BMJ

BMJ 2013;347:f4964 doi: 10.1136/bmj.f4964 (Published 20 August 2013)

CLINICAL REVIEW

Tourette's syndrome

Andrea E Cavanna *consultant in behavioural neurology and honorary professor in neuropsychiatry*[1 2 3], Stefano Seri *professor of clinical neurophysiology and developmental neuropsychiatry*[3]

[1]Department of Neuropsychiatry, Birmingham and Solihull Mental Health NHS Foundation Trust and University of Birmingham, Birmingham, UK; [2]Sobell Department of Motor Neuroscience and Movement Disorders, Institute of Neurology and University College London, London, UK; [3]School of Life and Health Sciences, Aston Brain Centre, Aston University, Birmingham, UK

Gilles de la Tourette's syndrome, or Tourette's syndrome, is a neurodevelopmental condition characterised by multiple motor and vocal tics, which appear in childhood and are often accompanied by behavioural symptoms.[1] Originally described by French physician Georges Gilles de la Tourette in 1885,[2] this syndrome has long been considered a rare medical condition, until large epidemiological studies showed that 0.3-1% of school age children fulfil established diagnostic criteria for this condition.[3 4] In the United Kingdom, it is estimated that as many as 200 000-330 000 people are affected, with different degrees of severity.[1 4] Although it is estimated that about two thirds of patients with GTS improve by adulthood the syndrome affects health related quality of life.[5] This article reviews current knowledge about the diagnosis and management of Tourette's syndrome, including drug treatments and behavioural interventions.

What is Tourette's syndrome and who gets it?

The chronic presence of at least two motor tics and one vocal tic since childhood is recognised as the key feature of Tourette's syndrome. Tics are defined as involuntary, sudden, rapid, recurrent, non-rhythmic movements (motor tics) and vocalisations (vocal or phonic tics). It is now known that the syndrome occurs worldwide, across all races and ethnicities, in both sexes (four times more prevalent in males than in females), and in children as well as in adults, although the average age at onset is around 6 years and adult onset of tics is rare.[3]

Motor tics generally precede the development of vocal tics, and the onset of simple tics often predates that of complex tics. Simple motor tics can manifest themselves as eye blinking, facial grimacing, shoulder shrugging, neck stretching, and abdominal contractions. The most common vocal tics are sniffing, grunting, and throat clearing. Gilles de la Tourette's original case series described nine patients who also presented with complex tics; namely, echolalia (repeating other people's words) and coprolalia (swearing as a tic).[2] Both coprolalia and copropraxia (involuntary production of rude gestures as complex tics) are relatively rare, occurring in about 10% of patients (20-30% in specialist clinics where more severe or complex cases are seen).[6]

Both simple and complex tics are characteristically preceded by a feeling of mounting inner tension, which is temporarily relieved by tic expression.[7] These sensations, also known as "premonitory urges," are a hallmark feature of tics, and they enable clinicians to reliably distinguish Tourette's syndrome from other hyperkinetic movement disorders. However, unequivocal reports of these sensations can prove difficult to elicit in younger children.

Tic symptoms vary in frequency, severity, and distribution throughout life. They have a waxing and waning course, usually with a peak in severity during early teenage years. Although large prognostic studies are lacking, clinical experience suggests that in most cases tics improve or stabilise after puberty. Tics tend to be exacerbated by anxiety and stress and alleviated by mental and physical tasks that require concentration, such as playing sports and music. Moreover, patients can voluntarily suppress their tics for short periods (usually seconds to minutes), at the expense of mounting inner tension and subsequent rebound in tic severity. This feature is particularly relevant for diagnostic purposes. Over the past few years, clinical studies on social cognition have shown that certain social situations and interactions with other people can play a central role in modulating tic symptoms, including the expression of socially inappropriate behaviours.[8]

Patients present with a wide range of tic severity, from mild symptoms that do not cause serious impairment and often go unnoticed, to loud noises and forceful movements that can result in self injury. Owing to the potentially disabling nature of the physical symptoms, some patients face problems with daily activities, above and beyond those caused by the social stigma associated with the disorder. The syndrome is not associated with intellectual disability, and patients can be talented people who achieve and often excel in different areas of life.

