Managing tic disorders: an update on Tourette syndrome

Gilles de la Tourette syndrome is a neuropsychiatric disorder characterised by multiple motor and vocal tics. Commonly seen in school-aged children, Tourette syndrome can mimic many hyperkinetic disorders, making the diagnosis challenging at times. Prompt and early diagnosis followed by appropriate treatment can improve the quality of life of affected individuals.

VALSAMMA EAPEN
PhD, FRCPsych, FRANZCP

PERMINDER SACHDEV
MD, PhD, FRANZCP

Professor Eapen is Professor and Chair of Infant, Child and Adolescent Psychiatry at the University of New South Wales, Liverpool Hospital, Sydney. Professor Sachdev is Professor of Neuropsychiatry at the University of New South Wales, and Director of the Neuropsychiatric Institute at the Prince of Wales Hospital, Sydney, NSW.

Gilles de la Tourette Syndrome is an inherited neuropsychiatric disorder characterised by the presence of multiple motor and one or more vocal tics, with an onset during childhood and a fluctuating course with periods of remission and exacerbation. The first medical description of Tourette syndrome has been attributed to Itard in 1825. Subsequently the prominent French neuropsychiatrist and pupil of Charcot, Georges Gilles de la Tourette described nine cases of Tourette syndrome in 1885, emphasising the triad of multiple tics, coprolalia and echolalia (see Table 1 for definitions of these and other symptoms). Until the 1970s, Tourette syndrome was considered a rare disorder and a medical curiosity. Owing to recent epidemiological work, we now recognise it to be relatively common but under recognised and a major cause of hidden disability.[1]

Clinical characteristics

Tourette syndrome occurs in people of all cultures, racial groups and social classes with some degree of uniformity of the core features but with variability in the comorbid conditions.[2] The age at onset of symptoms ranges from 2 to 15 years, with a mean age of 7 years. The most frequent symptoms are simple motor tics that involve the eyes (e.g. eye blinking, eye rolling), face (e.g. nose twitching,

IN SUMMARY

- **Tourette syndrome is a relatively common disorder affecting up to 1% of the population, but the diagnosis can often be missed.**
- **Characteristic features of Tourette syndrome include both multiple motor tics and one or more vocal tics that have been present for more than a year.**
- **Tics can be successfully treated with dopamine antagonists, alpha-adrenergic agonists or atypical antipsychotic agents.**
- **Common comorbid conditions include obsessive compulsive disorder and attention deficit hyperactivity disorder, which may necessitate treatment with selective serotonin reuptake inhibitors and stimulants (with caution), respectively.**
- **Although counselling, supportive psychotherapy and cognitive behaviour therapy for Tourette syndrome and associated symptoms may be beneficial, formal psychotherapy is not recommended for patients with tic disorders.**

Table 1. Definitions of symptoms of Tourette syndrome

Copropraxia
Involuntary and inappropriate obscene gestures

Coprolalia
Inappropriate and involuntary uttering of obscenities

Echopraxia
Imitation of movements or actions of others

Echolalia
Imitation of sounds or words of others

Palilalia
Repetition of the last word, phrase or syllable

grimacing), neck (jerking) and shoulders (shrugging). Complex motor tics may include licking, hitting, jumping, smelling, spitting, squatting, abnormalities of gait and forced touching.[3]

The onset of vocal tics is usually later, at a mean age of 11 years, with throat clearing, sniffing, grunting, coughing, barking, snorting, humming, clicking, colloquial emotional exclamations, and low- or high-pitched noises. Coprolalia occurs in less than one-third of clinic patients with Tourette syndrome, whereas copropraxia occurs in about one-fifth. Other symptoms such as echolalia and echopraxia have been described in 11 to 44% of patients with Tourette syndrome,[3] and palilalia in 6 to 15% of such patients (see Table 1 for definitions of these symptoms).

