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Pediatric Prevention: Tic Disorders

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Keywords

Tourette disorder, Tics, Children, Behavior therapy, CBIT

Key points

- It is not clear whether the development of tics can be prevented, but individuals with tics may be able to use various strategies to prevent the worsening of tics.
- Teaching families to shift attention to behaviors that reduce tics instead of attending to tics is an important part of decreasing tic severity.
- Various medications can serve as treatment options to reduce tic severity.
- Behavioral treatment is the gold standard psychotherapy intervention for tic disorders, with multiple studies demonstrating its efficacy and few side effects.
- CBIT is the most well-supported nonpharmacological treatment for children with tics.

Introduction

Tourette disorder (TD) is a childhood-onset neurologic condition, which involves the performance of sudden, repetitive, nonrhythmic motor movements and vocalizations that persist for at least 1 year.¹ The disorder is more prevalent in males, and cross-cultural studies suggest that it occurs in about 0.5% to 1% of youth.^{2, 3, 4, 5} The condition is believed to result from failed inhibition within cortico-striatal-thalamo-cortical circuits, because abnormally active striatal neurons in the basal ganglia lead to the release of unwanted motor movements and vocalizations.⁶

Although tic disorders have a neurologic basis, studies demonstrate that the environmental context plays a significant role in tic expression. Contextual factors, such as particular settings, participating in activities, reactions of other people to tics, and emotions have all been found to impact tic severity.⁷ These variables interact with biological processes to help explain the variability in tics. Typical tic onset occurs between the ages 5 and 7 years, and tics tend to increase in frequency and intensity until children are approximately 10 to 11 years.^{2, 8, 9, 10} Tics are categorized into simple and complex, motor and vocal movements. Most tics are simple movements or vocalizations, such as eye blinks, head jerks, throat clears, or grunts; however, other tics involve coordinated actions by multiple muscle groups. Examples of complex tics can include fixed sequences of simple tics, touching and tapping, and various vocalizations.

Premonitory urges, uncomfortable physical sensations, such as an itch or a burn, often precede tics.¹¹ Such experiences are reported by over 90% of individuals with tics, and children often experience but cannot reliably report urges until approximately age 10 years.¹² Premonitory urges may occur in specific regions of the body where the tic occurs, or they may be experienced as “generalized” across the entire body. The uncomfortable sensation is usually relieved by the completion of the tic, and some individuals describe the urge to be more bothersome than the actual tic.¹³

Children and adolescents seeking treatment of TD usually have mild to moderate tic severity and impairment related to tics.^{13, 14} Tic severity is greatest around age 10 years, with close to 85% of individuals reporting a reduction in severity as they enter adolescence and young adulthood.^{9, 15} In a longitudinal study by Bloch and colleagues,¹⁵ approximately 33% of participants were tic free by late adolescence, and less than 25% showed mild or greater tic severity according to the Yale Global Tic Severity Scale.¹⁶ Furthermore, studies have shown that more severe tics are positively correlated with tic-related impairment in multiple settings.^{17, 18} Unsurprisingly, tics greater in number, frequency, intensity, complexity, and interference usually are more distressing and difficult to manage at home, in school, and in other public places.¹⁹ Stiede and colleagues¹⁸ also demonstrated that motor tic complexity and vocal tic number and intensity tend to contribute the most to impairment.

Although TD is defined by tics, co-occurring conditions are often present. Approximately 78% to 90% of individuals with TD experience one or more comorbidities, with attention deficit-hyperactivity disorder (ADHD) and obsessive-compulsive disorder (OCD) being the most common.^{2, 14, 20, 21, 22} Comorbid ADHD is present in 30% to 50% of people with TD, and 10% to 50% have OCD.^{20, 23} Children with TD are also at a higher risk for anxiety disorders, oppositional defiant disorder, and mood disorders.^{2, 20} Studies have demonstrated that lower quality of life, lower self-esteem, and poorer social functioning are more common for individuals with tics plus comorbidities than individuals with only tics.^{24, 25, 26}

Variables affecting the expression of tics

It is not clear whether the development of tics can be prevented, but individuals with tics may be able to use various strategies to prevent the worsening of tics and related psychosocial problems. Numerous studies have examined the role behavior therapy can play in tic management. The behavioral model suggests that settings (eg, school, home, friend's house), activities (eg, sports, music), the presence or absence of specific stimuli (eg, people, emotions, sensations), and reactions of other people to tics (eg, parents, peers) can all directly influence the occurrence of tics.⁷ These contextual variables can be broken down into antecedent and consequence factors.

