC6A4* Encoding the Serotonin Transporter (SERT) in Gilles de la Tourette Syndrome

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Background:
Gilles de la Tourette syndrome (GTS) is a complex neurodevelopmental disorder characterized by motor and vocal tics. Most of the GTS individuals have comorbid diagnoses, of which obsessive-compulsive disorder (OCD) and attention deficit-hyperactivity disorder (ADHD) are the most common. Several neurotransmitter systems have been implicated in disease pathogenesis, and amongst these, the dopaminergic and the serotonergic pathways are the most widely studied. In this study, we aimed to investigate whether the serotonin transporter gene (*SLC6A4*) was differentially expressed among GTS individuals, and whether DNA variants (5-HTTLPR, rs25531, and rs25532) or promoter methylation was associated with GTS phenotype, or *SLC6A4* expression.

Methods:
DNA from peripheral blood samples was obtained from 72 GTS individuals and 87 controls, and RNA from 56 GTS individuals and 36 controls. All individuals were genotyped by PCR followed by sanger sequencing, and *SLC6A4* expression was quantified using RT-qPCR. Promoter methylation of *SLC6A4* was quantified using pyrosequencing.

Results:
We observed that *SLC6A4* expression is upregulated in GTS individuals compared to controls. Although no specific genotype, allele or haplotype was overrepresented in GTS individuals compared to controls, we observed that the LAC/LAC genotype of the 5-HTTLPR/rs25531/rs25532 three-locus haplotype was associated with higher *SLC6A4* mRNA expression levels in GTS individuals, but not in the control group. We observed no association between *SLC6A4* promoter methylation and phenotype, genotype, or expression levels.

Conclusions:
Our results show that *SLC6A4* expression is increased in GTS individuals, and that this difference is more pronounced in GTS individuals with the LAC/LAC genotype.

P10. Fine Motor Skills in Children with Tourette's Syndrome and Their Unaffected Siblings

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Background:
The exact etiology of Tourette's Syndrome (TS) remains unclear, making the search for impaired neuropsychological functions, possibly connected to the underlying cause of TS, as important as it is challenging. One neuropsychological domain of interest is the development of fine motor skills.

Methods:
This study compares fine motor skill performance on the Purdue Pegboard Task (PPT) in 19 children with TS with 24 unaffected first-degree siblings and 23 controls.
The presence of comorbid Attention Deficit Hyperactivity Disorder (ADHD) was assessed by ADHD-Rating Scale (ADHD-RS).

Results and Conclusions:
Children with TS, their siblings and controls did not differ significantly in fine motor skills as measured with the PPT. Performance on the PPT was not correlated with tic severity; however, an inverse correlation with severity of attention-deficit/hyperactivity disorder (ADHD) symptoms was found. Children with TS were found to have significantly higher parent reported ADHD-RS scores compared to controls, yet only 2 out of the 18 participants had been diagnosed with ADHD.

This study suggests that fine motor skill impairment in children with TS may be more strongly correlated with comorbid ADHD and related symptoms, even below the diagnostic cut-off, than to TS and tics themselves.

P11. Functional tic-like behaviors in patients with Gilles de la Tourette syndrome

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Background:
It is generally believed that functional tics are a rare presentation of functional movement disorders (FMD). Hence, possible co-occurrence of both tics – due to Gilles de la Tourette syndrome (GTS) - and functional tic-like behaviors – due to FMD - in one and the same patient is a heavily understudied clinical topic. This is the more surprising, since it is well known that patients may suffer from both a neurological disease and a functional neurological disorder (FND), for example non-epileptic seizures in patients with epilepsy. In GTS, up to now, only very few patients have been described suffering from "primary" tics and comorbid functional tic-like behaviors (FTB). With this study we want to raise awareness of comorbid FTB in patients with GTS, to present clinical characteristics of a large sample of patients suffering from both tics and FTB, and to give some advice, how to differentiate one from the other.

Methods:
Between 2002 and 2021, in our specialized Tourette outpatient clinic 71 patients were diagnosed with both GTS and comorbid FTB. We analyzed data of these patients retrospectively and compared the results with data obtained from a large GTS sample (n=1032) from the same center. Of note, in this sample we included no cases with recently described rapid onset functional tic-like behaviors related to COVID-19 or use of social media.

