

# Tourette's syndrome and its borderland

Jeremy S Stern

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## Correspondence to

Dr Jeremy S Stern, Department of Neurology, St George's University of London, London SW17 0RE, UK; [jestern@sgul.ac.uk](mailto:jestern@sgul.ac.uk)

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## ABSTRACT

The Gilles de la Tourette syndrome (or Tourette's syndrome) has a prevalence of 1% of children with a wide range of severity and associated comorbidities. The last 20 years have seen advances in the understanding of the syndrome's complex genetics and underlying neurobiology. Investigation with imaging and neurophysiology techniques indicate it is a neurodevelopmental condition with dysfunction of basal ganglia–cortical interactions, which are now also being studied in animal models. There is also increasing evidence for treatments although it often remains difficult to manage. First-line options include neuroleptics, other drugs and specialised behavioural treatments. Deep brain stimulation is an evolving field, not yet fully established. This review focuses on the phenomenology of tics, how to assess and manage the syndrome, and uses examples of atypical cases to explore the characteristics and limits of its clinical spectrum.

## THE HISTORY OF TOURETTE'S SYNDROME

Gilles de la Tourette was one of Charcot's favoured internes. Charcot had noted Beard's report of the 'jumping Frenchmen of Maine', an unusual condition comprising one of a range of obscure culture-bound startle syndromes that includes Latah (Malaysia) and Myriachit (Siberia). The search for a similar phenotype in Paris resulted in a clinical series (1885) describing tics, echolalia and obsessiveness. The report included the famous case of a cussing Marquise originally described by Itard in 1825. Trousseau, another Parisian physician, appears to have made a good description earlier than Gilles de la Tourette<sup>1</sup> but the condition was long ago credited to the Salpêtrière school (figure 1). For about 90 years Tourette's syndrome (TS) was recorded mainly as a bizarre footnote in psychiatric textbooks and worse, in psychoanalysts' formulations. It was rediscovered in New York in the 1970s. By the 1980s its

prevalence was thought to be 1/2000 but later community ascertainment studies in schools and other settings increased that to 1% of schoolchildren, a figure that is internationally robust. The condition is 2–4 times more common in males.<sup>2</sup>

## WHAT IS TS?

The Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-V) (box 1) lists the most used criteria for TS, describing a chronic multiple motor and vocal tic disorder starting by the age of 18 years.

Most cases manifest before adolescence and most often at 5–7 years of age, insidiously or more dramatically, usually with motor tics above the neck. It can be sufficiently mild to be of no clinical significance. Note that involuntary swearing (coprolalia) is not necessary for diagnosis, and this remains a reason for its underdiagnosis.

## Does TS get better?

TS is a persistent condition although usually bothers adults less than children, perhaps through a combination of tics improving with age and coping strategies. Thus its peak severity is on average at 13 years<sup>3</sup>, while some people develop tics for the first time later than that. There are relatively few prospective data as there are no lifelong studies. Patients attending adult clinics are numerous but represent a biased sample that are less typical. Patients when first seen often say they are worse than ever. It is hard to interpret distant memories of childhood symptoms particularly if the school experience was unhappy, so hearing from family members is valuable.

## What is a tic?

Tics are brief twitch-like movements of varying degrees of complexity, purposefulness and amplitude. They can be almost continuous but in other patients are sparse. In some people, they are milder



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**Figure 1** *Une leçon Clinique à la Salpêtrière*, Brouillet, 1887. Georges Gilles de la Tourette is seated in the front row wearing an apron, leaning attentively forward.

than usual in the context of the consultation room but then do become more noticeable as the appointment progresses. Occasionally a single examination cannot confirm a credible history of tics. All published descriptions use the idiom ‘wax and wane’, and most patients do describe some weeks or months as being more or less severe for no special reason. They are also generally aware of new tics appearing and old ones disappearing over time, and of having orchestrated sequences of certain tics. Some tics have a compulsive quality and merge into other obsessional symptoms. Examples are ticcing a certain number of times, ticcing until it feels ‘just right’ (eg, painfully tensing the neck,

supplementary video 5) and more dramatic examples of self-injurious behaviour. Tics can come in florid bouts, something the patient community refer to as ‘tic attacks’ or ‘tic fits’.

