

CASE IN CONTEXT

Case in Context: Tourette Syndrome

Kirsten Müller-Vahl*

Dr. Kirsten Müller-Vahl: Mr. Miller,* thank you very much for taking part in this interview. I would like to ask you to first explain how Tourette syndrome has impacted your life and what restrictions you experienced.

Miller: The first tics appeared approximately when I was 5 years old. Especially during my childhood, I had more intense vocal tics consisting of different sounds and noises. Later on, I suffered mainly from motor tics such as shaking my head or poking my tongue out. People did not understand why I did that and, as a result, I got bullied quite a lot at school. Especially outside my family, this was particularly painful. Owing to the fact that I was often bullied, I lost optimism and the willingness and motivation to take part in social activities or go to public places. However, I felt an inner urge to perform the tics without being able to do anything against them.

This phenomenon was accompanied by increased anger against myself, because the tics appeared again and again and were bothering me. Either because the tics hurt or because they distract from other activities and thereby also affect the ability to fully concentrate on something else. These are my main restrictions. For a long time, I could not understand why it was this way.

When I grew older and started working, the hurdles were mainly my self-perception rather than external perception. I worried a lot about what kind of impression I would leave with others and how they might perceive me once they witnessed my tics. I wondered whether this could cause any difficulties or disadvantages for me. Owing to the tics, I had a permanent weakness and this view accompanies everything and impacts daily life. The tics were a sensitive spot for me and forced me to be more careful than others.

*The patient's name has been changed to protect patient confidentiality.

Today, I work in a consulting firm. Besides calculations and analyses, a substantial share of my daily job is also to present and defend the results of my work. To this day, I sometimes feel certain disadvantages or restrictions. For example, when I worked for a client and took part in a meeting with high management attention, the mood and the meeting were fine and positive but during the presentation of a leader on the client side, I could not resist a tic and moved my eyebrows and nose a bit with the consequence that she interrupted the meeting and asked me to explain, why I looked in such a critical way—as she understood it as a reaction to her statement. Such experiences are accompanying me and still have a certain impact.

Dr. Müller-Vahl: What were the main reasons for you to start a cannabis-based therapy?

Miller: A driving reason was definitely the physical pain in the area of my neck caused by the tics. The stronger the tics are, the stronger is the pain. This depends on several factors, among them is also the number of sleeping hours. If I move the head or bend my neck too much into one direction, the pain appears. Another main motivation was my own psychological well-being: I strongly wanted to have a measure or an approach to overcome Tourette syndrome and finally be able to “switch it off,” whereas this is normally not possible. In certain parts, also self-impression played a role: if you enter for example new situations and in the same time you realize that there are tics coming, I wanted to be able to use something impactful and effective to feel safer and better.

Dr. Müller-Vahl: What are the changes to your life since you decided for cannabis-based therapy?

Miller: The cannabis-based therapy has changed my life in a very positive way. In the past, I tried several other medicines against the tics. Those came along with certain side effects. As a side effect of one medicine, I became almost panicking and unsafe. Those partially stronger side effects vanished and are not part of my life anymore. An absolute quantum leap is the possibility to reduce my tics by >95%. Depending on which cannabis-based medicine I use, the tics are reduced by 90% to up to 100% for a while. With none of the former medicines, I ever had the chance to yield similar results as with cannabis-based medicine. That is a great leap forward.

And there is an additional aspect: owing to the success of the cannabis therapy, it has an impact on the psychological condition as well. I now know that there is the possibility to be almost fully without tics for a while. At the same time the overall extent of the tics is reduced by the frequent and structured use of cannabis. This was not the case before and increases positivity and optimism regarding this topic that, in turn, improves my well-being. Furthermore, it supported my inner calm. Throughout my life I was rather a bit antsy, which also improved over the course of the therapy.

Dr. Müller-Vahl: What is changing for you if you have less tics?