According to the DSM-IV criteria, the presence of multiple motor tics and at least one vocal tic, not necessarily concurrently, for over one year is necessary for a diagnosis of Tourette syndrome (see the box on page 16 for the diagnostic criteria for Tourette syndrome).[4] Although the other clinical features are not essential in making the diagnosis, the presence of any of these behaviours would increase the clinician's diagnostic confidence.

The hallmark of a tic that separates it from other involuntary movements is that it is preceded by an 'urge to move or vocalise', which the patient may be variably able to suppress or postpone, and the movement or noise is said to be in response to this urge. Symptoms are suggestible and suppressible: patients are able to suppress symptoms voluntarily for brief periods of time at the expense of mounting inner tension. Many patients with Tourette syndrome also describe premonitory 'sensory' experiences such as a stretch, itch or tickling sensation just prior to the occurrence of the tic and this is relieved after the tic. Tics and vocalisations are aggravated by anxiety, stress, boredom, fatigue and excitement, whereas sleep, orgasm, relaxation or concentrating on an enjoyable task usually leads to temporary disappearance of symptoms.

The lifetime course is characterised by waxing and waning of symptoms, with the appearance of new tics replacing the older ones. Symptoms may

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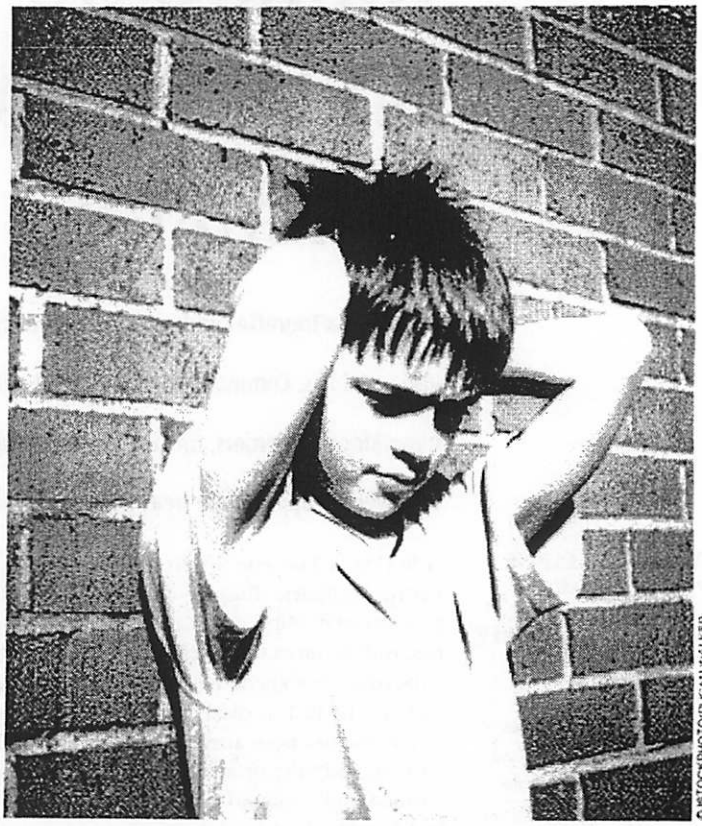


There is no cure for Tourette syndrome. The goals of treatment, therefore, are to reduce the severity, frequency and disruptive impact of symptoms, to manage associated psychiatric and learning problems, and to improve social functioning and quality of life.

Diagnostic criteria for Tourette syndrome (DSM-IV)[4]

- Both multiple motor tics and one or more vocal tics must be present at some time, although not necessarily concurrently.
- The tics must occur many times a day (usually in bouts) nearly every day or intermittently over more than one year, during which time there must not have been a tic-free period of more than three consecutive months.
- The onset must occurs before 18 years of age.
- The disturbance must not be caused by the direct physiological effects of a substance (e.g. stimulants) or a general medical condition (e.g. Huntington's disease, postviral encephalitis).

worsen in early and mid-adolescence, but in one-third of patients the tic symptoms will remit completely by late adolescence. An additional one-third of patients with Tourette syndrome will show significant improvement by early adulthood.

