HIGH SCHOOL EDITION
Journal of Student Research
Volume 13 Issue 2 (2024)

Modern Scope of Tourette Syndrome: History, Treatments, Comorbidities' Impact on Quality of Life

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ABSTRACT

Tourette Syndrome is a chronic neurological disorder characterized by uncontrollable motor and vocal outbursts. The disorder is usually accompanied by comorbidities such as attention-deficit hyperactivity disorder, obsessive-compulsive disorder, depression, and more. This review organizes current research regarding pathologies of these comorbidities, and how dopamine as well as other neurological sequences give rise to tics and other disorders. Furthermore, this review promotes the need for research to shed light on the negative quality of life that Tourettes has on individuals, especially children, and questions the role that social concern and inabilities act as mediators for the onset of such comorbid disorders. I begin by briefly going over Tourette Syndrome's history and explain the current scope of treatment options ranging from surgical procedures to behavioral options. Afterward, the paper discusses the current technology used for pathology detection and raises potential implications for technology use for comorbidity pathologies.

Modern Overview of Tourette Syndrome

Tourette syndrome (TS) is a neurological disorder developing in children ages 6-8 years old. Tourette Syndrome was first discovered in France in 1885 by Gilles de la Tourette and is thought to be hereditary (McNaught & Mink, 2011). This review explores the role of technological advancements in understanding the diagnoses, treatment, and management options for Tourette Syndrome, and suggests further research for clinical implications. Furthermore, I argue that Tourette-derived comorbidities have a greater impact on individuals' quality of life, stressing the need for a novel comprehensive treatment plan to counter other neurological disorders. This contention is contextualized within novel treatment methods as well as the effects of comorbid disorders on children and teen quality of life.

Background Information on Tourette Syndrome

Tourette Syndrome is characterized by a variety of motor tics and a vocal tic throughout the disorder (Faranak et al., 2022). Symptoms of Tourettes commonly include seemingly random, chronic, and involuntary twitching and sound-making. Billnitzer and Jankovic (2020) described the symptoms as being caused by uncontrollable urges or an unpleasant feeling of retention that needs to be released in the form of a tic. The prevalence of Tourette Syndrome is classified as common, with 0.30-0.77% of school-aged children being affected. Tourette Syndrome can occur in all ethnicities, and research also indicates that half to two-thirds of these children have their symptoms improve throughout adolescence and puberty. Furthermore, the severity of tics seems to vary with age in children. Children with Tourette have the most severe symptoms from ages 10-12 and less severe symptoms from 4-6 (Levine et al., 2019).

Currently, there is scant literature stating the exact pathologies and underlying neurological mechanisms of Tourette syndrome. It has been thought that imbalances in the Coritco-Striato-Thalamo-Cortical circuits of excitant and inhibiting factors are correlated with persistent tic symptoms (Shitova, et al., 2023). In addition, it is thought that the urge sensations preceding tics stem from the insular cortex (Rae, Critchley, 2022). However, recent research has shown that genetic variations and neurophysiological alterations have affected its pathogenesis (Johnson, Worbe, Foote, Butson, Gunduz, Okun, 2022). Environmental factors also play a role in the disorder's development, but genetic factors have been determined to have a bigger impact (Deng, Gao, Jankovic, 2012).

Individuals with Tourette syndrome face numerous quality-of-life issues and face emotional challenges that can be detrimental to their relationships. Tics resulting from Tourette syndrome can shape a person's experiences and interactions with their social community (Eapen, Cavanna, Robertson, 2016). An individual with Tourette syndrome has a high probability of being afflicted with other neurological and behavioral conditions as well. Common conditions include attention-deficit/hyperactivity disorder (ADHD), obsessive-compulsive disorder (OCD), conduct disorder, rage, depression, and anxiety (CDC.gov, no date). These other conditions can cause further impairment in an individual's life alongside Tourettes. Mood disorders such as intermittent explosive disorder and its symptoms such as physical aggression could cause tensions within families (CDC.gov, no date).

Other potential comorbidities include autism spectrum disorder and disruptive behaviors, which could amalgamate into deficient psychosocial functioning (Eapen, Cavanna, Robertson, 2016). The detrimental impacts on an individual's psychosocial functioning skills and quality of life are further amplified by the stigma surrounding Tourettes, which could lead to bullying, social exclusion, and discrimination (Eapen, Cavanna, Robertson, 2016). In a study by Sana Charania et al (2022), her group estimated bullying and perpetration frequencies in children ages 6-17 that were diagnosed with Tourettes. Results showed that 56.1% experience bullying victimization, and 20.7% experience bullying perpetration (Charania, et al., 2022). Results also found that 83.2% of children were diagnosed with Tourette Syndrome as a mental, behavioral, or developmental disorder (MBDD) (Charania, et al., 2022). From observations and studies alike, a general conclusion can be stated that children and teens diagnosed with Tourette Syndrome face severe social and relational hardships.