Antecedents are external or internal events that occur before tics that may change the likelihood of tic expression.⁷ Settings, activities, and other people are examples of external antecedents. Studies have suggested that watching television and playing video games are associated with increases in tic expression, whereas concentrating on artistic or creative activities, such as painting, taking photographs, and playing/listening to music, are related to reductions in tics.^{27, 28, 29, 30} Internal antecedents include feelings, such as stress, boredom, anger, and frustration. Himle and colleagues³¹ demonstrated that stressful situations worsened tics in 74% of children. Similarly, Silva and colleagues³⁰ showed that anxiety-producing situations, such as starting a new school year, waiting for test results, and family conflict were the most common factors that increased tic severity.

Consequence variables are events that occur in reaction to tics. Studies suggest that reactions to tics can maintain or strengthen future probability of tics via positive or negative reinforcement.⁷ For example, Capriotti and colleagues³² demonstrated that social-based (eg, another kid teases child; parent gives child a hug) and escape-based (eg, child allowed to stop doing homework) consequences of tics were positively correlated with several dimensions of tic severity. Himle and colleagues³¹ also showed that attention-based reactions to tics (eg, consoling, telling a child to stop ticcing) were related to increases in tic frequency. Furthermore, Watson and Sterling³³ examined the relationship between parental attention and the prevalence of a 4-year-old child's coughing tic. Results demonstrated that parental attention for the tic was associated with greater tic severity, whereas positive parental attention for the absence of the tic led to a decrease in tic expression. Combined, these studies suggest that reactions to mild tics may further exacerbate them, and actively ignoring tics may prevent the worsening of symptoms over time and lead to a less severe course.

Eaton and colleagues³⁴ examined the relationship between internalizing symptoms, reactions to tics, and tic severity. Results showed that children with higher levels of internalizing symptoms experienced more reactions to tics. In particular, children's total anxiety symptoms (ie, separation anxiety and social anxiety) were significantly positively correlated with consequences they received for their tics and total tic severity. Results also demonstrated that children with persistent tic disorders and increased depression received more accommodations for and reactions to displaying tics. Finally, a regression analysis indicated that total environmental consequences was a significant predictor of total tic severity. Overall, these studies suggest that teaching families to shift attention to behaviors that reduce tics instead of attending to tics is an important part of decreasing tic severity. Families that do not learn this concept run the potential risk of creating an environment that could exacerbate tics. In addition, with multiple studies demonstrating the influence of stress/anxiety on tics, the use of relaxation techniques may be beneficial.

There is also some evidence that the ability of children with recent-onset tics to suppress their tics can predict future tic severity. Kim and colleagues³⁵ had 45 children with recent-onset tics complete multiple tic suppression tasks in which they were asked to tic freely, to inhibit their tics, and to inhibit their tics in the presence of a reward. Researchers examined the children's tic severity at baseline and at a 12-month follow-up. Results showed that participants who showed better tic suppression in the presence of a reward exhibited reduced tic severity at the 12-month follow-up visit. These results suggest that better tic-inhibitory ability at tic onset may be associated with longer-term remission and/or reduction of tics, but future studies are needed to confirm this claim. Interestingly, simply asking a child to inhibit tics in the absence of a reward did not predict future tic outcome; therefore, the reward seems to be a key element in reducing the expression of tics.

Treatment options

Because ADHD and OCD are often more impairing than tics, and these comorbidities can influence the effectiveness of behavioral treatment, such comorbid conditions should be managed before tic-specific treatment begins.^{36,37} Furthermore, if children have provisional or mild tics, psychoeducation about tic disorders and the impact of the environment on tics may be enough to alleviate concerns.³⁸ However, if tics are associated with impairment, such as distress in school, bullying, or physical pain, then behavior therapy and pharmacotherapy are the 2 primary evidence-based interventions that should be considered.

Recently, the American Academy of Neurology (AAN) published recommendations for the assessment and treatment of tics, which were established by a multidisciplinary panel of tic experts.³⁹ The panel recommended that alpha-agonists should be considered in the treatment of tics, and that antipsychotic medication may be considered when the benefits of treatment outweigh the risks. Similarly, relative to other initial treatment options, such as other psychosocial/behavioral interventions and medication, the most well-supported behavioral treatment, Comprehensive Behavioral Intervention for Tics (CBIT), should be considered when treating tics.