Tics are situational and often worsen when stressed or bored, but improve when engaged, for instance, in music or sport. Coprolalia usually develops in childhood and affects about 10% of clinic cases. It is distinct from excessive swearing in social context; swearing is often interjected out of any grammatical sense and covered by other vocalisation. Echolalia and echopraxia are more often described as an urge than actually witnessed in the clinic (see Figure 2 and supplementary video 1).

Certain clinical features can help to distinguish tics from other involuntary movements. Tics are usually preceded by premonitory sensory experiences. These were first described by Joseph Bliss, a physician with TS,<sup>4</sup> and originally conceptualised as an analogous tic of the sensory system. Urges are now regarded as an intimate component of the tic, which can be resisted for a while, with the tic itself almost a response—perhaps more semivoluntary than strictly involuntary—and bringing a sense of relief. We can reproduce this by thinking of trying not to blink, sneeze or yawn, although this obvious interpretation can still be debated. Perhaps premonitory sensations develop over time as a response to experiencing tics. There have been experimental explorations of the dissociation between urges and suppression of tics.<sup>5</sup>

### Box 1 Diagnostic and Statistical Manual of Mental Disorders, 5th edition

#### Tourette's disorder

*Note:* A tic is a sudden, rapid, recurrent, non-rhythmic motor movement or vocalisation.

- ▶ Both multiple motor and one or more vocal tics have been present at some time during the illness, although not necessarily concurrently.
- ▶ The tics may wax and wane in frequency but have persisted for >1 year since first tic onset.
- ▶ Onset is before age 18 years.
- ▶ Disturbance is not attributable to the physiological effects of a substance (eg, cocaine) or another medical condition (eg, Huntington's disease, postviral encephalitis).



**Figure 2** Still of video 1: complex motor tics.

Patients with other movement disorders do not generally describe this arc of urge–suppressibility–tic–relief. For some people, the urge is a focal feeling of the part of the body that has to move; for others it is more diffuse or not articulated in such somatic terms. Tic suppression is sometimes a physical tensing; for others it is a more psychic process that is hard to explain. For a few patients the urge and/or effort of suppression is so unpleasant that

### Box 2 Supporting history points for diagnosing tics

- ▶ Are you able to hold the tics in?
- ▶ Do you feel an urge to tic that gets worse when you hold them in?
- ▶ Is there a sense of relief when you have done the tic?
- ▶ Do the tics vary if you are stressed or bored?
- ▶ Do the tics improve if you are more focused on an activity, for example, sport?
- ▶ Do the tics increase or decrease in severity for no particular reason so some weeks or months are worse than others?
- ▶ Do new tics come and some others disappear over the years?
- ▶ Do you have an urge to repeat words (echolalia) or to copy what people say, or their gestures (echopraxia)?

it symptomatically outweighs the tic itself. **Box 2** summarises some features of tics that are useful to raise in history taking.

### DIFFERENTIAL DIAGNOSIS OF TICS

Although tics vary in their morphology, complexity and amplitude, they are distinctive but still prone to overinvestigation or underdiagnosis. Adults (and children) with a typical multiple tic disorder do not require brain imaging. There are also many examples of unnecessary electroencephalography and primary care referral to ear, nose, and throat or immunology for sniffing or throat clearing.

Parents are often advised that tics are ‘habits’ that the child will grow out of. This is frequently correct for mild motor tics as 15%–20% of boys have a provisional (transient) tic disorder that lasts for less than a year; however, a combination of motor and vocal tics for 12 months is likely to persist to a diagnosis of TS.

The traditional textbook list of neurological differentials is perhaps more useful for non-neurologists as it contains rare disorders that usually look rather different, for example, DYT1 dystonia and myoclonus. Some tics have a more sustained quality, termed dystonic tics,<sup>6</sup> and occasional patients have both tics and a focal dystonia.<sup>7</sup>

Myoclonic conditions have diverse presentations reflecting their range of causes and anatomical origins. An individual myoclonic jerk can appear indistinguishable from a simple tic but myoclonus is neither suppressible nor patterned in the same way as multiple tics. Chorea has a more continuous and less purposeful quality but tic-like movements occur in Huntington’s disease, especially of the face.

