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Tremor and Other Hyperkinetic Movements

Reviews

Sources of Disability in Tourette Syndrome: Children vs. Adults

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Abstract

Background: Tourette syndrome (TS) is a neurodevelopmental disorder characterized by tics and neuropsychiatric co-morbidities like Obsessive Compulsive Disorder (OCD) and Attention Deficit Disorder (ADHD), among others. In many instances tics get better with age but this is not always true regarding the psychiatric co-morbidities.

Methods: This manuscript reviews the disease-specific Quality of Life (QOL) instruments used to measure disability in TS and the existing literature on sources of functional impairment in children and adults with TS.

Results: Traditionally, disability in TS has been recorded using objective measures. In recent years there has been a development of disease-specific instruments to measure subjectively the impact of the different aspects of TS on the patient's daily function. The differential impact of tics vs. the psychiatric co-morbidities in children with TS is an issue of debate in the existing literature. In adults with TS, the literature is scant, therefore the sources of disability in this group are even less defined compared to children.

Discussion: As clinicians, we need to focus on determining the sources of disability in children and adults with TS so we can target our interventions successfully.

Keywords: Tics, quality of life, Gilles de la Tourette syndrome

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Introduction

Tourette syndrome (TS) is a neuropsychiatric developmental disorder characterized by multiple motor tics and at least one vocal tic, which tend to occur multiple times a day and frequently in bouts. They usually start before the age of 18 years and should be present for at least 1 year before the diagnosis of TS is made, to distinguish them from transient tic disorders of childhood. It is characteristic for tic disorders that the tic number, frequency, and complexity change over time. Even though tics are the hallmark of TS, up to 90% of patients with TS evaluated in specialty clinics present with additional problems, mostly neuropsychiatric manifestations, which can range from complex tic-like symptoms (self-injurious behaviors; non-obscene, socially inappropriate behaviors; coprophenomena; echophenomena; and paliphenomena) to attention deficit hyperactivity disorder (ADHD), obsessive compulsive disorder (OCD), mood disorders, and impulse control disorders.[1] Other behavioral problems such as aggression, temper outbursts and rage, oppositional defiant disorder, conduct disorder, and learning disabilities are also evaluated in TS. Although the definition of the spectrum of the clinical presentation of TS has evolved over recent decades, it is still under debate which one of these psychiatric comorbidities is an integral part of TS and subsequently genetically linked to it.[2]

As our understanding evolves and the definition of what constitutes TS changes, so does the consensus about its prevalence. TS was once considered to be rare, but newer studies conducted in the community/schools rather than specialty clinics have suggested a prevalence range between 0.4% and 3.8% in the population between 5 and 18 years of age, with a calculated overall prevalence of 1%.[3] The prevalence is even higher in special education populations. Likewise, the prognosis of TS has been extensively researched in the medical literature. Data gathered from longitudinal studies suggest that tic frequency and severity decline with age in a large proportion of patients. Overall, the

average age at tic onset is 5.6 years, with a fluctuating course, worst severity early in the second decade,[4] and eventual decline in frequency and severity after puberty in a large proportion of patients (59–85%).[5] Even though prognosis is good with regard to tic symptomatology as the individual grows up, many elements of the psychopathology may persist until later in life.

Although there is a wide spectrum of severity in TS, many patients with tics only and no other psychiatric comorbidities do fairly well, and in many instances do not need to be medicated for their tics. There is an extensive body of literature debating the primary sources of disability in patients with TS during childhood and, to a lesser degree, adulthood.[6–12] Unfortunately this literature is not conclusive, does not, in many instances, take into account the patient's own perception of their disease, and does not separate disease impact in childhood vs. adulthood. The purpose of this article is to review the existing literature on measures of disability in TS and the differential impact of tics vs. psychiatric comorbidities in children and adults with TS.

Measures of disability in TS

The concept of health-related quality of life

Research on the functional impact of TS suggests that it is associated with impairment across several domains.[9] Furthermore, given the number of potential clinical phenotypes and the different conditions associated with TS, it can at times be difficult to delineate the disabilities and determine the differential impact on patient function in order to appropriately direct treatment.

Scales used to measure tics in TS are usually geared toward quantifying motor and vocal tics by measuring different aspects of tics such as number, frequency, severity, complexity, interference, and impairment.[13] They are not as good at measuring the effect of tics on different dimensions of life, the differential effect of tics vs. other psychiatric comorbidities on the patient's life, and the patient's view of the disease. Moreover, the patient's perception of disease impact on different aspects of life and the physician's assessment on disease-generated disability can often diverge from each other. Therefore, the concept of health-related quality of life (HR-QOL) has been used to close this gap.[14]

QOL data are routinely used in the evaluation of interventions, as an endpoint in clinical trials, in outcome studies, and cross-cultural comparisons of health and well-being. Although no single definition of QOL is universally accepted, there are two types of information gathered in assessing QOL: the functional status of an individual and the individual's appraisal of how their health impacts their life.[12] It is generally agreed that HR-QOL is a construct of three domains: physical, psychological, and social well-being.