Medication

Several medications serve as treatment options for tics. For milder tics, nonneuroleptic medications, such as clonidine and guanfacine, are the recommended option. These alpha-2 adrenergic agonists are regularly used to treat tics because they have relatively few side effects, but their effectiveness in reducing tic severity is usually modest.⁴⁰

For more severe tics, typical (eg, haloperidol, pimozide) and atypical neuroleptics (eg, aripiprazole, risperidone) seem to be more effective than alpha-2 adrenergic agonists in reducing tic severity.⁴¹ The efficacy of traditional neuroleptics (eg, haloperidol, pimozide, fluphenazine) has been demonstrated in multiple placebo-controlled trials.^{42, 43, 44} In addition, studies suggested that pimozide may have fewer side effects than haloperidol.^{45,46} Atypical neuroleptics, such as risperidone and aripiprazole have also been shown to be more effective than placebo, equally effective to pimozide and clonidine, and helpful for individuals with neuropsychiatric comorbidities.⁴¹ Unfortunately, side effects, such as dyskinesia, acute dystonia, depression, weight gain, drowsiness, and cardiac concerns can occur.⁴¹ Although these medications can reduce up to 70% of tics, side effects may restrict their use.⁴⁷

Other Emerging Medical Therapies

Although not rated as having high empirical support in the AAN review, there are other emerging medical therapies with some evidence for reducing tic severity. Recent studies have shown that tetrabenazine and deutetrabenazine may improve tic severity.^{48, 49, 50} Furthermore, patients with severe TD who have unsuccessfully tried medication and behavior therapy may benefit from deep brain stimulation (DBS), a treatment in which a neurostimulator sends electrical impulses into areas within the brain that have been associated with tics. Studies with adult patients have demonstrated decreases in tic severity after DBS; however, research on DBS for children is minimal.^{51,52} Finally, although there is some evidence that cannabinoids can significantly reduce tics, to date there is little evidence that cannabis-based medication reduces tics in youth.^{53,54}

Behavior Therapy

Behavioral treatment is considered the gold standard psychotherapy intervention for tic disorders, with multiple randomized controlled trials demonstrating its efficacy and no side effects reported.^{36,38} Habit reversal training (HRT), a type of behavior therapy, has shown efficacy in multiple clinical trials and meta-analyses.^{55, 56, 57, 58} Initially, it included 14 components, but Woods and colleagues⁵⁹ suggested that awareness training, competing response training, and social support are the 3 main therapeutic skills needed for the intervention. CBIT extended HRT to include psychoeducation and functional assessment/interventions.

Currently, CBIT is the most well-supported nonpharmacological treatment for children with tics.^{36,37,39,60} CBIT consists of psychoeducation, functional assessment/intervention, HRT, relaxation training, and a motivational reward program.⁶¹ In CBIT, therapists first provide the client with psychoeducation about tic disorders to minimize blame, stigma, and negative feelings related to the client's symptoms. Next, a functional assessment is completed to assess how the environment may impact tic expression. The therapist and client discuss internal and external antecedents, such as emotions, settings, and activities that are associated with increases in tic severity. For those antecedents identified as being associated with tic exacerbation, therapists examine attention, aversive, and escape-based consequences to tics that occur within these identified antecedents.

Following the functional assessment, functional interventions are developed to manage the antecedents and consequences associated with worsening tic severity.⁶¹ Next, the clinician implements HRT for each tic, which involves 3 elements. First, awareness training is completed to teach the client to recognize each tic and its associated premonitory urge. This step is important because if clients are not aware of their tics/urges, then it will be difficult to implement competing response exercises. After clients are aware of approximately 80% of tic occurrence, competing response training begins. Competing responses are behaviors that are physically incompatible with the target tic. Clients are instructed to use the competing response contingent on the tic or premonitory urge for 1 minute or until the urge goes away, whichever is longer. Finally, social support training is introduced to teach a social support person, in most cases a parent, how to assist the child in the implementation of the competing response. The support person's job is to praise correct implementation of the competing response and to prompt the children when they forget to do their competing response.⁶¹

Piacentini and colleagues⁶² demonstrated that CBIT is more effective than nonspecific supportive therapy in reducing tics and tic-related impairment in children with tic disorders, with 53% of participants showing significant improvement at the end of the 8-week intervention and 87% of responders exhibiting continued benefit 6 months after treatment. Furthermore, Woods and colleagues⁶³ showed that CBIT does not lead to adverse effects on disruptive behavior, attention, mood, and anxiety regulation, and Rizzo and colleagues⁶⁴ suggested that behavior therapy is as effective as neuroleptic medication in treating children and adolescents with tics.

Exposure and response prevention (ERP) for tics is another behavior therapy shown to reduce tics.^{65,66} In ERP, clients are asked to suppress their tics for gradually longer periods of time, with each 2-hour session consisting of exposure to sensory experiences and response prevention of tics. Unlike CBIT, all tics are targeted at once, and the therapist uses techniques, such as focusing on the urge, talking about tics, and describing situations or activities related to increases in tics, to elicit the premonitory urge. When tics occur, the therapist encourages the client to try even harder to suppress the tics, reminding them of what they would gain if they ignore the urge to tic. In a randomized controlled trial (RCT), Verdellen and colleagues⁶⁶ found no differences in posttreatment tic severity scores between participants given ERP or HRT. Pringsheim and colleagues³⁹ noted that if CBIT is unavailable, ERP may be an acceptable behavioral intervention.