Social problems are prevalent in Tourette syndrome patients, primarily due to non-obscene socially inappropriate behaviors (NOSI) and other copro phenomena (Eapen, et al., 2016). These patients face difficulties sustaining personal and peer relationships, exemplified by a clinical study examining TS patients with ages ranging from 16-54 (Eapen, et al., 2016). The study found that 29% reported difficulties with family relationships, 27% reported troubles with friends, and 20% reported general issues relating to their social life (Eapen, et al., 2016).

Treatments, Diagnosis, and Assessment

New technological advancements have enhanced the understanding of the pathogenesis of Tourette Syndrome and its diagnosis. Medical imaging technology developments in electrophysiology and neuroimaging have hinted at cortical volume limitations and reduced connectivity from the frontal lobe to other brain areas (Chou, Agin-Liebes, Kuo, 2022). Research has also shown that urge generation and the ability to control these urges correlate with abnormal connectivity between cortical regions responsible for interceptive processing and the cortico-subcortical networks responsible for regulating motor output (Cothros, Martino, 2022).

Other research has also contributed to the understanding of the pathogenesis of TS.

In recent years, the histidine decarboxylase mutation has been considered high penetrance in individuals with Tourette Syndrome. Scientists are testing this theory on mice as mice with HDC-knockout seem to have similar neurochemical irregularities as patients with Tourette syndrome (Xu, Zhang, et al., 2022).

Recent research has shown that supplementary motor area (SMA) activity is correlated with the activation of tics in patients with Tourette syndrome (Larsh, Huddleston, et al., 2022). Based on this information, scientists can make a diagnosis, and even develop potential treatment options using medical imaging. One Yale study conducted by Denis Sukhodolsky and his colleagues (2020) observed 21 patients for tic reductions after being treated by neurofeedback created through functional magnetic resonance imaging (fMRI). Although this technique has not been widely used to treat neuropsychiatric disorders in the past, Michelle Hampson, an associate professor within the Department of Radiology and Biomedical Imaging at Yale, supports the idea that it can be used as a minimally invasive procedure for improving tic functions (Vaca, 2019). This sheds light on new methods of treatment that could speed up the tic reduction process.

Furthermore, new research regarding the pathology of Tourette syndrome has uncovered that alterations to the basal ganglia are a vital source of tic development (Bloch, State, Pittenger, 2011). In patients with TS, the caudate and putamen were observed to be smaller than those without TS (Bloch, State, Pittenger, 2011). Additionally, increased activation of the striatum, the largest structure of the basal ganglia, is thought to be correlated with tics, as well as increased activity in the orbitofrontal and varying cortical regions (Bloch, State, Pittenger, 2011).

Expeditious advancements in digital technologies have increased access to the remote delivery of behavioral therapy in forms such as telemedicine. Specifically, remote access to digital health interventions (DHI) has garnered attention due to its high efficacy in treating tic disorders and the ability to provide remote therapy for patients diagnosed with Tourette Syndrome. Unfortunately, a problem still stands as DHIs are not widely implemented in clinical services. Instead, behavioral treatment methods such as HRT, CBIT, and ERP have been used to lessen the severity of tics in individuals with Tourettes (Khan, Hollis, Murphy, Hall, 2022). During HRT, patients are taught to become self-aware of their tics and learn new habits to cancel out or create a polar response to suppress their tics (Wetterneck, Woods, 2006).

Similarly, Exposure and Response Prevention is a behavior suppression method to make the patient more resistant to performing a certain behavior in a stimulated state (Wetterneck, Woods, 2006). In a clinical trial by Wetterneck and Woods (2006), an 11-year-old boy was presented with different scenarios in which he had to resist being artificially provoked to perform a behavior. After only three treatment sessions, the behavior decreased to zero, which demonstrates the efficacy of behavioral therapies on patients with Tourettes (Wetterneck, Woods, 2006).