Generic measures of QOL in TS

The majority of studies that have examined functioning in patients with TS have used measures like the Yale Global Tic Severity Scale (YGTSS).[13] The YGTSS impairment subscale specifically assesses tic-related impairment without measuring general QOL. Several studies using generic instruments to assess HR-QOL have employed the 36-Item Short-Form Survey (SF-36),[15] the Child Health Questionnaire Form 50 (CHQ50),[11] and the EuroQOL-50 (EQ-5D).[10] The SF-36 has been used to compare QOL in adults with TS to patients with epilepsy.[15] The EQ-5D was applied in a cohort of adults with TS, concluding that the main independent factors for determining HR-QOL in adults with TS were depression, severity of symptoms, and age.[10] Surprisingly, when the CHQ50 was used to determine the factors that influence QOL in children with TS, it was found that psychosocial health was not different from that of the normative population in the majority of domains tested.[10]

Disease-specific measures of QOL in TS

A disease-specific QOL instrument has been published and used in a few different studies of TS patients. The Gilles de la Tourette Syndrome Quality of Life Scale (GTS-QOL) was developed with input from patients, caregivers, clinicians, and literature review. The 27-item scale with four subscales (psychological, physical, obsessional, and cognitive) demonstrated satisfactory scaling assumptions and acceptability; high internal consistency, reliability, and test–retest reliability (Cronbach alpha $\geqslant$0.8 and intra-class correlation coefficient $\geqslant$0.8); good validity; confirmatory factor analysis; and correlation patterns with other rating scales and clinical variables.[16]

This disease-specific instrument was used in a study investigating the HR-QOL in 75 patients with TS with and without behavioral comorbidities.[8] This research involved children and adolescents recruited at three specialty clinics for TS, which resulted in a sample characterized by marked tic severity. After splitting this cohort into two groups according to the presence or absence of psychiatric comorbid conditions, the investigators found that the TS plus group scored significantly higher than the pure TS group on a number of measures, in particular OCD.[8] Even though this study involved a small number of patients from specialty clinics, it provided evidence that the GTS-QOL may be a useful additional subjective measure complementing available objective rating scales. To further complicate things, the impact of tics and comorbid conditions on the HR-QOL of children was viewed differently from the point of view of the children compared with their parents, with children placing more emphasis on the tics and parents placing more emphasis on the psychiatric comorbidities, which they perceive to be worse than tics.[7] In another study, parent reports of their child's QOL were weakly related to tics, with children's self-reported QOL inversely correlated to a measure of tic severity.[12] Correlations between parent and child ratings of QOL for children aged 8–11 years were generally higher than those for youth aged 12–17 years.[12] Whether children are more likely to notice the impact of the tics and whether their parents place more emphasis on the comorbidities are questions that warrant further investigation and likewise reinforce the importance of using QOL measures along with the objective symptom assessing scales to determine disability.

Conclusion

Even though the generic instruments measuring QOL in TS have the advantage of allowing comparison between different disease

entities, they are not sensitive to the specific features that are important to patients with TS. More specifically, they have limited applicability to the neuropsychiatric conditions and are not sensitive to motor and vocal tics, repetitive behaviors, and other tic-related symptoms.[8] The GTS-QOL is a disease-specific scale that has been found to have good clinimetric properties and has already been used in the literature;[7,16] therefore, it should be considered when designing a study to elucidate the most likely source of disability or to investigate new interventions in TS.

Determinants of disability in children with TS

The relationship between functional impairment and tic severity in children remains unclear. Some research has yielded significant positive correlations between tic severity and functional impairment[17] and other research has failed to demonstrate a significant relationship.[18] These conflicting data can be difficult to interpret because of multiple variables that can influence the results, including the type of clinic population (specialty vs. community), type of sample (mild vs. severe tics), age group (children vs. adolescents), study methodology (direct questionnaire, internet, or mail survey).

Studies supporting tics as the main source of disability in TS

In a clinic-based sample of children with TS, Storch et al.[12] rated the degree to which tics interfered with children's school, home, and social functioning, as defined by multiple "problem areas" within each of these three functional domains. The majority of the sample reported tic-related impairment in at least one significant problem area; 37% reported two or more problem areas.