Dissemination of behavior therapy

Although CBIT is effective at reducing tic severity and is rated as highly acceptable by clients, accessibility remains a problem.⁶⁷ A survey by Woods and colleagues⁶⁸ demonstrated that most clients desire CBIT, but only approximately 6% of treatment-seeking children/families and 4% of treatment-seeking adults have received CBIT. The most common reason given for not receiving CBIT was a lack of knowledgeable and trained providers. Because CBIT's limited availability, efforts have been made to enhance its dissemination using telehealth and a self-guided Web-based treatment. Because there are few providers trained in CBIT, these adaptations could provide greater access to the intervention.

To examine the effectiveness of CBIT delivered via telehealth, Himle and colleagues⁶⁷ had 20 children with TD complete 10 weeks of CBIT delivered either face-to-face or via videoconferencing. Regardless of format, individuals demonstrated significant equivalent decreases in tic severity, which suggests that receiving telehealth CBIT is a viable option for therapy. TicHelper.com ("TicHelper") is another treatment option if CBIT providers are inaccessible. TicHelper is an online, interactive self-help program, based on CBIT, for individuals with tics from 8 years old to adolescence.⁶⁹ The program was developed using an iterative testing and feedback process involving CBIT professionals, children with persistent tics, and their parents. An RCT comparing TicHelper with an Internet-based resources condition has been completed but has not yet been published. However, the site is based on the therapist manual used in Piacentini and colleagues,⁶² who showed that CBIT is more effective in reducing tics and tic-related impairment in children than supportive therapy.

In another attempt to disseminate CBIT treatment, the Tourette Association of America (TA) offers the TA-Behavior Therapy Institute, a 2-day in-person didactic and skills-based training for licensed social workers, health, or mental health practitioners.⁷⁰ After the training, each attendee can participate in 3 consultation calls with CBIT experts to discuss their training cases. An online training program, based

on the CBIT manual, is also being developed to provide therapists with another opportunity to become trained in CBIT.

Predictors of treatment outcome

Few studies have examined moderators and predictors of response to behavior therapy for children with tic disorders. Sukhodolsky and colleagues⁷¹ used data from 2 studies that compared CBIT with psychoeducation and supportive therapy to investigate moderators and predictors of treatment response. The combined sample consisted of 248 participants (177 male; 71 female), and selected variables included presence of baseline tic medication, tic phenomenology, age, sex, family functioning, treatment expectancy, and co-occurring ADHD, OCD, and anxiety disorders. Results demonstrated that the treatment effect of CBIT was significantly larger for participants not on tic medication compared with those on tic medication; yet, participants on tic medication still showed improvements with CBIT. The remaining variables tested did not moderate outcome.

Furthermore, Sukhodolsky and colleagues⁷¹ suggested that co-occurring anxiety disorders, severity of premonitory urges, participant positive expectancy, and higher overall severity, as measured by the Clinical Global Impression – Severity (CGI-S), predicted tic severity outcomes regardless of treatment assignment. For example, individuals with a comorbid anxiety disorder demonstrated less tic reduction after 10 weeks of treatment. Similar results were found by Nissen and colleagues⁷² who showed that high anxiety scores predicted less improvement in functional impairment after treatment. Thus, although relaxation training is an element of the behavioral program, these findings suggest that additional techniques to manage anxiety and stress may be beneficial for individuals with tics.

Premonitory urge severity was associated with lower tic reduction, suggesting that it may be more difficult for children with stronger premonitory urges to manage tics.⁷¹ Furthermore, Sukhodolsky and colleagues⁷¹ showed that optimism related to treatment outcome may be an important factor, as parents' and children's positive expectancy for change was associated with greater tic reduction. Similarly, Nissen and colleagues⁷² demonstrated that patients who believed that it is extremely difficult to suppress tics, experienced poorer treatment outcome. Therefore, building rapport with clients to increase optimism and beginning HRT with a tic in which there is a better chance for success may be important elements for better treatment outcome. Both of these factors are emphasized in CBIT. Finally, Sukhodolsky and colleagues⁷¹ showed that participants with higher initial tic severity demonstrated greater tic reduction over time regardless of treatment condition.