Miller: I have higher self-confidence because the tics were my most sensitive and vulnerable spot. In the meantime, I approach things differently, especially in public. In the past, when I had to give a presentation or speech during school or university, my tics got worse. This was noticed by the other participants, even though they did not criticize or question me every time. This generally decreased and I could thereby gain a better inner balance experiencing less pressure. Some time ago, I felt the tics as a permanent weakness and, therefore, tried to be better than others in other spots and areas, somehow compensating my disadvantage. This disappeared to a certain extent.

Dr. Müller-Vahl: Some people with tics try to avoid certain situations. Did you experience the same?

Miller: I did not allow myself to fully avoid certain situations but rather forced myself quite a lot. There were many things that I would have preferred not to do but was pushed by my social environment or developed the

wish to still try to take part myself. Thereby I was quite stressed sometimes. A very typical example was if I started working for a new company or joined any other group of new people and nobody knew me. We had meetings with 10–15 people sitting around a round table watching each other in a competitive environment. This was something I absolutely hated. Now I manage those situations better and the tics are more under control.

Dr. Müller-Vahl: Do you think that this could have an impact on your further professional career?

Miller: Yes, sure. For example, I like to present certain topics, be in close touch and interaction with colleagues and be on a stage explaining things. For a long while I hated this due to the inability to keep my tics under control. In the past, I thought, I would never end up in a position, which requires me to speak in front of people. This was excluded in my life choices and I tried to find my way around. This disappeared. I know that I am now able to have the tics under better control. Some mental blocks that I had imposed to myself are dissolving now. I cannot really quantify this, but have the personal impression that it helps.

Dr. Müller-Vahl: Are there similar changes also in your private life?

Miller: Yes, when starting the cannabis therapy, my parents and siblings had the impression that I am generally more balanced and happier. I would confirm this.

Dr. Müller-Vahl: Do the tics have or had an impact on your social contacts? Did it change through cannabis therapy?

Miller: Yes, there was a certain impact, but it was not too strong. I managed to handle social contacts quite well. The ability to meet new people and friends was affected a bit by Tourette's effects. But not in a way that I had serious problems to meet and get to know new people. This is probably due to the reason that my Tourette condition is not accompanied by strong vocal or even insulting tics.

Dr. Müller-Vahl: Mr. Miller, thank you very much for this interview and for being willing to answer all the questions so openly. I wish you all the best for your future, both professionally and privately.

Tourette Syndrome

Definition and clinical course

Tourette syndrome is a chronic neuropsychiatric disorder. Tics are the hallmark of the disease. Motor tics are involuntary movements that are most commonly located at the face and head such as eye blinking, grimacing, and head jerking. However, in more severely affected patients, motor tics may also involve other parts of the body and become more complex. In addition to motor tics, patients with Tourette syndrome suffer from one or more vocal tics, most often coughing, sniffing, or clearing one's throat. With increasing severity of the disease, vocal tics may become louder and more complex. In ~20–30% of patients, obscene vocal tics occur, called coprolalia.

Although the age at onset is in early childhood around the age of 6–8 years, the maximum of tics is typically reached at age 10–12 years. Although tics often improve during the later course of the disease, complete recovery is rare. Depending on the number, frequency, intensity, location, and complexity of the tics, quality of life is significantly impaired. However, even mild tics may cause reduced self-esteem and result in social withdrawal, teasing, and bullying. About 80% of patients with Tourette syndrome suffer in addition from psychiatric comorbidities such as attention deficit/hyperactivity disorder, obsessive compulsive disorder, depression, anxiety, rage attacks, self-injurious behavior, and sleeping problems, which impacts quality of life in many cases as well.

Pathology

The underlying cause of the disease is still unknown. Most evidence supports an involvement of corticostriato-thalamo-cortical circuits. Based on the fact that antidopaminergic drugs improve tics, a dopaminergic hypothesis has been postulated. However, there is also evidence for an involvement of other neurotransmitter systems including gamma-aminobutyric acid (GABA), glutamate, noradrenaline, and serotonin.