Results:
27/71 patients (38%) with GTS+FTB (mean age=23.9, SD 13.1, range 11-55 years) were female, which represents a slightly higher proportion of female compared to our GTS sample (23%, p=0.003). While in the GTS+FTB group, tic onset was in early childhood (mean age: 6.3 years, SD 2.3, range, 3-12 years) and thus did not differ from our large GTS sample (mean age: 6.97 years, SD 3.17, range, 0–21 years, p=0.13), comorbid FTB started on average 14 years later (mean age: 20.8 years, SD 11.8) with a remarkably wide age range between 9 and 47 years. Most typically onset of FTB was abrupt (n=38, 54%) enabling all patients (n=38) to precisely indicate the exact date of onset of FTB. Based on patients' reports and clinical judgement, more than half of patients reported a concrete triggering factor (n=38, 54%). Different from tics, in most cases, FTB presented with complex motor tic-like behaviors not following the typical rostro-caudal distribution of tics and/or complex vocalizations. Accordingly, coprophenomena were much more common in GTS+FTB compared to GTS (44% vs 28%). Different from tics, FTB did not show the typical waxing and waning course. Furthermore, self-injurious behaviors such as self-hitting were more common in GTS+FTB than GTS (55% vs. 30%). While most patients reported stress being the strongest influencing factor for their tics, FBT was mainly influenced by situations that usually have no major impact on tic severity such as long intervals of sitting or unhealthy food. Remarkably, presence and severity of FTB strongly depended on contact with particular people. Regarding treatment response, 47% of patients with

GTS+FTB were regarded as “treatment-resistant” or reported unusual or even unknown side effects after use of typical anti-tic medications.

Conclusions:
The additional diagnosis of FTB in patients with GTS should be taken into consideration, when mainly complex motor (including self-hitting) and vocal tic-like behaviors occur, which so far were not present in the course of the disease, with abrupt onset several years after tic onset characterized by completely different influential factors and response to treatment compared to preexisting tics. Based on our sample, it can be assumed that FTB is common in patients with GTS. The diagnosis of FTB should not be missed to avoid inappropriate treatments.

P12. Mycoplasma pneumoniae IgG is positivity is associated with tic severity in chronic tic disorders

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Background:
Infectious pathogens may represent an environmental risk factor for chronic tic disorders (CTD). This cross-sectional study aimed to determine whether Mycoplasma pneumoniae IgG positivity is associated with the presence or severity of tics.

Methods:
Baseline serum samples from the European Multicentre Tics in Children Studies (EMTICS) cohorts were used. We compared Mycoplasma pneumoniae IgG positivity across three groups: children and adolescents (3-16 years) with CTD (CTD group; n=302); siblings (3-10 years) of people with CTD who developed tics within a seven-year follow-up period (tic onset group; n=51); siblings (4-10 years) who did not develop tics within the study period and were ≥10-years-old at their last assessment (unaffected group; n=88). The relationship between Mycoplasma pneumoniae IgG positivity and the presence and severity of tics was analysed using multilevel models controlling for site, family relatedness, sex, age, presence of comorbid obsessive-compulsive and/or attention-deficit/hyperactivity disorder and use of psychotropic medication.

Results and Conclusions:
Mycoplasma pneumoniae IgG positivity was not associated with the presence of CTD, or the first onset of tics as compared to siblings who remained unaffected. Mycoplasma pneumoniae IgG positivity was associated with a moderately higher tic severity score within the CTD group (β= 2.64, s.e.=1.15, p =0.03). It may be that Mycoplasma pneumoniae infection influences tic severity in CTD or, that having more severe tics, increases the risk of infection. However, it is also possible that the two are not causally linked and that both infection and greater tic severity are epiphenomena of shared underlying mechanisms, with neither influencing the other directly.

P13. Questioning the definition of Tourette syndrome – evidence from machine learning

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Background:
The clinical diagnosis of Tourette syndrome is not always clear and straightforward because motor and vocal tics are often difficult to discern from single spontaneous movements or vocalizations in healthy people. We applied machine learning to independent video ratings of motor and vocal tics using the well-established Modified Rush Videotape Rating Scale to detect, which aspects of Tourette syndrome phenomenology are most useful in diagnosing an individual with Tourette syndrome.

Methods:
A standardized video of patients with Tourette syndrome as well as healthy controls was taken using the Modified Rush Videotape Rating Scale. According to the protocol, five categories (number of body areas, frequency of motor tics, frequency of vocal tics, severity of motor tics, severity of vocal tics) were scored yielding a total score ranging from 0-20. Furthermore, tic count per minute was computed. A support vector machine based analysis of video ratings was conducted to examine the impact of each category of the Modified Rush Videotape Rating Scale, the motor tic count per minute, as well as age and gender, for the classification of individuals into the groups “Tourette syndrome” and “no Tourette syndrome”. N=101 patients with Tourette syndrome (71 males, 30 females, mean age 17.36 years ± 10.46 standard deviation (SD)) and n=109 healthy controls (57 males, 52 females, mean age 17.62 years ± 8.78 SD) were included.