Deckersbach and colleagues⁷³ also examined predictors of treatment response. They used a visuospatial priming task to investigate whether pretreatment response inhibition impairment in individuals given HRT predicted reductions in tic severity. Results suggested that participants with greater deficits in response inhibition did not respond as well to HRT, suggesting that it may be harder for individuals with poor baseline response inhibition to use competing response exercises. Similarly, other studies have found that attention problems are related to poorer tic suppressibility; thus, problems with attention could predict poorer response to behavioral treatments.^{74,75}

Summary

Although there is no information on how to prevent the development of tics, various strategies have been shown to be effective in secondary and tertiary prevention of tics and related psychosocial problems. A behavioral model indicates that contextual variables can impact tic expression; therefore, functional assessments are used to identify antecedents and consequences related to tic exacerbation and attenuation. Functional interventions also are used to modify antecedents and consequences associated with greater tic severity. Furthermore, medication can be prescribed to reduce tic severity; however, side effects may restrict their use. Finally, in CBIT, competing responses are implemented to give individuals an exercise that they can use when they feel the urge to tic. Overall, although children may be unable to prevent the development of tics, they can still use several strategies to reduce their tic severity and impairment.

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References

- 1 American Psychiatric Association. **Diagnostic and statistical manual of mental disorders.** (5th edirion), American Psychiatric Association, Washington, DC (2013)
- 2 R.D. Freeman, D.K. Fast, L. Burd, *et al.* **An international perspective on Tourette syndrome: selected findings from 3500 individuals in 22 countries.** *Dev Med Child Neurol*, 42 (2000), pp. 436-447
- 3 N. Khalifa, A.L. Von Knorring. **Prevalence of tic disorders and Tourette syndrome in a Swedish school population.** *Dev Med Child Neurol*, 45 (2003), pp. 315-319
- 4 T. Knight, T. Steeves, L. Day, *et al.* **Prevalence of tic disorders: a systematic review and meta-analysis.** *Pediatr Neurol*, 47 (2012), pp. 77-90
- 5 J.M. Scharf, L.L. Miller, C.A. Mathews, *et al.* **Prevalence of Tourette syndrome and chronic tics in the population-based Avon longitudinal study of parents and children cohort.** *J Am Acad Child Adolesc Psychiatry*, 51 (2012), pp. 192-201
- 6 T. Deckersbach, T. Chou, J.C. Britton, *et al.* **Neural correlates of behavior therapy for Tourette's disorder.** *Psychiatry Res*, 224 (2014), pp. 269-274
- 7 C.A. Conelea, D.W. Woods. **The influence of contextual factors on tic expression in Tourette's syndrome: a review.** *J Psychosom Res*, 65 (2008), pp. 487-496
- 8 J.T. Kraft, S. Dalsgaard, C. Obel, *et al.* **Prevalence and clinical correlates of tic disorders in a community sample of school-age children.** *Eur Child Adolesc Psychiatry*, 21 (2012), pp. 5-13
- 9 J.F. Leckman, H. Zhang, A. Vitale, *et al.* **Course of tic severity in Tourette syndrome: the first two decades.** *Pediatrics*, 102 (1998), pp. 14-19
- 10 C.A. Mathews, L.D. Herrera Amighetti, T.L. Lowe, *et al.* **Cultural influences on diagnosis and perception of Tourette syndrome in Costa Rica.** *J Am Acad Child Adolesc Psychiatry*, 40 (2001), pp. 456-463
- 11 J.F. Leckman, D.E. Walker, D.J. Cohen. **Premonitory urges in Tourette's syndrome.** *Am J Psychiatry*, 150 (1993), pp. 98-102
- 12 D.W. Woods, J. Piacentini, M.B. Himle, *et al.* **Premonitory Urge for Tics Scale (PUTS): initial psychometric results and examination of the premonitory urge phenomenon in youths with tic disorders.** *J Dev Behav Pediatr*, 26 (2005), pp. 397-403