Certain situations merit investigation, although this is often negative, leaving a diagnosis of TS with supposedly atypical features. These situations include an abrupt or dramatic late presentation or one that follows infection, where one would consider MR scan of brain, anti-streptolysin-O titre and antibasal ganglia antibodies (with the proviso given below). Occasional patients with tics have movements that look more choreiform or have a relevant family history (consider genetic testing for Huntington’s disease). There may be a role for array comparative genomic hybridisation testing in patients with neurodevelopmental syndromes including learning disability. The technique is currently more familiar in paediatric neurology, and its usefulness in managing adults with tics has not been established.

Neuroacanthocytosis occasionally needs to be considered. An example was a woman with tics who had consanguineous parents, unexpected progressive bulbar features and tongue biting among her movements (and abnormal imaging). Tongue and cheek biting can occur as a tic or self-injurious compulsion in TS but it is appropriate to check a blood film in these cases.

The concept of psychogenic tics is difficult as patients with tics share some features of psychogenic movement disorders, particularly distractibility and suggestibility, but paradoxically they have more possibility for voluntary control/suppression. Stereotypies also need to be considered in the context of autistic children and in older patients with focal symptoms. These movements also lack premonitory urge and are generally easy to stop when the person's attention is drawn to them. This can be a confused concept in the literature and has been very usefully reviewed.<sup>8</sup>

### COMORBID CONDITIONS

Tic syndromes show a gradient of comorbidity: TS has a high rate of comorbidity, people with chronic vocal tics have some comorbidity, those with chronic motor tics have less comorbidity and children with provisional tic disorder have a baseline level.<sup>9</sup> The condition's features have been repeatedly documented in clinical populations, including an international study of 3500 patients attending specialist clinics<sup>10</sup>; with few exceptions they do not differ by geographical location. TS can be divided clinically into a pure tic disorder without comorbidity (only 12% of clinic patients), 'full-blown TS' with echophenomena and coprolalia and the most common form 'TS-plus' with overlaps into a range of comorbidities, each of which themselves more often present without tics.<sup>11</sup> The most strongly associated conditions are obsessive-compulsive disorder and attention-deficit hyperactivity disorder (Figure 3). Thirty-six per cent of patients have more than one comorbidity.<sup>9</sup> Patients with no comorbidities tend to do better in their early development and integrate better into the workplace or higher education.<sup>12</sup>

Obsessive-compulsive disorder occurs in 11%–80% of cases.<sup>2</sup> Less intrusive obsessionality is clearly very common, and is known in this context as obsessive-compulsive behaviour. Tourette's obsessionality is clinically distinct from pure obsessive-compulsive disorder. Patients usually have checking behaviours, concerns about order and symmetry and a need to 'even things up'. Many have counting habits and can

be surprised when a doctor asks about this. Obsessional thoughts relating to violent, morbid or sexual themes are important symptoms. Other content such as hand washing/hygiene is less common.

Attention-deficit hyperactivity disorder occurs in 20%–90%.<sup>2</sup> The treatment of this disorder in adults is a growing field; although sometimes controversial, it is probably significantly underprovided. Tic suppression by children in the classroom may mimic inattention through a different mechanism.

Depression and anxiety are both frequent. Autistic spectrum disorder is more common in people with tics<sup>13</sup> and is often undiagnosed when the tics are being considered in a neurology clinic. TS has a higher prevalence in people with learning disabilities but generally there is an average IQ.

Some people with TS have an urge to do what they should not—for instance, having to walk on the grass despite a sign forbidding it or to make rude or personal comments that are not in their character. This can be as a tic or as a behavioural response that seems more complex and is known as non-obscene socially inappropriate behaviour.<sup>11</sup> See online supplementary video 3 for a possible example, explained by the patient.