The development of machine learning and artificial intelligence technologies has paved the way for accurate and efficient analysis of neuromedical diseases. In a study conducted by Nele Brugge et al. (2023) concerning the detection of motor tics using machine learning, she developed two machine learning algorithms to automate the detection of tics to improve diagnosis methods through video. The tests resulted in an 88.5% accuracy of tic automatic tic detection using the deep neural network approach making use of machine learning algorithms (Brugge, et al., 2023).

Telemedicine is a technology that allows for virtual appointments for patients. This makes meetings more convenient, as you can meet and consult with your doctor from the comfort of your own home, or any place with access to the internet (Hasselfeld, no date). Relating to the treatment of Tourette Syndrome, telemedicine can be used to more efficiently manage patients with tics, and allow for earlier evaluation and diagnoses leading to quicker treatment plans (Cen, Yu, Wang, et al, 2020). What makes this development in Telemedicine significant is that it improved the ease of access to which patients with tic-related disorders can communicate with healthcare professionals, resulting in earlier diagnosis, evaluations, and ultimately the treatment of their disorders (Cen, Yu, Wang, et al. 2020).

As an alternative to therapy, pharmacological treatments are also an excellent option for patients with Tourette Syndrome. However, pharmacological treatments contain a risk of unpleasant side effects, and should be considered when the patient has limited access to CBIT (Comprehensive Behavioral Intervention for Tics)

(Billnitzer and Jankovic, 2020). Pharmaceuticals used to treat TS are classified into two main categories: medications for tics and medications for comorbidities (Tourette.org, no date). Medications for tics primarily function to restrict or lessen dopamine release. Alpha-2 agonists are a class of drugs used in children for milder tics due to their low-risk factors. Alpha-2 agonists such as clonidine and guanfacine work by reducing arousal resulting in better regulation of norepinephrine. In the case of guanfacine, the medication stimulates postsynaptic alpha-2A receptors on dendritic spines . The dendritic spines are located in the frontal cortex, meaning the drug gives stronger control to the designated area leading to better-controlled tics (Billnitzer and Jankovic, 2020).

With modern technological advancements, two prominent treatment options emerged to combat tic symptoms in patients: Deep Brain Stimulation (DBS) and transcranial magnetic stimulation (TMS). DBS is a neurological procedure that involves sending electrical pulses to the thalamus through an implanted device called a neurostimulator. DBS was originally developed as a treatment option for patients with Parkinson's disease. This procedure is considered a last resort when a patient's tic symptoms do not subside or go away into their twenties. As DBS is a surgical procedure, it does carry most surgical risks relating to brain surgery. Infection, blurred vision, loss of energy, and bleeding can all be adverse effects as a result of an imperfect operation (Müller-Vahl, 2013).

Additionally, there are many assistive technologies including smart devices that enhance the quality of life for patients diagnosed with Tourette Syndrome. One such example of this type of technology would be Dragon Naturally Speaking, a smart speech recognition software that helps individuals with motor tics that impair their ability to write or type (Illinois Library, no date). Other software also assists in reading, such as scanning pens that use optical character recognition (Illinois Library, no date). These pens can scan words and gather the meaning of words. They can also convert written work to digital text and allow the individual to hear the sentences vocalized digitally for easier comprehension (Illinois Library, no date).

Future Technological Implications in Tourette Syndrome

With new emerging developments in technologies and their applications in mental health research, there is promising research for better diagnoses and treatment options for neurodevelopmental disorders (Ribas, Micai, et al., 2023). This especially includes the growth in understanding of artificial intelligence provides opportunities for better detection of neurodegenerative disorders through machine learning and deep learning algorithms (Mathew, Pillai, 2022). An example of applied technologies can be seen when treating Parkinson's disease by analyzing the vocal characteristics of patients with Parkinson's disease. Multivariate visualization of the vocalization data could allow for pinpointing and characterization of vocal vibration signals produced by the patients (Pillai, Menon, Bartkowiak, 2022).

There are also technological interventions that may be invasive, but still effective at treating Tourette syndrome symptoms in patients. Botulinum toxin (botox) injections are usually used in plastic surgery for aesthetic procedures by inhibiting the local release of acetylcholine to reduce muscle activity to improve lines and wrinkles on the face (Eddy, Rickards, Cavanna 2011). However, when used for administration for the treatment of tics, they are directly injected into the muscle group included in a motor tic, and even into the laryngeal muscles for vocal tics. This treatment method has been seen to improve tic symptoms, but due to the severity of the treatment, it is only used to treat patients with self-injurious behaviors and tics.