- 13 L. Scahill, M.G. Aman, C.J. McDougle, *et al.* **Trial design challenges when combining medication and parent training in children with pervasive developmental disorders.** *J Autism Dev Disord*, 39 (2009), pp. 720-729
- 14 M.W. Specht, D.W. Woods, J. Piacentini, *et al.* **Clinical characteristics of children and adolescents with a primary tic disorder.** *J Dev Phys Disabil*, 23 (2011), pp. 15-31
- 15 M.H. Bloch, B.S. Peterson, L. Scahill, *et al.* **Adulthood outcome of tic and obsessive-compulsive symptom severity in children with Tourette syndrome.** *Arch Pediatr Adolesc Med*, 160 (2006), pp. 65-69
- 16 J.F. Leckman, M.A. Riddle, M.T. Hardin, *et al.* **The Yale Global Tic Severity scale: initial testing of a clinician-rated scale of tic severity.** *J Am Acad Child Adolesc Psychiatry*, 28 (1989), pp. 566-573
- 17 K.I. Cloes, K.S.F. Barfell, P.S. Horn, *et al.* **Preliminary evaluation of child self-rating using the Child Tourette Syndrome Impairment Scale.** *Dev Med Child Neurol*, 59 (2017), pp. 284-290
- 18 J.T. Stiede, J.R. Alexander, B. Wellen, *et al.* **Differentiating tic-related from non-tic-related impairment in children with persistent tic disorders.** *Compr Psychiatry*, 87 (2018), pp. 38-45
- 19 E.A. Storch, C.W. Lack, L.E. Simons, *et al.* **A measure of functional impairment in youth with Tourette's syndrome.** *J Pediatr Psychol*, 32 (2007), pp. 950-959
- 20 M.E. Hirschtritt, P.C. Lee, D.L. Pauls, *et al.* **Lifetime prevalence, age of risk, and genetic relationships of comorbid psychiatric disorders in Tourette syndrome.** *JAMA Psychiatry*, 72 (2015), pp. 325-333
- 21 E.R. Lebowitz, M.G. Motlagh, L. Katsovich, *et al.* **Tourette syndrome in youth with and without obsessive compulsive disorder and attention deficit hyperactivity disorder.** *Eur Child Adolesc Psychiatry*, 21 (2012), pp. 451-457
- 22 T. Sambrani, E. Jakubowski, K.R. Muller-Vahl. **New insights into clinical characteristics of Gilles de la Tourette syndrome: findings in 1032 patients from a single German center.** *Front Neurosci*, 10 (2016), p. 415
- 23 R. Kurlan, P.G. Como, B. Miller, *et al.* **The behavioral spectrum of tic disorders: a community-based study.** *Neurology*, 59 (2002)
- 24 N. Debes, H. Hjalgrim, L. Skov. **The presence of attention-deficit hyperactivity disorder (ADHD) and obsessive-compulsive disorder worsen psychosocial and educational problems in Tourette syndrome.** *J Child Neurol*, 25 (2010), pp. 171-181
- 25 V. Eapen, R. Črnčec, S. McPherson, *et al.* **Tic disorders and learning disability: clinical characteristics, cognitive performance and comorbidity.** *Australas J Spec Educ*, 37 (2013), pp. 162-172
- 26 V. Eapen, A.E. Cavanna, M.M. Robertson. **Comorbidities, social impact, and quality of life in Tourette syndrome.** *Front Psychiatry*, 7 (2016), p. 97
- 27 M. Barnea, N. Benaroya-Milshtein, E. Gilboa-Sechtman, *et al.* **Subjective versus objective measures of tic severity in Tourette syndrome: the influence of environment.** *Psychiatry Res*, 242 (2016), pp. 204-209
- 28 B. Caurín, M. Serrano, E. Fernández-Alvarez, *et al.* **Environmental circumstances influencing tic expression in children.** *Eur J Paediatr Neurol*, 18 (2014), pp. 157-162
- 29 S. Bodeck, C. Lappe, S. Evers. **Tic-reducing effects of music in patients with Tourette's syndrome: self-reported and objective analysis.** *J Neurol Sci*, 352 (2015), pp. 41-47
- 30 R.R. Silva, D.M. Munoz, J. Barickman, *et al.* **Environmental factors and related fluctuation of symptoms in children and adolescents with Tourette's disorder.** *J Child Psychol Psychiatry*, 36 (1995), pp. 305-312