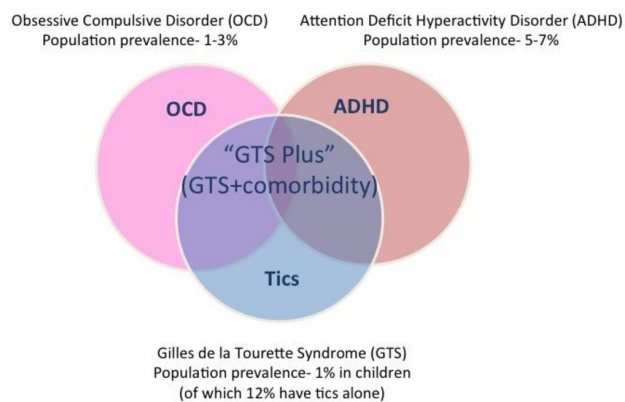
### ASSESSING SEVERITY

The syndrome has a wide range of severity and a wide range of how well individuals cope with it. The vast majority of adults with mild TS are probably not medicalised although they may still have comorbidities that have impaired them in childhood or later life. Some people with mild tics are very self-conscious, for instance, those who, despite distress, have never discussed their twitches with their partner. Others tolerate noticeable or even quite severe tics. The gold standard for research is the Yale Global Tic Severity Scale, which assesses tics and includes a crude measure of the impact of tics alone on quality of life; it is useful for at least a routine baseline clinical measure. A more recent disease-related self-reported quality-of-life instrument is very helpful in rating disease-specific symptomatic items and captures aspects of the overall impact of comorbid conditions.<sup>14 15</sup>

### MANAGING TS

The first management step is to formulate the diagnoses and decide with the patient the treatment priorities. Often all that is needed is the diagnosis, some information and signposting to the patient group Tourette's Action (<http://tourettes-action.org.uk>). Tics are commonly the primary complaint of the patient or referrer, yet they are not the main determinant of quality of life; this requires clinical judgement to decide the relative importance of the different aspects.

Attention-deficit hyperactivity disorder, obsessive-compulsive disorder, autistic spectrum disorder and depression can be managed as usual, often combined with treatment for other aspects, such as



**Figure 3** Overlapping neurodevelopmental syndromes.

tics. Where these comorbidities affect quality of life, regardless of the tic severity, neurologists should consider managing patients jointly with psychiatric services, although of course many neurologists are comfortable recommending the use of antidepressants. SSRIs are also commonly used for obsessive-compulsive disorder but do not improve tics. Stimulants given for attention-deficit hyperactivity disorder do not usually exacerbate tics; this is an outdated concern. A trial of the non-stimulant ADHD agent atomoxetine in TS showed an improvement in tics.<sup>16</sup>

### Drugs for tics

The data are relatively weak and limited by the variability of response, the difficulty in objectively measuring a fluctuating severity and the lack of sustained long-term beneficial responses to drugs in many patients. There is no single best first-line drug. There are European and Canadian guidelines based on systematic reviews<sup>17,18</sup> and a National Institute for Health Research Health Technology Assessment of 70 controlled studies in patients aged under 18 years (selected from >6000 citations) that used meta-analyses where possible.<sup>19</sup> This most rigorous view of the evidence concluded that only antipsychotic and noradrenergic drugs (clonidine, guanfacine) have clear randomised-controlled trial (RCT) evidence for clinically meaningful (but short-term) benefit for tics and that the main distinction among neuroleptic drugs is in their adverse effects. The effect size was judged moderate to large, with no difference between the two classes of drug. However, many clinicians consider noradrenergic drugs to be less effective, at least in adults where there is less evidence. Some other agents do have RCT data, for instance, topiramate, but this evidence is weak and undermined by the risk of adverse effects in younger patients. Despite the inadequacies of both the drugs and the evidence, there are patients who show a sustained and effective response and more who have a useful response, regardless of severity. Despite the lack of literature on this variability of effectiveness of medication, it is a dominant issue in the clinic.

There is little evidence to guide the safety and effectiveness of drug combinations or serial use of different options; however, the latter would be a standard approach, depending on patient wishes. Sometimes a successful treatment can be found after trying several failed alternatives.<sup>20</sup> There are no data to guide how long a trial of treatment should be, aside from the timescale of positive results in controlled trials that often last for weeks only. If patients are not having adverse effects, I encourage them to maintain a new drug for 3 months to allow review. The duration of treatment with any particular drug beyond an initial trial is empirical, depending on the benefit that the patient/family perceive in the longer term and any later adverse effects.

Patients older than 20 years with fairly mild tics who are coming for first treatment may find the drug

options unhelpful. There may be several reasons, including the difficulty in improving quality of life where the problem is a mild motor disorder that is unlikely to be suppressed completely by treatment.

### Neuroleptics

Haloperidol was the first drug used for TS in the 1950s, and the first randomised studies in the 1980s focused on haloperidol against pimozide. Since then almost every neuroleptic has been tried in at least case reports. Adverse effects are common and differ between patients; they include sedation, weight gain, occasional worsened depression or anxiety and concerns over potential metabolic, cardiac and extrapyramidal side effects.