Correspondence to: A E Cavanna, Department of Neuropsychiatry, Barberry National Centre for Mental Health, Birmingham B15 2FG, UK
a.cavanna@ion.ucl.ac.uk

Summary points

- Tourette's syndrome is a tic disorder that is often associated with behavioural symptoms
- Diagnostic criteria are based on the presence of both motor and vocal tics; because of its varied presentations, the syndrome has the potential to be misdiagnosed
- Prevalence is higher than commonly assumed; coprolalia is relatively rare (10-30%) and not required for diagnosis
- The syndrome can cause serious distress and compromise health related quality of life
- The main management strategies include psychoeducation, behavioural techniques, and drugs
- Service provision is patchy even in developed countries and patients of all ages often "fall through the net" between neurology and psychiatry

Sources and selection criteria

We based this review on articles found by searching Medline, the Cochrane Collaboration Library, Clinical Evidence, and the National Institute for Health and Care Excellence website with the term "Tourette". Our search was limited to English language articles published between 2005 and 2012. We also used evidence from published studies and guidelines on the management and treatment of Tourette's syndrome by the European Society for the Study of Tourette Syndrome and the Movement Disorders Society taskforces. Priority was given to evidence obtained from systematic literature reviews, meta-analyses, and randomised controlled trials when possible.

How is Tourette's syndrome diagnosed?

The diagnosis is clinical and relies on skilful observation and comprehensive history taking. Updated diagnostic criteria for tic disorders, including Tourette's syndrome, have recently been published in the *Diagnostic and Statistical Manual of Mental Disorders*, fifth edition (box).[9] The complex symptoms that were originally described by Gilles de la Tourette (such as coprolalia and echolalia) are not included in the diagnostic criteria, which do not distinguish between simple and complex tics. The differential diagnosis of tics includes myoclonic jerks, mannerisms, and stereotypies (especially in the context of autistic spectrum disorders), in addition to other hyperkinetic movement disorders with onset in childhood. Specific investigations, including laboratory tests and neuroimaging, are indicated only to rule out other possible causes of tics in patients with atypical presentations, which include acute onset, onset in adulthood, or sustained/dystonic tics.

Does Tourette's syndrome occur with other disorders?

Most patients with Tourette's syndrome also have specific behavioural symptoms, which can complicate the clinical picture considerably. Converging evidence from large clinical studies conducted in specialist clinics,[10 11] and in the community,[12] indicates that only 10% of patients have no associated psychiatric comorbidity (pure Tourette's syndrome). Consequently, the behavioural spectrum of the condition is multifaceted (figure⇓) and the management of patients with "Tourette's syndrome plus" can pose considerable challenges even to experienced clinicians. Obsessive-compulsive disorders and attention-deficit/hyperactivity disorder (ADHD) are the most common comorbidities, with an estimated prevalence of around 60%.[6] Interestingly, the obsessive-compulsive disorder symptoms associated with tics overlap only partially with the clinical presentation of patients with primary obsessive-compulsive disorder. For instance, patients with Tourette's syndrome report a significantly higher prevalence of concerns about symmetry, "evening-up" behaviours, obsessional counting (arithmomania), and "just right" perceptions, whereas patients with pure obsessive-compulsive disorder have a higher rate of cleaning rituals, compulsive washing, and fears of contamination.[13] These differences probably result from different pathophysiological mechanisms, because only certain obsessive-compulsive disorder symptoms are considered intrinsic to Tourette's syndrome. Similarly, some complex tics can be misdiagnosed as compulsions, possibly leading to overdiagnosis of comorbid obsessive-compulsive disorder, as it seems to be suggested by the results of recent epidemiological studies.[4]

The high prevalence of comorbidity between Tourette's syndrome and ADHD complicates the diagnosis and management of children and adolescents with the syndrome. By definition, tics involve hyperactivity and the constant effort to suppress them can interfere with the ability to concentrate at school. The diagnosis of comorbid ADHD should therefore be established by experienced child and adolescent psychiatrists, paediatricians, or adult psychiatrists or neuropsychiatrists after a comprehensive clinical assessment. The decision of whether to prioritise treatment of ADHD or tic symptoms is not easy, because psychostimulants used to treat ADHD can increase tic severity. Over the past few years, experts have reached an evidence based consensus that patients with tics should be treated with psychostimulants if the ADHD symptoms seriously impair their quality of life. Particular attention to adequate titration and avoidance of supratherapeutic doses is required.[14]