Results:
The results showed that only a single feature, the severity of motor tics, is sufficient to identify an individual as having Tourette syndrome with an accuracy of 91,4%. Adding more features to the analysis did not significantly improve predictability.

Conclusions:
Tourette syndrome is a multi-faceted disorder, but the results of the present study showed that only a single feature of the Modified Rush Videotape Rating Scale, the severity of motor tics, is sufficient to identify an individual as having Tourette syndrome with an accuracy of more than 90%. This finding is of great relevance for the conceptualization of Tourette syndrome because it questions the validity of current diagnostic criteria for Tourette syndrome requiring the presence of both motor and vocal tics. In addition, the negligible importance of vocalizations has implications for medical practice, because current recommendations for Tourette syndrome probably also apply to the large group with chronic motor tic disorders.

P14. Reduction of tics after CBIT is not associated with change in EEG alpha coherence during a Go/No-Go task in children with Tourette syndrome

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Background:
Comprehensive Behavioral Intervention for Tics (CBIT) is a first-line treatment for Tourette syndrome (TS). However, the brain mechanisms involved in successful reduction in tic symptoms following CBIT are poorly understood. Enhanced EEG coherence in the alpha frequency band (8-13 Hz) over frontomesial electrodes during a response inhibition task has been suggested as a mechanism by which individuals with TS may gain control over their tics (Serrien et al., 2005). In this study, we tested whether alpha coherence during a Go/NoGo task represented a possible mechanism of tic reduction after CBIT. We hypothesized that alpha coherence would increase from baseline to endpoint in children undergoing CBIT relative to a Treatment-as-Usual (TAU) control condition. We also hypothesized that children with larger baseline alpha coherence would be those showing larger decreases in tic severity after CBIT.

Methods:
This was a randomized-controlled trial of CBIT vs TAU that included 32 children with TS (mean age ± SD: 11.3 ± 1.6, range: 8 – 13; 84.4% boys). Children were randomly assigned to the CBIT condition, consisting of 8 sessions of behavioral therapy over a 10-week period (n = 16), or to a TAU condition (n = 16). The primary outcomes measures included the Yale Global Tic Severity Scale (YGTSS) and the Clinical Global Impression – Improvement Scale (CGI-I), which were conducted by an independent evaluator who was blinded to the treatment allocation. High-density EEG was recorded during a Go/NoGo task at both baseline and endpoint in all 32 subjects. In the Go/NoGo task, a visual cue was first presented and indicated the location of the target stimulus that would be presented 3 seconds later. The target indicated whether a response must be given (Go) or inhibited (NoGo). EEG coherence was assessed in the alpha-band (8-13 Hz) between 4 channel pairs (F3-C3, FCz-C3, F4-C4 & FCz-C4). Event related EEG coherence to the NoGo trials was computed as a percentage score ((post-target – pre-cue) / pre-cue) indicating coherence increase from pre-cue to post-target.

Results:
All randomized participants completed the endpoint assessment. Tic severity decreased from 23.8 ± 6.0 at baseline to 16.9 ± 4.9 at endpoint in the CBIT group and it increased from 24.4 ± 5.0 to 24.9 ± 5.0 in the TAU group (Time X Treatment interaction: $F(1,30) = 41.08$, $p < .001$, d: 1.34). Ten children (62.5%) in the CBIT group and none in the TAU group were considered as responders according to the CGI-I (Fisher's exact test: $p < .001$). CBIT had no impact on alpha coherence. Mean ± SD values for NoGo alpha coherence changed from 0.03 ± 0.20 at baseline to 0.00 ± 0.12 at endpoint in CBIT condition, and from 0.09 ± 0.20 to 0.14 ± 0.24 in the TAU group (Time X treatment interaction: $F(1,30) = 0.59$, $p = .45$, $d = .37$). Also, baseline levels of EEG alpha coherence during NoGo trials did not predict the change in YGTSS scores after CBIT relative to TAU (Treatment by NoGo coherence interaction: $F(1,30) = 2.37$, $p = .14$).

Conclusions:
Consistent with previous studies (Piacentini et al, 2010), CBIT resulted in significant reduction of tics in children with TS. However, contrary to our hypothesis, there was no effect of CBIT on EEG alpha coherence related to response inhibition.

P15. Substance Use in Tourette's Syndrome

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Background:
The neurobiological underpinning of Tourette's Syndrome (TS) is still under investigation, but current research has implicated dysfunctions in the brain's dopaminergic, endogenous opioid and endocannabinoid systems—suggesting a correlation with substance use. A few small-scale studies have shown an increased risk of substance abuse in TS, possibly mediated by its common comorbidities, Obsessive Compulsive Disorder (OCD) and Attention Deficit Hyperactivity Disorder (ADHD). First, this study examined the correlation between TS, its comorbidities and substance abuse in a large longitudinal clinical sample of children and adolescents with TS. Second, this study aimed to establish whether tic, ADHD and OCD severity in children with TS can predict their substance use as young adults.