- 31 M.B. Himle, M.R. Capriotti, L.P. Hayes, *et al.* **Variables associated with tic exacerbation in children with chronic tic disorders.** *Behav Modif*, 38 (2014), pp. 163-183
- 32 M.R. Capriotti, J.C. Piacentini, M.B. Himle, *et al.* **Assessing environmental consequences of ticcing in youth with chronic tic disorders: the Tic Accommodation and Reactions Scale.** *Child Health Care*, 44 (2015), pp. 205-220
- 33 T.S. Watson, H.E. Sterling. **Brief functional analysis and treatment of a vocal tic.** *J Appl Behav Anal*, 31 (1998), pp. 471-474
- 34 C.K. Eaton, A.M. Jones, A.M. Gutierrez-Colina, *et al.* **The influence of environmental consequences and internalizing symptoms on children's tic severity.** *Child Psychiatry Hum Dev*, 48 (2017), pp. 327-334
- 35 S. Kim, D.J. Greene, A. Robichaux-Viehoever, *et al.* **Tic suppression in children with recent-onset tics predicts 1-year tic outcome.** *J Child Neurol*, 34 (2019), pp. 757-764
- 36 T.K. Murphy, A.B. Lewin, E.A. Storch, *et al.* **Practice parameter for the assessment and treatment of children and adolescents with tic disorders: Committee on Quality Issues (CQI).** *J Am Acad Child Adolesc Psychiatry*, 52 (2013), pp. 1341-1349
- 37 C. Verdellen, J. Van De Griendt, A. Hartmann, *et al.* **European clinical guidelines for Tourette syndrome and other tic disorders. Part III: Behavioural and psychosocial interventions.** *Eur Child Adolesc Psychiatry*, 20 (2011), pp. 197-207
- 38 D. Martino, T.M. Pringsheim. **Tourette syndrome and other chronic tic disorders: an update on clinical management.** *Expert Rev Neurother*, 18 (2018), pp. 125-137
- 39 T. Pringsheim, M.S. Okun, K. Müller-Vahl, *et al.* **Practice guideline recommendations summary: treatment of tics in people with Tourette syndrome and chronic tic disorders.** *Neurology*, 92 (2019), pp. 896-906
- 40 H. Weisman, I.A. Qureshi, J.F. Leckman, *et al.* **Systematic review: pharmacological treatment of tic disorders—efficacy of antipsychotic and alpha-2 adrenergic agonist agents.** *Neurosci Biobehav Rev*, 37 (2013), pp. 1162-1171
- 41 J. Quezada, K.A. Coffman. **Current approaches and new developments in the pharmacological management of Tourette syndrome.** *CNS Drugs*, 32 (2018), pp. 33-45
- 42 M.S. Ross, H. Moldofsky. **A comparison of pimozide and haloperidol in the treatment of Gilles de la Tourette's syndrome.** *Am J Psychiatry*, 135 (1978), pp. 585-587
- 43 A.K. Shapiro, E. Shapiro. **Controlled study of pimozide vs. placebo in Tourette's syndrome.** *J Am Acad Child Psychiatry*, 23 (1984), pp. 161-173
- 44 E. Shapiro, A.K. Shapiro, G. Fulop, *et al.* **Controlled study of haloperidol, pimozide, and placebo for the treatment of Gilles de la Tourette's syndrome.** *Arch Gen Psychiatry*, 46 (1989), pp. 722-730
- 45 C.L. Budman. **The role of atypical antipsychotics for treatment of Tourette's syndrome: an overview.** *Drugs*, 74 (2014), pp. 1177-1193
- 46 V. Roessner, K.J. Plessen, A. Rothenberger, *et al.* **European clinical guidelines for Tourette syndrome and other tic disorders. Part II: pharmacological treatment.** *Eur Child Adolesc Psychiatry*, 20 (2011), pp. 173-196
- 47 D. Huys, K. Hardenacke, P. Poppe, *et al.* **Update on the role of antipsychotics in the treatment of Tourette syndrome.** *Neuropsychiatr Dis Treat*, 8 (2012), pp. 95-104
- 48 J.J. Chen, W.G. Ondo, K. Dashtipour, *et al.* **Tetrabenazine for the treatment of hyperkinetic movement disorders: a review of the literature.** *Clin Ther*, 34 (2012), pp. 1487-1504
- 49 J. Jankovic. **Dopamine depleters in the treatment of hyperkinetic movement disorders.** *Expert Opin Pharmacother*, 17 (2016), pp. 2461-2470