Associated psychopathology

The relation between Tourette syndrome and obsessive compulsive disorder (OCD) has been well documented.[5] An association between attention deficit hyperactivity disorder (ADHD) and some types of self-injurious behaviour with Tourette syndrome is also well known. Sleep problems are commonly encountered, and depression and anxiety have been shown to occur more often in patients with Tourette syndrome than in controls. However, these may be secondary phenomena caused by the severe and socially handicapping nature of Tourette syndrome, the effects of medication or the effects of comorbidity and ascertainment bias within clinic population. A possible genetic mechanism and coexistence by chance due to the high life-time prevalence of anxiety and depression are other possible explanations.

Some investigators have suggested that a number of psychiatric disorders, including anxiety, phobias, depression, bipolar disorder, schizophreniform psychosis, learning disability, eating disorder, substance use and pathological gambling, may be alternative phenotypic expressions of the same Tourette syndrome gene(s), but this is controversial.[1]

Prevalence

It is believed that the earlier widely accepted prevalence rate of Tourette syndrome of 0.5/1000 may be an underestimate, with the more recent studies reporting rates of 1 to 3% and a male to female ratio of 3 to 4:1.[6] Some recent prevalence studies conducted in schools suggest a prevalence rate of Tourette syndrome of between 0.6 and 1.0% in children aged 5 to 17 years and much higher rates for tic disorders – 6.6% in a Swedish study[7] and 2.9% in an Italian study.[8]

The prevalence of tic disorders and Tourette syndrome is even higher in certain select populations such as in those with mental retardation and autistic spectrum disorders. Rates of 28% for tics and 12% for Tourette syndrome were reported among 3034 pupils referred for psychoeducational assessments in California.[9] In a study from the UK, tics were noted in 65% of students with behavioural and emotional problems, 24% of those with learning difficulties and 6% of those with other problems, compared with children who showed no symptoms of tics and had no problems.[10] Tourette syndrome does not, however, appear to be over represented in adult psychiatric inpatients.[11]

Neurobiological findings

With regard to the neurobiological substrates of Tourette syndrome, the role of basal ganglia and frontal-subcortical circuits, as well as dopaminergic neurotransmission, have attracted much attention. There is growing evidence of the role of multiple parallel neuronal circuits involving fronto-striato-pallido-thalamo-frontal circuits in Tourette syndrome. Of the neuotransmitters, dopamine has received the most attention because of the beneficial effects of dopamine antagonists in reducing the tic symptoms, whereas stimulants such as dexamphetamine and methylphenidate exacerbate the symptoms. There is also support for dopamine involvement from imaging studies.[12]

In 1995 it was also suggested that tics and associated behaviours including OCD might develop from streptococcal infection by the process of molecular mimicry, whereby antibodies directed against bacterial antigens cross-react with brain targets. This spectrum of neurobehavioural disorders has been termed paediatric autoimmune neuropsychiatric disorders associated with streptococcal infection (PANDAS). However, there is debate as to whether this may have a direct aetiological role or whether it merely precipitates tics in a predisposed individual and modulates the phenotypic expression of Tourette syndrome.

In a review of immune abnormalities in Tourette syndrome, OCD and PANDAS, it was reported that there is a subset of patients with Tourette syndrome and OCD, perhaps 10%, in whom there is a clear streptococcal trigger.[13] This may have implications for diagnosis and treatment, particularly in children in whom there is a clear temporal relation between streptococcal infection and the onset of tics, followed by remission of tics with improvement of the infection.[14]

There is a widely held belief among both the lay public and patients with Tourette syndrome that symptoms are associated with allergy,[15] but there is little scientific evidence to support this.[16] However, one study of 300 patients with Tourette syndrome showed that although there is no evidence that allergies cause Tourette syndrome, symptom exacerbation

is often associated with seasonal allergy responses and the ingestion of allergens in food, as well as by the drugs used to treat allergies.[17] A study using multiple allergen simultaneous tests (MAST) showed that the prevalence of allergy in patients with Tourette syndrome is significantly higher than in the general population.[18]

Genetic studies

Available evidence from twin, family and molecular genetic studies strongly suggest a genetic aetiology to Tourette syndrome with a number of candidate genes being implicated.[19] The mechanisms involved seem more complicated than a single gene. Previous studies have identified different genetic loci and chromosomal regions of interest and suggest the possibility of multiple alleles and genetic heterogeneity, as well as multifactorial inheritance with genetic and environmental contributions.