Risperidone and aripiprazole are the consensus first-line agents in adults. Aripiprazole is a partial D2-agonist with serotonergic and adrenergic actions and RCT data support its use.<sup>21</sup> It has lower rates of weight gain, metabolic effects and hyperprolactinaemia, and may not cause QTc prolongation; it is my preferred drug in personal practice. As with all options, it is best to start low and increase slowly; I start with 2.5 mg at night increasing every 2 weeks by 2.5 mg to 15–20 mg. If one neuroleptic does not work or is not well tolerated, it is worth trying others.

Monitoring of the metabolic and cardiac effects of these medications follows guidelines from psychosis, although in that situation the cardiovascular risk and vulnerability to diabetes may differ. It is reasonable at baseline to check ECG, weight and blood pressure, glucose, lipids and prolactin. At each subsequent visit it is useful to review weight and blood pressure and to look out for extrapyramidal side effects. These are more common with first-generation antipsychotics; parkinsonism, tremor, acute akathisia and dystonias do occasionally emerge with older or newer drugs. Tardive dyskinesia develops in TS only very rarely. During continuing therapy, patients need annual blood tests; they require repeat ECG if changes to their health or drug history increase their risk of a prolonged QTc or if they are taking agents with a higher risk such as pimozide or risperidone.

### Non-neuroleptics

The alpha-2 adrenergic agonist clonidine is used widely for children, supported by literature, though opinion on it for adults is divided. Guanfacine is an alternative with less frequent adverse effects (postural hypotension, dry mouth, headache, initial sedation); it has long been used in other countries and is now available in the UK. Prescribing these drugs requires a baseline ECG, with blood pressure and pulse checked at each visit, and tapered withdrawal if necessary.

Other drugs for which there is no best evidence outlined above are topiramate<sup>22</sup> and tetrabenazine, which are alternatives for adults when needed. Benzodiazepines such as clonazepam sometimes help but should not be used first line. Many other drugs have

**Table 1** Suggested drug treatment of Tourette's syndrome

Drug treatment		Starting dose	Gradual increase as needed to
<b>Tics</b>			
First line	Aripiprazole	2.5 mg at night	15–20 mg at night
Alternative	Sulpiride	100 mg	300–400 mg twice daily
	Risperidone	1 mg	5 mg (ECG monitoring)
Second line	Clonidine (more often used first line in children)	25 µg	75 µg twice daily (ECG, taper withdrawal)
Alternative	Guanfacine	1 mg	5–7 mg
Third line	Topiramate	25 mg	100 mg twice daily
	Pimozide	1 mg	5 mg (ECG monitoring)
	Tetrabenazine	25 mg	25 mg three times a day
Fourth Line	Clonazepam	500 µg	1.5 mg
	Haloperidol	1 mg	5 mg
Botulinum toxin injection for selected focal motor tics (neck, eyes), and severe vocal tics			
<b>Obsessive-compulsive disorder</b>			
SSRIs	Sertraline		
Tricyclics	Clomipramine		
<b>Attention-deficit hyperactivity disorder</b>			
Stimulants	Methylphenidate, dextroamphetamine		
Non-stimulants	Atomoxetine, clonidine, guanfacine		

These recommendations reflect personal preference given the limitations of the evidence. If there is poor tolerability, it is worth trying alternative agents of the same class before those of different classes; responses vary between patients. See text for further details of monitoring of neuroleptic drugs.

been reported in case studies or series but such open-label data are especially vulnerable to giving falsely encouraging results. Preliminary trials of cannabinoids have generated interest, and the D1 antagonist ecopipam is also being investigated.

Botulinum toxin can be used for focal tics, especially if these involve the eyes or neck, but also for vocal cord injections to help vocal tics and coprolalia, usually marred by hoarse voice.

Table 1 lists drug options and suggested doses, based on the evidence; given the limitations of the data, these are also my personal practice.