Tourette's syndrome can lead to the development of affective disorders through several mechanisms.[15] Firstly, depression can be an understandable psychological reaction to living with a potentially disabling condition and its serious social stigma; secondly, the multiple neurotransmitter abnormalities in corticostriatal systems responsible for the involuntary movements (tics) may also account for the impairment in affective tone; finally, certain drugs commonly used to manage tics (especially antidopaminergic agents) can cause depression. Importantly, tics and Tourette's syndrome are also more common in patients with autistic spectrum disorders, and recent studies found a significant association between Tourette's syndrome and impulse control disorders in adults (especially intermittent explosive disorder),[16] which can have relevant medico-legal implications.[17] Finally, the association with personality disorders, which are over-represented in patients with Tourette's syndrome, especially those with comorbid psychiatric disorders, requires further investigation.[18]

What impact does Tourette's syndrome have on health?

Over the past decade, there has been increased interest in the assessment of the impact of Tourette's syndrome on health related quality of life. A controlled study that used generic quality of life rating instruments demonstrated decreased quality

Current diagnostic criteria for Tourette's syndrome[9]

- At least two motor and one vocal tic (not necessarily concurrently)
- Presence of tics for at least 12 months
- Onset before age 18 years
- Tics not caused by the physiological effects of substances (such as stimulants) or other medical conditions (such as Huntington's disease)

of life.[19] Of note, the associated behavioural comorbidities often compromise overall wellbeing much more than tic severity. This observation is reflected in the multidimensional structure of the only disease specific quality of life scale for Tourette's syndrome, which encompasses four domains: physical, psychological, obsessional, and cognitive.[20]

What causes Tourette's syndrome?

Little is known about the exact brain mechanisms associated with tic development and expression, although preliminary evidence from neurochemical and neuroimaging investigations suggests a primary role for dysfunction of the dopaminergic pathways within the cortico-striato-cortico-frontal circuitry.[21] Neuropathological studies of patients with Tourette's syndrome are rare, but a few studies have provided evidence for deficits in cerebral maturation, in particular at the level of striatal interneurone migration.[21] Genetic predisposition has a major role in the development of the syndrome, as shown by early family studies. Although segregation analyses of large kindreds with multiple affected generations initially suggested an autosomal dominant transmission model, polygenic and bilineal transmission were also postulated, and subsequent investigations found that the syndrome is a genetically heterogeneous disorder.[22]

Findings from epidemiological and laboratory studies have also drawn attention to the role of environmental factors, including infections and autoimmune dysfunction, as well as prenatal and perinatal problems, in at least a subset of patients. The hypothesis that Tourette's syndrome can be subsumed in a group of conditions called paediatric autoimmune neuropsychiatric disorders associated with streptococcal infections is still controversial and requires further investigations.[23] The concepts of genetic and aetiological heterogeneity are in line with recent clinical phenomenology studies, which confirmed the existence of multiple phenotypes within the disease spectrum by using principal component factor analysis and hierarchical cluster analysis.[6]

Whom should I refer to a specialist?

Patients with suspected Tourette's syndrome should be referred to a specialist clinic, often part of a wider neuropsychiatric service, where multidisciplinary input can be provided. Because such clinics are few and far between, GPs can initially refer younger patients to local child and adolescent mental health services or community paediatrics services for a general neurodevelopmental and behavioural assessment. Specialist clinics could then be involved if the diagnosis is uncertain (for example, when comorbidities are present) or to deliver specific treatments. In adults, the pathway would be from primary care to adult neurology or neuropsychiatry. Once the diagnosis is established, patients should be reviewed at least once a year by a clinician with knowledge about the complexities of the disorder and its evolving treatment. Specialist services for these patients are in great demand because this fascinating area of neuropsychiatric medicine is underdeveloped in the UK.

How is Tourette's syndrome managed?