Clinical evaluation

Tourette syndrome is a neuropsychiatric disorder par excellence, and both neurological and psychiatric symptoms deserve attention. A detailed medical and psychiatric history and thorough physical and neurological examinations are indicated. Special attention should be given to the evaluation of comorbid disorders such as obsessive compulsive symptoms or disorder, ADHD, disruptive behaviours or personality disorder, depression and anxiety.

An educational assessment is often helpful because of the frequent presence of learning difficulties and attentional problems; this can be carried out through the child's school. Assessment of Tourette syndrome should include the involvement of family members, teachers and significant others who are affected and whose reactions in turn affect the symptoms.

Differential diagnoses

The characteristic features described above, as well as the stereotypic nature of the tics, are so distinctive that a diagnosis can be made on history alone. Despite this, diagnostic difficulties can sometimes occur. At the time of first onset, children are often referred to multiple specialists for possible eye, nose and throat problems or the problem is dismissed as 'nervousness'. Unfortunately, it is still not uncommon for children to be undiagnosed for many years.

One of the differential diagnoses at the early stage of Tourette syndrome is that of tics of childhood. These tics commence between the ages of 5 to 10 years, but they are not multiple nor persistent and remit spontaneously within weeks or months. If the symptoms persist beyond a year, a chronic tic disorder is diagnosed and if both motor and vocal tics have manifested, the condition is referred to as Tourette syndrome. There is evidence from family genetic studies that Tourette syndrome, chronic tic disorder and simple tic disorder may in fact be on a continuum of severity with a shared genetic vulnerability.[20]