While the use of technology has improved treatment options for Tourette patients, it has also raised numerous ethical concerns due to risks associated with treatment. One ethical concern regards fair patient selection, in which patients are evaluated to receive treatments such as deep brain stimulation due to chances of natural remission during their adolescent years (Smeets, Duits, et al., 2018). In a case study regarding the ethics of Deep Brain Stimulation in Tourette patients, one patient's tic severity reduced after two rounds of behavioral therapy. In his first round of treatment, the patient did not complete all of his therapy assignments. This incomplete compliance led to a stunt in his improvement (Smeets, Duits, et al., 2018). However, during his second

round of therapy, he completed all the homework exercises, which led to his improvement in tic symptoms (Smeets, Duits, et al., 2018). This case study shows that behavioral therapy can significantly benefit tic symptoms. Accordingly, surgical interventions should not be considered until after going through non-surgical treatment. The patient's treatment needs must be thoroughly evaluated before initiating more invasive treatment options.

Comorbidities

The new emergence of Tourette treatment options has allowed for a more comprehensive treatment course for individuals. Developing novel treatment courses is crucial to respond to the high rates of comorbidities that affect individuals diagnosed with Tourettes. Comorbidities are conditions or disorders that simultaneously afflict individuals in addition to pure Tourettes. Cravedi and her group explored different studies and reviews to highlight statistics that displayed comorbidity rates. In one survey with a sample consisting of three schools in Los Angeles, Tourette syndrome frequency was 14 out of 3034, or 0.46%. Out of those 14 individuals, 70% had comorbid ADHD. In the second study of 435 children, 22% had comorbid ASD, 24% had development coordinate disorder, and 36% had dyslexia out of a 0.15% Tourette syndrome frequency. In a Swedish study the group reviewed, the rampancy of comorbid ADHD was higher at 68% while ASD remained similar at 20%. Other disorders such as dyslexia were reported at 16% while the development coordination disorder was reported at 20% (Cravedi, et al., 2017). According to these statistics, we can infer that ADHD is a common comorbidity among individuals with Tourettes and that comorbidities commonly afflict individuals with Tourette syndrome.

Additionally, another study by Eapen and others supports this conclusion by claiming the presence of comorbidities is acutely correlated with Tourette syndrome, with ADHD, OCD, and autism spectrum disorder being the most prevalent. These disorders create severe psychosocial deficiencies, which can critically impair children and teenagers' social functioning and subsequently their quality of life. Tics caused by Tourette syndrome in tandem with a detriment in focusing ability cause poorer performance in school or at work than those that aren't afflicted with these disorders (Eapen, et al., 2016).

However, this correlation between Tourette and comorbid disorders and poor quality of life is questioned by a review examining anxiety and depression rates in adult Tourette patients. The study found tic severity was not significantly correlated with quality of life. Rather, obsessive-compulsive symptoms were the only variable significantly correlated with tic severity (Huisman-van Dijk, et al., 2019). These studies bring forth a potential correlation with comorbid disorders which have to do with quality of life instead of pure Tourettes. The lack of association between pure tic severity and poor quality of life is vital in understanding the extent to which comorbidities affect individuals with Tourettes, and to develop treatment options to tackle problems outside of pure Tourette symptoms. The combination of Tourettes and ADHD is one of many significant determinants of quality of life. Examining the impact of comorbidities and identifying them in Tourette patients should be stressed as the first order of action instead of being put aside and probing the tic severity (Cravedi, et al., 2017).

Conclusion

Through conducting this review, I explored the use of technology and its vital impacts on improving tic symptoms and severity. Furthermore, the integration of technological developments such as telemedicine allows for new modes of behavioral therapy, ultimately helping increase patient outcomes through a more efficient healthcare delivery system. Technology use has been shown to improve tic symptoms and quality of life in individuals diagnosed with Tourette Syndrome. The future landscape of Tourette treatment looks bright with

emerging developments in neuroimaging, neurofeedback using wearable devices tracking neuroactivity, and virtual reality-based behavioral therapies. However, the current scope of treatment does not consider comorbidities as a primary indicator for treatment course development. Since disorders such as ADHD and OCD have severe impacts on school life and cause other psychosocial problems, new behavioral therapies should be tailored to treat these comorbid disorders and tic symptoms simultaneously. Although more research needs to be done to understand the exact pathology of Tourette Syndrome, technology will play a crucial role in helping advance treatment options and possibly prevent patients from not only this disorder but other neurological conditions as well.

Acknowledgments

I would like to thank my advisor for the valuable insight provided to me on this topic.

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