Tourette's syndrome is a lifelong condition with far reaching implications. Relevant and accurate information, alongside reassurance and explanation, should be provided to the patient, relatives, teachers, employers, and medical professionals involved. It is important to highlight that the syndrome is compatible with success at school and in the workplace. However, schools should be encouraged to implement appropriate arrangements for affected children, and career choices should take account of the practical implications of having tics and behavioural symptoms. The European Society for the Study of Tourette Syndrome recently published the first European assessment and management guidelines, which cover behavioural interventions, drug treatment, and surgical options for severe treatment refractory cases.[24-28]

What behavioural treatments are available?

A wide range of behavioural interventions have been developed or adapted to help patients maximise tic control.[29] Habit reversal training or exposure and response prevention seem to be the most promising approaches. These methods aim to enable patients to recognise premonitory urges and modify the response to their occurrence, so that tic expression is delayed and eventually abolished. Recently, two large randomised controlled trials in children and adolescents[30] and adults[31] with Tourette's syndrome or chronic tic disorders found that a comprehensive behavioural intervention for tics that incorporated habit reversal training significantly reduced tic severity in about half of the patients. Motivation to engage in the therapy sessions and full awareness of the premonitory urge are important factors that can increase response rate. In addition to enhancing tic suppression, psychological interventions can improve patients' awareness of the environmental factors that affect their tic severity and can provide valuable support and skills to deal with tic associated behavioural symptoms. Access to behavioural treatment is currently limited even in developed countries. In the future, telemedicine or remote consultations might widen access to specialist diagnostic and therapy services.

When should drugs be prescribed?

Drugs should be considered in specialist settings, in addition to psychoeducation and as an alternative or add-on to behavioural therapy for patients whose tics are associated with clear impairment. The European Society for the Study of Tourette Syndrome recently published expert consensus on indications for drug treatment. These included tics that cause subjective discomfort (such as pain or injury), sustained social problems (such as social isolation or bullying), social and emotional problems (such as reactive depressive symptoms), or functional interference (such as impairment of academic achievements).[26]

Which drugs are effective?

Few double blind randomised controlled trials have been conducted to test the efficacy of drugs for tic management, especially newer ones, for which recommendations are based on case series and open label trials.[32 33] The first drugs to show effectiveness in tic control were neuroleptics, especially haloperidol and pimozide. These are still considered among the most effective tic suppressants, and in many countries they are the only drugs licensed for Tourette's syndrome, based on multiple randomised controlled trials. However, their poor tolerability profile, mainly due to extrapyramidal and metabolic side effects, restricts their use to second line or third line options, and only in selected patients.

Over the past couple of decades these drugs have been replaced by the newer antidopaminergic agents—the atypical antipsychotics—which are better tolerated overall and have similar efficacy for tic control. Within this group, there are positive data from randomised controlled studies for risperidone and promising findings from open label studies for aripiprazole, which has the best tolerability profile thanks to its partial dopamine agonist action. Aripiprazole has led to tic reduction in 65-85% of patients treated in open label trials, whereas rates of discontinuation due to adverse effects have been lower than 25%.[26] Substitute benzamides (such as sulpiride) and presynaptic dopamine depletors (such as tetrabenazine) offer valuable alternatives, although both these drug classes and the newer antipsychotics can still have serious metabolic side effects, especially hyperprolactinaemia and weight gain. Importantly, antidopaminergic agents can also be useful as augmentation therapy in patients treated with selective serotonin reuptake inhibitors or serotonergic agents because of severe comorbid obsessive-compulsive disorder.

Centrally acting α2 adrenergic agonists, such as clonidine and guanfacine, can be considered as first line treatment for young patients, because they have fewer adverse effects than other classes and their antinoradrenergic action can also be effective for comorbid ADHD. Evidence of efficacy against tics is also robust (randomised placebo controlled double blind trials), and mild side effects related to their hypotensive action should be monitored.[33] Benzodiazepines should be avoided for the long term management of tics because of addiction and tolerance. However, positive results from open label and double blind controlled trials indicate that other agents that enhance γ-aminobutyric acid (GABA) activity, particularly antiepileptic drugs such as topiramate, have shown some benefit in small open label and double blind controlled trials, although further studies are needed to confirm this.[26] Likewise, preliminary evidence for tic suppressing properties from controlled trials on Δ9-tetrahydrocannabinol should prompt further investigations on the efficacy and tolerability of purified cannabinoids, especially in adults who are refractory to treatment.[26] Despite the paucity of evidence based data, the recently published European guidelines offer useful treatment algorithms based on the consensus of a large number of experts.[26]

Is there any other treatment?