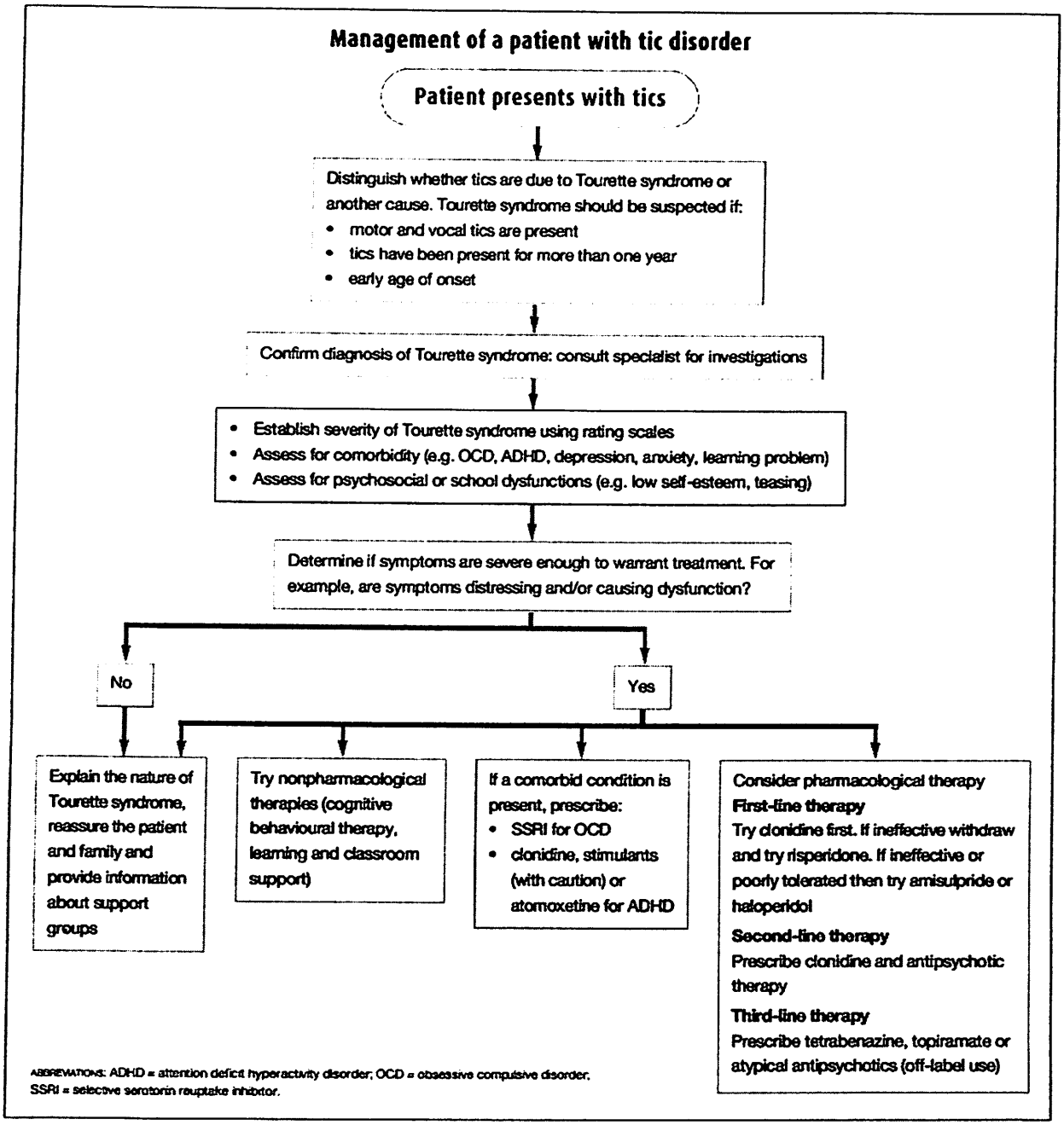
Conditions that should be considered in the differential diagnoses of Tourette syndrome are detailed in Table 2. Most of these have distinctive clinical features and classical courses and are associated with characteristic types of movements that usually make it possible to differentiate them from Tourette syndrome. Other conditions to be excluded are restless leg syndrome, myoclonus and epilepsy, especially myoclonic epilepsy.

Table 2. Differential diagnoses of tics and Tourette syndrome

Condition	Differentiating feature
Athetoid type of cerebral palsy	Onset between birth and 3 years of age; static course; associated neurological deficit and learning disability
Dystonia musculorum deformans	Torsion dystonia of legs – progressive; crippling 10 to 15 years after onset
Spasmodic torticollis	Associated with spastic speech; static or progressive
Encephalitis lethargica	History of encephalitis; parkinsonian symptoms
Huntington's chorea	Onset in 3rd to 5th decades (1% in early childhood); usually a positive family history of Huntington's chorea; presence of choreoathetoid movements; progression to dementia; progression to death in 10 to 20 years
Tardive tourettism	History of long-term use of antipsychotics or other drugs such as levodopa, phenytoin, cocaine, stimulants, carbamazepine and lamotrigine; dyskinetic movements are common
Other neurological disorders	Associated with signs and symptoms specific to the disorder such as autistic disorder, poststroke, Sydenham's chorea, multiple sclerosis, Wilson's disease, Hallervorden-Spatz disease, Jakob-Creutzfeldt disease, choreoathetosis, neurofibromatosis, Arnold-Chiari malformation and status dysmyelinatus
Acquired tourettism	Trauma, carbon monoxide poisoning

Management

There is no cure for Tourette syndrome. The goals of treatment, therefore, are to



reduce the severity, frequency and disruptive impact of symptoms, to manage associated psychiatric and learning problems, and to improve social functioning and quality of life.