The cannabinoid hypothesis of Tourette syndrome

A cannabinoid hypothesis of Tourette syndrome has been proposed. This idea is primarily based on the fact that a large number of patients report beneficial effects not only on their tics, but also on psychiatric comorbidities after use of cannabis or cannabis-based medicines. Until today, several single case studies and case series including altogether >200 patients with

Tourette syndrome have been published reporting beneficial effects and good tolerability after use of different cannabis-based medicines, including inhaled (smoked or vaporized) cannabis, cannabis extracts such as nabiximols, and pure tetrahydrocannabinol (THC). The first such report dates back to 1988 describing three male patients, who reported a reduction of their tics and the preceding premonitory urges, but also an improvement of self-injurious behavior, attention, and hypersexuality as well as a general relaxation, when smoking 0.5–2 cannabis cigarettes per day.

Until today, two small randomized double-blind placebo-controlled trials using THC have been performed, including 12 and 24 adult patients with Tourette syndrome. Although limited in size, both studies suggested that THC may be effective and safe in the treatment of tics with no detrimental effects on neuropsychological performance. These data are in line with a single case report describing a patient, whose driving ability improved after use of 15 mg THC.

The cannabinoid hypothesis of Tourette syndrome is further supported by the finding of elevated cerebrospinal fluid levels of the endocannabinoids anandamide and 2-arachidonoylglycerol, the endocannabinoid-like molecule palmitoylethanolamide, and arachidonic acid in adult patients with Tourette syndrome. Assuming an involvement of the endocannabinoid system (ECS) in the pathobiology of Tourette syndrome, observed changes can be secondary due to the alterations in other transmitter systems such as the dopaminergic system. Alternatively, it can be speculated that Tourette syndrome is caused by a primary dysfunction in the ECS, which, in turn, would result in changes in several other neurotransmitter systems because of the paramount role of the ECS as a neuromodulatory system in the brain. Accordingly, activation of central cannabinoid receptors—which are expressed with high density in the basal ganglia—by use of cannabis-based medicines may result in a decrease of dopaminergic activity resulting in a reduction of tics.

Treatment

According to current guidelines, treatment of tics shall start with psychoeducation and behavioral therapy. In those patients, who do not respond sufficiently to this kind of treatment, pharmacotherapy must be initiated. First-line pharmacotherapy for tics is antipsychotics, namely aripiprazole, and other dopamine receptor antagonists such as risperidone, sulpiride, and tiapride. However, in a substantial number of patients, these

treatment strategies either fail to improve the tics sufficiently or cause clinically relevant side effects. Therefore, new treatments are urgently needed.

Based on preliminary findings, it is suggested that cannabis-based medicines might be such an alternative treatment option for patients with Tourette syndrome. Most importantly, the available data suggest that cannabis-based medicines might be the first treatment that improves not only tics, but at the same time also various psychiatric comorbidities. Currently, a well-designed large multicenter placebo controlled randomized trial is ongoing investigating efficacy and safety (including fitness to drive) of the cannabis extract nabiximols in the treatment of 96 adult patients with Tourette syndrome (ClinicalTrials.gov Identifier: NCT03087201). Thus, further robust data can be expected in the near future. Of note, only recently, the selective endocannabinoid modulator and monoacylglycerol lipase inhibitor Lu AG06466 (former ABX-1431) was found to be ineffective in the treatment of

tics in adults with Tourette syndrome.¹ This result opens the window for further discussion on the mechanisms underlying tic improvement after use of exocannabinoids.

Reference

1. Lundbeck. Lundbeck announces phase IIa study results of Lu AG06466 in adults with Tourette Syndrome. March 27, 2020. Available at: https://investor.lundbeck.com/news-releases/news-release-details/lundbeck-announces-phase-ii-a-study-results-lu-ag06466-adults?source=content_type%3Areact%7Cfirst_level_url%3Anews%7Csection%3Amain_content%7Cbutton%3Abody_link

Abbreviations Used

ECS = endocannabinoid system
THC = tetrahydrocannabinol

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