Botulinum toxin injections are indicated for the symptomatic treatment of isolated tics (including vocal tics), with positive results from open label studies, especially in patients with focal dystonic tics.[26] Finally, a few selected patients with severe tics who do not respond to conventional interventions might be considered for surgery.[28] The first patient with Tourette's syndrome who successfully underwent the functional neurosurgical procedure of thalamic deep brain stimulation was reported in 1999.[34] Since then, more than 100 procedures have been reported, mainly single case reports and small case series, with varying degrees of success.[35] There is therefore little evidence on which surgeons can determine the suitability of a candidate and the optimal brain target because deep brain stimulation of the globus pallidus-pars interna and thalamic ventromedian-parafascicular nucleus often yield similar results in terms of efficacy, with the first option showing a better side effect profile. Currently, this procedure is still considered as a last resort and is rarely recommended.

Contributors: Both authors contributed equally to this article's conception and design, drafting, and final approval of the version to be published. They are both guarantors.

Competing interests: We have read and understood the BMJ Group policy on declaration of interests and declare the following interests: None.

Provenance and peer review: Commissioned; externally peer reviewed.

1 Stern JS, Burza S, Robertson MM. Gilles de la Tourette's syndrome and its impact in the UK. *Postgrad Med J* 2005;81:12-9.
2 Gilles de la Tourette G. Etude sur une affection nerveuse caracterisée par de l'incoordination motrice accompagnée d'écholalie et de copralalie. *Arch Neurol (Paris)* 1885;9:19-42;158-200.
3 Robertson MM, Eapen V, Cavanna AE. The international prevalence, epidemiology and clinical phenomenology of Tourette syndrome: a cross-cultural perspective. *J Psychosom Res* 2009;67:475-83.
4 Scharf JM, Miller LL, Mathews CA, Ben-Schlomo Y. Longitudinal study of parents and children cohort. *J Am Acad Child Adolesc Psychiatry* 2012;51:192-201.
5 Hassan N, Cavanna AE. The prognosis of Tourette syndrome: Implications for clinical practice. *Funct Neurol* 2012;27:23-7.
6 Cavanna AE, Rickards H. The psychopathological spectrum of Gilles de la Tourette syndrome. *Neurosci Biobehav Rev* 2013;37:1008-15.
7 Crossley E, Cavanna AE. Sensory phenomena: clinical correlates and impact on quality of life in adult patients with Tourette syndrome. *Psychiatry Res* [forthcoming].
8 Eddy CM, Cavanna AE. Altered social cognition in Tourette syndrome: nature and implications. *Behav Neurol* 2013;27:15-22.
9 American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 5th ed. APA, 2013.
10 Freeman RD, Fast DK, Burd L, Kerbeshian J, Robertson MM, Sandor P. An international perspective on Tourette syndrome: selected findings from 3500 individuals in 22 countries. *Dev Med Child Neurol* 2000;42:436-47.
11 Cavanna AE, Critchley HD, Orth M, Stern JS, Young M-B, Robertson MM. Dissecting the Gilles de la Tourette spectrum: a factor analytic study on 639 patients. *J Neurol Neurosurg Psychiatry* 2011;82:1320-3.
12 Khalifa N, Von Knorring A-L. Tourette syndrome and other tic disorders in a total population of children: clinical assessment and background. *Acta Paediatr* 2005;94:1608-14.
13 Worbe Y, Mallet L, Golmard JL, Béhar C, Durif F, Jalenques I, et al. Repetitive behaviours in patients with Gilles de la Tourette syndrome: tics, compulsions, or both? *PLoS One* 2010;5:e12959.
14 Bloch MH, Panza KE, Landeros-Weisenberger A, Leckman JF. Meta-analysis: treatment of attention-deficit hyperactivity disorder in children with comorbid tic disorders. *J Am Acad Child Adolesc Psychiatry* 2009;48:884-93.