Methods:
At time 1 (T1), patients were recruited from the national Tourette's Clinic, Glostrup University Hospital, Denmark. Healthy controls were recruited from the patients' neighborhood, totaling 314 patients and 81 controls. Patients and controls were assessed for tic severity and comorbidities with validated diagnostic instruments. At time 2 (T2), between 4 and 8 years later, (mean 5.6 years) participants (n=227) and controls (n=53) were re-examined with the same measures. Furthermore, they were asked about alcohol, cigarettes, cannabis and hard drugs consumption and whether substance use alleviated their tics or comorbidities. These measurements were primarily categorical with only one alcohol and one smoking measure being continuous. The mean age in both groups was 18.5 at T2, with a variance of 8 in the patient cohort and 7 in the control group.

Results and Conclusions:
For the continuous variables, the sample was split by patient/control group and diagnoses at both T1 and T2. Controls consumed more alcohol than TS patients and TS+ADHD patients at T1 consumed more than other patient groups. No difference was found for smoking. For the categorical values, these group differences were assessed with descriptive statistics. A higher percentage of patients consumed hard drugs and cannabis compared to controls. TS+ADHD patients at T1 along with TS+OCD and TS+OCD+ADHD patients at T2 had the highest levels of consumption among patients. Severity of ADHD, OCD and tics were all correlated with increased substance use. A strong relationship between ADHD severity and all included forms of substance use was seen; OCD and tic severity were only correlated to cannabis and hard drug use. ADHD and OCD severity both showed predictive power, as ADHD severity at T1 led to increased consumption of all substances, while OCD severity at T1 was connected to cannabis use.
Generally, patients with high comorbidity severity scores at both T1 and T2 found that consumption of all substances reduced symptoms, including tic severity. The exception for this was hard drugs—only patients with high ADHD severity found this helpful. The

strong relationship between tic, ADHD and OCD severity and the belief that substance use reduces tics and comorbidities, indicates substance use could be explained as a form of self-medication.

P16. The severity of tics in patients with Gilles de la Tourette syndrome and comorbid Autism Spectrum Disorder

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Background:
Autism Spectrum Disorder (ASD) is one of comorbidities in patients with Gilles de la Tourette Syndrome (GTS). It is characterized by persistent deficits in social communication and social interaction with restricted and repetitive patterns of behaviour, interests or activities. The prevalence of ASD in patients with GTS ranges from about 3% to 20%. The aim of this study was to compare characteristics and severity of tics in patients with GTS and comorbid ASD to patients without ASD diagnosis.

Methods:
We performed a one-time registration study in a cohort of 390 consecutive patients with GTS aged 5–66 years (mean age 16.0±9.5, 292 males, 255 children). Duration of GTS was 8.7±7.6 years. All patients were personally interviewed and examined. The diagnosis of ASD was in each case made prior to our evaluation in specialized centers dedicated to ASD diagnosis by psychiatrists experienced in the field of ASD. All patients were assessed using Yale Global Tic Severity Scale (YGTSS) and the statistical analysis of obtained results was performed.

Results:
Statistical analysis of 5 dimensions of YGTSS (number, frequency, intensity, complexity, and interference) related to motor and phonic tics showed a significantly higher score for complexity of motor tics ($p=0.002$) and frequency ($p=0.036$), intensity ($p=0.013$), complexity ($p=0.011$), and interference ($p=0.022$) of vocal tics in patients with GTS and comorbid ASD compared to patients with GTS only. A statistical analysis of total scores on YGTSS was also performed. Patients with a dual diagnosis of GTS and ASD had a significantly higher total scores on YGTSS compared to patients with GTS without comorbid ASD: total motor tic score (Me 18 vs 14; Q1-Q3 14-19 vs 11-18; $p=0.003$), total phonic tic score (Me 13.5 vs 10; Q1-Q3 9-19 vs 6-14; $p=0.002$), impairment score (Me 30 vs 20; Q1-Q3 20-35 vs 10-30; $p=0.001$), total Yale Global Tic Severity Score (Me 57.5 vs 42; Q1-Q3 45-75 vs 26-61; $p<0.001$).

Conclusions:
Patients with dual diagnosis of GTS and ASD have more severe tics which cause significant impairment of daily living. Such GTS patients require clinicians' special attention not only due to the presence of ASD symptoms but also because of the more severe course of GTS itself.

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