In an internet-based survey, 740 parents of children with chronic tic disorders and 232 children (aged 10–17 years) were questioned regarding the functional impairment of tics across different domains (physical, social, academic, and psychological), HR-QOL, and perceptions of discriminations resulting from tics. The survey results were consistent with notable functional impairment in children as a result of tics. Functional impairment was associated with tic severity.[12] Additional co-occurring conditions tended to further increase the functional impairment in another sample.[9]

Studies supporting psychiatric comorbidities as the main source of disability in TS

There is a large body of literature where disability is associated with psychiatric comorbidities rather than the tics. Characteristically, in one study, even though 88% of the patients reported that tics interfered with their life, a high proportion of them suffered from behavioral problems and/or other psychopathologies, which in half of the patients had a greater impact on functioning than the tics themselves.[19] Similarly, a total of 53% of the members of a TS cohort in another study had sought mental health counseling for the psychiatric manifestations of their disease.[20]

In a sample of patients with TS, albeit with mild to moderate tics, tic severity did not predict QOL, while both ADHD and OCD were strong predictors.[6] In another study investigating the relationship between tics, obsessive compulsive symptoms (OCSs), and impulsivity, and their effects on global functioning in children and adult patients with TS, the impact of OCSs on global functioning was greater than that of tics in children, despite a moderate correlation between tic severity and OCSs.[21] Similarly, in a cross-sectional study of children evaluated at two TS clinics, using a multiple linear regression model, including diagnosis, age, sex, and TS, OCD, and ADHD symptom severity, it was concluded that the most significant predictor of the psychosocial summary score was ADHD symptom severity.[11] Children with both TS and ADHD compared to those with TS alone had significantly more behavioral problems, poorer social adaptation, and worse QOL.[11]

Conclusion

Even though the literature is not conclusive, it appears that in many instances, especially in children with TS, the psychiatric comorbidities may be causing more impairment than the tics themselves. These findings underscore the need for neurologists to broaden their attention when assessing children with TS and tailor their treatment to the specific manifestations with the greatest impact on function.

This finding is particularly important given that for decades there has been some reluctance by clinicians to treat symptoms of ADHD in children with tics, even though it is often the driving force of disability, because of the fear of worsening the tics. The Tourette's Syndrome Study Group[22] conducted a study on the treatment of ADHD in children with tics that provided evidence that the risk of worsening tics in children treated for ADHD with stimulants is not different than placebo.

Determinants of disability in adults with TS

As most studies on TS have focused on children, there is limited information on natural history, comorbidities, and tic characteristics of TS in the adult population. Furthermore, most of the information we have about adults is gathered by assessing the patients who seek medical attention, and therefore it does not take into account the patients whose symptoms are too mild or who are disillusioned with medical care.

Tic progression into adulthood

In a study designed to address the long-term outcome of children with TS as they reach adulthood, 46 children with TS underwent a structured interview at age 11.4 ± 1.6 years, which was repeated at 19.0 ± 1.8 years.[23] On average, subjects in the cohort experienced their worst-ever tics at 10–11 years of age, and most experienced a marked attenuation of tic severity during adolescence. Slightly less than one-quarter (22%) continued to experience mild or greater tic symptoms (YGTSS score ≥ 10) at follow-up, while nearly one-third were in complete remission for tic symptoms at follow-up. The only childhood clinical measure significantly associated with higher tic severity at follow-up was increased tic severity at the time of baseline assessment during childhood (<14 years).[23] Worst-ever OCD symptoms occurred approximately 2 years later than worst-ever tic symptoms. Increased childhood intelligence quotient was strongly

associated with increased OCD severity at follow-up. Furthermore, OCSs in children with TS became more severe at a later age and was more likely to persist than tic symptoms.[23] Cavanna et al.,[7] investigating the childhood predictors of future HR-QOL, concluded that tic severity associated with characteristic premonitory urges in childhood, indicating more complex tics, and family history of tic disorders was predictive of poor HR-QOL in adulthood. In another study designed to investigate the same question, the authors recruited 31 adult patients with TS who had been evaluated as children or adolescents at the same clinic and had undergone a standardized 5-minute filming protocol to come to the clinic, be assessed, and record another video under the same protocol.[24] Ninety percent of the adult patients re-evaluated still had tics, but the mean objective tic disability had diminished compared to childhood (mean composite tic disability score childhood 9.58 vs. adulthood 7.52, $p=0.014$). The improvement in tic disability score did not relate to medication use, as only 13% of adults received medications for tics, compared with 81% of children.[24]

Jankovic et al.[25] also reviewed medical records of 43 adults with tics who had been evaluated in the same clinic as children and found adult patients with TS had significantly more facial and truncal tics and a greater prevalence of substance abuse and mood disorders, but fewer vocal tics, and lower rates of ADHD and oppositional behavior than children with TS. They also found that the majority of tics presenting during adulthood represented recurrences of childhood-onset tics.