Pharmacological therapy

Although tics can attract a great deal of attention, it is not always necessary to suppress them except when it is felt that there is a deleterious effect on the patient's social, educational or occupational functioning. Drug therapy is, at present, the mainstay of treatment for the motor and vocal symptoms. The medications most commonly used are dopamine

antagonists and alpha-adrenergic drugs. Other medications, however, are also useful in the treatment of tics as well as the associated behaviours.

Since Tourette syndrome is a remitting-relapsing disorder, a few 'indicator tics' help assess the status of the disorder (the term indicator tic is used to denote any tic that is present during the assessment, the quality and nature of which would be indicative of the problem and serve as a prototype). We recommend a trial of clonidine (Catapres) first; if this is ineffective we suggest withdrawing it and then trying risperidone (Risperdal). If risperidone up to a dose of 4 mg per day is ineffective or poorly tolerated, amisulpride (Solian Tablets) or haloperidol (Haldol Decanoate, Serenace) may be tried (see the flowchart on page 18).

Dopamine antagonists

The butyrophenone haloperidol was the first drug used successfully for Tourette syndrome, and since then dopamine antagonists have been widely and successfully used. Doses are relatively small, beginning with, for example, in the case of haloperidol, a small dose of 0.25 to 0.5 mg daily and increasing slowly by 0.5 mg increments as needed. Extrapyramidal side effects, sedation and dysphoric states are common with haloperidol. School phobia and avoidance have also been reported as unwanted side effects of haloperidol. Typical antipsychotics may also impair concentration and scholastic achievement and may cause tardive dyskinesia.

Atypical antipsychotics

Atypical antipsychotics such as risperidone have also been found to be effective in treating symptoms of Tourette syndrome (at a mean daily dose of 1.5 mg per day [range of 0.5 to 4.0 mg/day]). It is recommended that risperidone be started at a dose of 0.25 mg and then titrated up by increments of 0.25 mg every four to five days. Commonly encountered side effects of risperidone include drowsiness, dizziness, weight gain and headache. Extrapyramidal side effects may occur but are less common. These can be reduced by starting at a low dose and increasing the dose gradually. Although clozapine has been found to be ineffective in treating symptoms of Tourette syndrome, other atypical antipsychotics, including olanzapine (Zyprexa) 5 to 10 mg, ziprasidone (Zeldox) 5 mg titrated up to 40 mg per day and aripiprazole (Abilify) 10 to 20 mg per day, have been reported to be of benefit.

Tiapride and sulpiride (both are not available in Australia) have been used successfully to treat Tourette syndrome in the UK; amisulpride, which belongs to the same group of medications, is available in Australia and has also been shown to be effective. The recommended dose of amisulpride is 200 to 1200 mg per day and the side effects include sedation and weight gain, as well as galactorrhoea and amenorrhoea in women.

Alpha-adrenergic agonists

The alpha-adrenergic agonists clonidine and guanfacine (the latter is not marketed in Australia) have been used successfully in patients with Tourette syndrome and they are the agents of choice particularly if a child has Tourette syndrome and associated ADHD.

The usual effective dose of clonidine is 100 to 300 µg per day in two to three divided doses. The major side effects are sedation and postural hypotension. To reduce the impact of these side effects it is usual to start at a low dose (25 µg twice daily) and up titrate by increments of 25 µg per day every week or so until the optimal dose is reached. A trial of six to eight weeks is necessary before the drug is considered to be ineffective. If so, it should be withdrawn gradually over two to three weeks to avoid rebound hypertension.

Other therapies

Benzodiazepines are generally not effective for the symptoms of Tourette syndrome. Other drugs that have been tried with some success include tetrabenazine, fluphenazine (Modecate), clomipramine (Anafranil, Placil) topiramate (Topamax), clonazepam (Paxam, Rivotril) carbamazepine (Tegretol, Teril) and local injections of botulinum toxin (Botox, Dysport).[21] For medically refractory tics, deep brain stimulation has been tried in some selected cases with varying success (see the box on page 20).[22]