15 Robertson MM. Mood disorders and Gilles de la Tourette's syndrome: an update on prevalence, etiology, comorbidity, clinical associations, and implications. *J Psychosom Res* 2006;61:349-58.
16 Wright A, Rickards H, Cavanna AE. Impulse control disorders in Gilles de la Tourette syndrome. *J Neuropsychiatry Clin Neurosci* 2012;24:16-27.
17 Cavanna AE, Robertson MM, Critchley HD. Schizotypal personality traits in Gilles de la Tourette syndrome. *Acta Neurol Scand* 2007;116:385-91.
18 Jankovic J, Kwak C, Frankoff R. Tourette syndrome and the law. *J Neuropsychiatry Clin Neurosci* 2006;18:86-95.
19 Eddy CM, Rizzo R, Gulisano M, Agodi A, Barchitta M, Calì P, et al. Quality of life in young people with Tourette syndrome: a controlled study. *J Neurol* 2011;258:291-301.
20 Cavanna AE, Schrag A, Morley D, Orth M, Robertson MM, Joyce E, et al. The Gilles de la Tourette syndrome-quality of life scale (GTS-QOL): development and validation. *Neurology* 2008;71:1410-6.
21 Felling RJ, Singer HS. Neurobiology of Tourette syndrome: current status and need for further investigation. *J Neurosci* 2011;31:12387-95.
22 Ali F, Morrison KE, Cavanna AE. The complex genetics of Gilles de la Tourette syndrome: implications for clinical practice. *Neuropsychiatry* 2013;3:321-30.
23 Madhusudan N, Cavanna AE. The role of immune dysfunction in the development of tics and susceptibility to infections in Tourette syndrome: a systematic review. *Basal Ganglia* 2013;3:77-84.
24 Cavanna AE, Rickards H, Worrall R, Hoekstra PJ, Plessen KJ, Roessner V. From ipse dixit to evidence-based guidelines: on the optimal management of Tourette syndrome. *Eur J Paediatr Neurol* 2012;16:310-1.
25 Cath DC, Hedderly T, Ludolph AG, Stern JS, Murphy T, Hartmann A, et al. European clinical guidelines for Tourette syndrome and other tic disorders. Part I: assessment. *Eur Child Adolesc Psychiatry* 2011;20:155-71.
26 Roessner V, Plessen KJ, Rothenberger A, Ludolph AG, Rizzo R, Skov L, et al. European clinical guidelines for Tourette syndrome and other tic disorders. Part II: pharmacological treatment. *Eur Child Adolesc Psychiatry* 2011;20:173-96.
27 Verdellen C, van de Griendt J, Hartmann A, Murphy T; ESSTS Guidelines Group. European clinical guidelines for Tourette syndrome and other tic disorders. Part III: behavioural and psychosocial interventions. *Eur Child Adolesc Psychiatry* 2011;20:197-207.

Tips for non-specialists

- Tics are not just habits and should not be ignored if they cause distress
- Tics tend to run in families and can be motor or vocal-phonic
- Involuntary swearing is a socially disabling tic symptom that is present in only 10-30% of patients with Tourette's syndrome
- The presence of comorbid behavioural symptoms often makes the diagnosis more difficult
- Multidisciplinary care within specialist settings is recommended when the clinical picture is unclear, complex, or challenging
- Offer psychoeducation and discuss behavioural and drug treatments with patients
- Refer patients to useful sources of information, such as the Tourettes Action or Tourette Syndrome Association's websites

Additional educational resources

Resources for healthcare professionals

- BMJ Best Practice (http://bestpractice.bmj.com/best-practice/monograph/1042.html)—Useful best practice module on Tourette's syndrome
- Martino D, Leckman JF, eds. Tourette syndrome. Oxford University Press, 2013. Multi-authored textbook covering all aspects of the condition from a large group of experts
- Robertson MM, Cavanna AE. Tourette syndrome: the facts. Oxford University Press, 2008. Concise reference that provides an evidence based overview
- Movement Disorders Society (www.movementdisorders.org)—Main international society dedicated to the research and care of patients with movement disorders, including Tourette's syndrome
- European Multicentre Study on Tics (www.emtics.eu)—First large-scale European collaborative study on Tourette syndrome