Nevertheless, life continues to be hard for those patients who do not experience improvement in their tics as adults. In studies of adult TS patients, it has been found that TS patients end up in a lower social class than their parents[26] and experience higher unemployment rates.[15] Decreased self-esteem and increased social anxiety have also been reported among adults who suffer from tics.[27] The existing literature though is not clear as to the major source of disability in adulthood, whether it stems from the tics vs. other psychopathologies.

A study investigating the impact of tics, OCSs, and impulsivity in 53 (33 under 17 and 20 over 18 years) Japanese patients with TS found that, despite a moderate correlation between tics and OCSs severity, the impact of OCSs on global functioning was greater than that of tics in children. For the adult group, global functioning scores were significantly and negatively correlated with only the YGTSS global severity scores ($r=-0.515$, $p=0.020$).[21]

Traditionally, TS has been viewed as a disease that is more common in men, thus women have always been under-represented in research. However, a large international sample with 3,500 individuals with TS (69% from North American samples) found that among adult patients the male preponderance was less pronounced.[28] In a study conducted to provide a phenomenological characterization of tic disorders among 185 adult women with tics, 61% reported clinically significant tics (YGTSS total severity $\geq$20; separating motor and vocal tics, 68% of women reported a motor tic total $\geq$12 and 30% reported a phonic tic total of $\geq$12). Almost a third of adult women with tics (28%) reported severe tic symptoms (YGTSS $\geq$30).[29] A sizeable number of adult women with persistent tics were suffering from psychiatric comorbidity and psychosocial consequences such as underachievement and social distress.[29]

TS psychiatric comorbidities in adulthood

Thibert et al.[27] assessed self-concept and self-consciousness in 98 adults with TS and found that people with TS and significant OCSs tend to have impaired self-concept and increased social anxiety, concluding that OCSs may be the main driving force of the negative functional consequences of tics. In contrast, TS patients with low OCSs did not significantly differ from the norm. The authors thus concluded that the presence of prominent OCSs rather than tics alone contributed to impaired self-concept, decreased self-esteem, and increased anxiety in this group of adult patients with TS.[27]

In another cohort of adult patients, 103 outpatients with TS completed a semi-structured interview and 90 completed questionnaires screening for depression, anxiety, and OCSs. QOL was measured with the Medical Outcomes Study SF-36 and the Quality of Life Assessment Schedule. Patients with TS showed significantly worse QOL than a general population sample, although they had better QOL than epilepsy. Factors that influenced QOL domains were employment status, tic severity, OCSs, anxiety, and depression.[15]

Conclusion

Even though tics improve with age, the adults who continue to have tics have significant problems with self-image, social adjustment, social anxiety, and incorporation in the work force. The presence of psychiatric comorbidities can further worsen this situation. Even though the literature is not conclusive, it appears that while the tics are usually not the main source of disability in childhood, they can be severe when they persist in adulthood and they are often the major impairment resulting from TS in adulthood. It is unclear how many patients continue to have problems in adulthood since the only information we have is from those who seek medical attention. Furthermore, patient organizations and networks are mostly geared toward children, leaving adult patients with TS in many instances isolated from their peers.

The available literature suggests that tic severity in childhood is the strongest predictor of increased tic severity at follow-up later in life.[7,24] We know that ADHD can be a major factor influencing functioning at multiple levels in children with TS, mostly during the school years, and OCD although appearing later is more persistent and disruptive in adulthood and needs to be addressed when it is severe enough to affect function. Although common sense suggests that early treatment of ADHD, OCD, and other psychiatric comorbidities in childhood will help produce better adjusted adults, to date there are no data confirming that more aggressive treatment of psychiatric comorbidities in childhood will improve disability in adulthood.

The future

It is generally agreed that a large but undetermined proportion of individuals with TS remains undiagnosed in the community.[30] Among the patients who present themselves to the medical establishment for treatment, each one has a specific combination of problems. Although the phenomenology of TS is becoming clearer, what is included in the TS spectrum remains under debate. TS is a multifaceted clinical

syndrome and the clinician is often asked to recognize and rank the presenting symptoms. As clinicians, we need to improve our understanding of what symptoms produce the most disability in children, adults, and other demographic subgroups of patients with TS and use sensitive instruments to measure them both subjectively and objectively.

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