Nonpharmacological therapy

Successful management of patients with Tourette syndrome requires psychosocial measures and support to the patient and his or her family, as well as pharmacological intervention. For many children and adults with mild Tourette syndrome (around 50% of all patients with Tourette syndrome), explanation and reassurance are often sufficient along with information about self-help groups, and booklets for teachers and families. Assessment of impairment and comorbidity should guide the need for treatment and this can be carried out using assessment tools such as the National Hospital Interview Schedule for the assessment of Tourette syndrome and related behaviours.[23]

Behavioural therapy has limited value in ameliorating the tics and vocalisations of Tourette syndrome, although for the tic symptoms massed practice (over rehearsal of the target tic) and other forms of behavioural therapy can sometimes be helpful in substituting a more acceptable movement for a particularly difficult or socially unacceptable one. Relaxation training and meditative techniques may have a nonspecific ameliorating effect on tics. A referral of the patient to a clinical psychologist specialising in behavioural treatment is therefore a useful strategy. Similarly, parent management training has been found to be effective in the overall management of Tourette syndrome,

Deep brain stimulation

Deep brain stimulation (DBS) involves the implantation of electrodes deep in the brain for chronic stimulation and is aimed at disrupting neural activity in the target regions. DBS is a well-established treatment for severe and intractable Parkinson's disease, dystonia and essential tremor. There have been a few reports of DBS for severe tic disorders, including one recent case in Australia. Since this is symptomatic treatment with potential risks, it should be considered only in adult patients with chronic and severe tic disorders who are medically intractable and have severe functional impairment. They should be evaluated by a team with expertise in the management of tic disorders. Guidelines for patient selection and assessment recommendations have been developed[22] and a comprehensive research protocol is recommended. There is no consensus on the best target for DBS. Previous targets have included the centromedian–parafascicular complex of the thalamus, the internal segment of the globus pallidus and the anterior limb of the internal capsule.

particularly in dealing with disruptive behaviours.

Teachers and principals should be informed about Tourette syndrome and its associated behaviours (especially ADHD, which may simultaneously affect concentration and disrupt a class). It may be appropriate to suggest that a child with Tourette syndrome be given individual tuition, special educational input and extra time in examinations, allowing the use of word processors or computers in the classroom, or to state that the child is unlikely to be of danger to others in, for example, a chemistry class or swimming pool.

Management of associated features

For the severely affected patient with Tourette syndrome who may have associated features such as ADHD, self-injurious behaviour and aggressive behaviour, the management is complex. In these cases, management includes counselling, regular assessment of mood and danger to the individual (depression and self-injurious behaviour), and often the prescribing of more than one medication – for example, a selective serotonin reuptake inhibitor for OCD symptoms, or alpha-adrenergic drugs such as clonidine or stimulants such as methylphenidate (Attenta, Concerta Extended-Release Tablets, Ritalin) for ADHD. Although stimulants have been implicated in precipitating or worsening tics, a recent large study by the Tourette Syndrome Study Group suggests that long-term use of methylphenidate is safe and does not exacerbate tics.[21] However, stimulants should be used cautiously and patients monitored carefully. Nonstimulants such as atomoxetine (Strattera) may be effective, but the clinical experience with these agents varies.

In some patients, allergy may have an effect on Tourette syndrome, making the tic or hyperactivity symptoms worse. Dietary manipulation and antiallergy treatment may well be an area worth pursuing in this subgroup of patients. However, the input of a physician specialising in allergies is recommended.

Conclusion

Tourette syndrome is no longer the rarity it was once thought to be. The core symptomatology is uniform and genetically determined (motor and vocal tics), whereas the associated symptoms are variable (e.g. OCD, ADHD, self-injurious behaviour and sleep problems) and are likely to be the result of a variety of genetic and environmental factors in predisposed individuals.

Self-help groups such as the Tourette Syndrome Association of Australia (www.tourette.org.au) have played a vital role in education and support, and we recommend that all patients and their families should be referred to this association. Extensive materials for patients and their families as well as for teachers, social workers and physicians are available on the association's website and through membership. MT

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COMPETING INTERESTS: None.