Resources for patients

- Tourette's syndrome: NHS choices (www.nhs.uk/Conditions/Tourette-syndrome/Pages/Introduction.aspx)—NHS website that provides advice on Tourette's syndrome, how it is diagnosed, and common treatments
- European Society for the Study of Tourette Syndrome (http://tourette-eu.org/)—European collaborative website that provides support and advice for patients
- Tourette Syndrome Association (www.tsa-usa.org)—US based charity providing information about the condition and ongoing research
- Tourettes Action (www.tourettes-action.org.uk)—UK based organisation providing information and support to patients

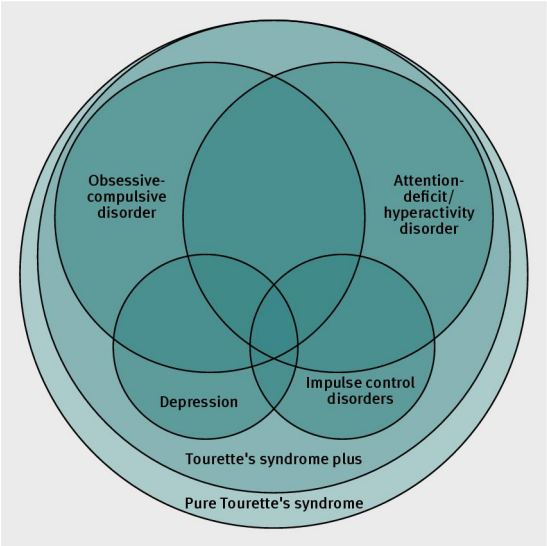
Questions for future research

- What factors trigger the waxing of tics and how can waxing episodes be recognised earlier and prevented?
- What behavioural symptoms are integral to Tourette's syndrome?
- What are the different clinical phenotypes of the syndrome?
- What is the relative contribution of genetic and environmental factors in the development of this syndrome?
- Which is the primary brain pathophysiological process?
- How can we define treatment refractoriness in this syndrome?
- Is deep brain stimulation a feasible treatment option and for whom?
- Is behaviour therapy as effective as drugs, and is the combination of the two treatments more effective than either one alone?

28 Muller-Vahl KR, Cath DC, Cavanna AE, Dehning S, Porta M, Robertson MM, et al. European clinical guidelines for Tourette syndrome and other tic disorders. Part IV: deep brain stimulation. *Eur Child Adolesc Psychiatry* 2011;20:209-17.
29 Frank M, Cavanna AE. Behavioural treatments for Tourette syndrome: an evidence-based review. *Behav Neurol* 2013;27:105-17.
30 Piacentini J, Woods DW, Scahill L, Wilhelm S, Peterson AL, Chang S, et al. Behavior therapy for children with Tourette disorder: a randomized controlled trial. *JAMA* 2010;303:1929-37.
31 Wilhelm S, Peterson AL, Piacentini J, Woods DW, Deckersbach T, Sukhodolsky DG, et al. Randomized trial of behavior therapy for adults with Tourette syndrome. *Arch Gen Psychiatry* 2012;69:795-803.
32 Waldon K, Hill S, Termine C, Balottin U, Cavanna AE. Trials of pharmacological interventions for Tourette syndrome: a systematic review. *Behav Neurol* 2013;26:265-73.
33 Thomas R, Cavanna AE. The pharmacology of Tourette syndrome. *J Neural Transm* 2013;120:689-94.
34 Vandewalle V, van der Linden C, Groenewegen HJ, Caemaert J. Stereotactic treatment of Gilles de la Tourette syndrome by high frequency stimulation of thalamus. *Lancet* 1999;353:724.
35 Piedad JCP, Rickards HE, Cavanna AE. What patients with Gilles de la Tourette syndrome should be treated with deep brain stimulation and what is the best target? *Neurosurgery* 2012;71:173-92.

Cite this as: *BMJ* 2013;347:f4964

Figure



Schematic representation of the behavioural spectrum in Tourette's syndrome: the size of each area is proportional to the estimated prevalence of the symptoms; the background colour intensity is proportional to the complexity of the clinical presentation