- 50 C. Kenney, C. Hunter, J. Jankovic. **Long-term tolerability of tetrabenazine in the treatment of hyperkinetic movement disorders.** *Mov Disord*, 22 (2007), pp. 193-197
- 51 W. Deeb, P.J. Rossi, M. Porta, *et al.* **The international deep brain stimulation registry and database for Gilles de la Tourette syndrome: how does it work?** *Front Neurosci*, 10 (2016), p. 170
- 52 P.J. Rossi, E. Opri, J.B. Shute, *et al.* **Scheduled, intermittent stimulation of the thalamus reduces tics in Tourette syndrome.** *Parkinsonism Relat Disord*, 29 (2016), pp. 35-41
- 53 P.F. Whiting, R.F. Wolff, S. Deshpande, *et al.* **Cannabinoids for medical use: a systematic review and meta-analysis.** *JAMA*, 313 (2015), pp. 2456-2473
- 54 Tourette Association of America position statement on the use of medical marijuana for Tourette Syndrome, Tourette Association of America (2019). Available at: <https://tourette.org/research-medical/medical-marijuana/> Accessed October 25, 2019
- 55 N.H. Azrin, R.G. Nunn. **Habit-reversal: a method of eliminating nervous habits and tics.** *Behav Res Ther*, 11 (1973), pp. 619-628
- 56 N.H. Azrin, A.L. Peterson. **Treatment of Tourette syndrome by habit reversal: a waiting-list control group comparison.** *Behav Ther*, 21 (1990), pp. 305-318
- 57 K.S. Bate, J.M. Malouff, E.T. Thorsteinsson, *et al.* **The efficacy of habit reversal therapy for tics, habit disorders, and stuttering: a meta-analytic review.** *Clin Psychol Rev*, 31 (2011), pp. 865-871
- 58 J.F. McGuire, J. Piacentini, E.A. Brennan, *et al.* **A meta-analysis of behavior therapy for Tourette syndrome.** *J Psychiatr Res*, 50 (2014), pp. 106-112
- 59 D.W. Woods, R.G. Miltenberger. **A review of habit reversal with childhood habit disorders.** *Educ Treat Children*, 19 (1996), pp. 197-214
- 60 T. Steeves, B.D. McKinlay, D. Gorman, *et al.* **Canadian guidelines for the evidence-based treatment of tic disorders: behavioural therapy, deep brain stimulation, and transcranial magnetic stimulation.** *Can J Psychiatry*, 57 (2012), pp. 144-151
- 61 D.W. Woods, J.C. Piacentini, S.W. Chang, *et al.* **Managing Tourette syndrome: a behavioral intervention for children and adults.** Oxford University Press, New York (2008)
- 62 J. Piacentini, D.W. Woods, L. Scahill, *et al.* **Behavior therapy for children with Tourette disorder: a randomized controlled trial.** *J Am Med Assoc*, 303 (2010), pp. 1929-1937
- 63 D.W. Woods, J.C. Piacentini, L. Scahill, *et al.* **Behavior therapy for tics in children: acute and long-term effects on psychiatric and psychosocial functioning.** *J Child Neurol*, 26 (2011), pp. 858-865
- 64 R. Rizzo, A. Pellico, P.R. Silvestri, *et al.* **A randomized controlled trial comparing behavioral, educational, and pharmacological treatments in youths with chronic tic disorder or Tourette syndrome.** *Front Psychiatry*, 9 (2018), p. 100
- 65 K. Hoogduin, C. Verdellen, D. Cath. **Exposure and response prevention in the treatment of Gilles de la Tourette's syndrome: four case studies.** *Clin Psychol Psychother*, 4 (1997), pp. 125-135
- 66 C.W.J. Verdellen, G.P.J. Keijsers, D.C. Cath, *et al.* **Exposure with response prevention versus habit reversal in Tourette's syndrome: a controlled study.** *Behav Res Ther*, 42 (2004), pp. 501-511
- 67 M.B. Himle, M. Freitag, M. Walther, *et al.* **A randomized pilot trial comparing videoconference versus face-to-face delivery of behavior therapy for childhood tic disorders.** *Behav Res Ther*, 50 (2012), pp. 565-570
- 68 D.W. Woods, C.A. Conelea, M.B. Himle. **Behavior therapy for Tourette's disorder: utilization in a community sample and an emerging area of practice for psychologists.** *Prof Psychol Res Pract*, 41 (2010), pp. 518-525

- 69 C.A. Conelea, B.C.M. Wellen. **Tic treatment goes tech: a review of TicHelper.com.** *Cogn Behav Pract*, 24 (2017), pp. 374-381
- 70 Tourette syndrome behavior therapy institute (TS-BTI), Tourette Association of America (2019). Available at: <https://tourette.org/cbit-bti-training/> Accessed October 25, 2019
- 71 D.G. Sukhodolsky, D.W. Woods, J. Piacentini, *et al.* **Moderators and predictors of response to behavior therapy for tics in Tourette syndrome.** *Neurology*, 88 (2017), pp. 1029-1036
- 72 J.B. Nissen, E.T. Partner, P.H. Thomsen. **Predictors of therapeutic treatment outcome in adolescent chronic tic disorders.** *BJPsych Open*, 5 (2019), pp. 1-6
- 73 T. Deckersbach, S. Rauch, U. Buhlmann, *et al.* **Habit reversal versus supportive psychotherapy in Tourette's disorder: a randomized controlled trial and predictors of treatment response.** *Behav Res Ther*, 44 (2006), pp. 1079-1090
- 74 B.S. Peterson, P. Skudlarski, A.W. Anderson, *et al.* **A functional magnetic resonance imaging study of tic suppression in Tourette syndrome.** *Arch Gen Psychiatry*, 55 (1998), pp. 326-333
- 75 M.B. Himle, D.W. Woods. **An experimental evaluation of tic suppression and the tic rebound effect.** *Behav Res Ther*, 43 (2005), pp. 1443-1451