### Behavioural treatments

Cognitive-behavioural techniques for tics have a long history with good evidence for two particular approaches. One is called comprehensive behavioural intervention for tics, which is built on an older concept of habit retraining therapy in which the patient counters the urge to tic with a muscular action that prevents the tic. Trials of 10 weekly sessions in children and adults showed the effect is as good as that for drugs, can be sustained and was not matched by psychoeducation and relaxation strategies alone.<sup>23 24</sup> The other method is exposure and response prevention in which patients learn to tolerate the urge to tic without performing the movement.<sup>25</sup> Not all patients are suitable for these treatments since motivation, learning disability or other comorbidities can get in the way. Ideally, each patient requiring intervention

for tics—unless there is a bar to effective engagement—would be offered psychological intervention if they wish, after discussing the pharmacological options. The main barrier to treatment is the availability of specialised clinical psychologists. The charity Tourette's Action have a list of UK therapists and organise training sessions for psychologists. Online treatment (web-based or via video consultation) is an area of active investigation that may improve access.

### Deep brain stimulation

Deep brain stimulation is extensively reviewed elsewhere, with >150 cases published so far including a controlled trial.<sup>26</sup> It could be an important treatment in selected cases but the appropriateness of referral to a neurosurgical unit with experience in treating TS depends on local availability, and it is not currently available in the National Health Service. Patients that may be suitable are generally older than the age of final maturation of the brain in the early 20s and have severe tics that are refractory to multiple drug classes and (ideally) to behavioural therapies. It is not yet clear how this interacts with comorbidities. There is little consensus on the best target but most documented cases have targeted the thalamic nuclei and globus pallidus interna.<sup>26</sup> Although there is some positive long-term follow-up information, it is already clear that not all patients benefit. While treatment on compassionate grounds is understandable, ideally we

need to set up procedures within research trials or the international registry for this purpose.<sup>27</sup>

### ABBREVIATED NEUROBIOLOGY OF TS

TS has an important genetic component, with a population-based heritability estimate of 0.77 and variable severity and comorbidities within family members. Premillennial genetic techniques failed to find the autosomal-dominant single gene that had once been expected. As with many other neuropsychiatric conditions, the focus is now on polygenic mechanisms using genome-wide association studies, copy number variants and epigenetic investigation. By 2018, international genetic consortia should have collected 12 500 cases and several susceptibility genes of interest, including *NRXN1*, should be confirmed.<sup>28 29</sup> There is evidence that TS presentations with and without comorbidities each have distinct genetic architecture, and there are overlaps in candidate genes between TS and conditions such as obsessive-compulsive disorder.<sup>29</sup> Non-genetic components include maternal alcohol and cannabis use<sup>30</sup> and possibly streptococcal autoimmunity as a provoking cause in genetically vulnerable individuals.

These non-genetic components, and particularly the relationship to paediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS), remain controversial; there is an ongoing prospective European study<sup>31</sup> but the current evidence is against using immune treatments.<sup>32</sup> About 25% of TS cases have serum antibasal ganglia antibodies, not fulfilling the criteria for PANDAS and of uncertain significance; our current knowledge suggests that in most cases this test is not useful for diagnosis or management. The classical literature on the encephalitis lethargica epidemic, starting in 1917, included a hyperkinetic subtype with tics as one component. The cause is still debated but similar contemporary sporadic cases suggest a possible postinfective autoimmune condition with associated basal ganglia antibodies.<sup>33</sup>

The cause of tic production and the resting state of the brain in TS has been explored with neurophysiology and structural/functional imaging (each using many modalities), small scale but influential postmortem and transcriptome work<sup>34</sup> and increasingly relevant animal models.<sup>35</sup> There is very clearly a neurological substrate but it is not yet fully understood. Neurophysiological investigations overall suggest altered synaptic excitability and intracortical inhibition with increased gain of sensory input to motor areas, increased cortico-cortical coherence and possible abnormal plasticity mechanisms. A broad-brush summary anatomical hypothesis would be that there is a neurodevelopmental disorder with subtle atrophy of parts of the basal ganglia thalamocortical circuitry with a likely complex neurochemistry. Clinical improvement may be associated with later brain maturation giving increasing frontal control.<sup>36</sup> Recent imaging work has included the concept of endophenotypes depending

on the severity of tics and presence of comorbidities, with some evidence of differential atrophy or differing measures on functional imaging.

### THE BORDERLAND: ATYPICAL CASES

Sir William Gowers used the term 'borderland' to describe the differential diagnoses of epilepsy and identified a range of conditions that he regarded as 'near it, but not of it' (1907), some of which remain relevant to the first fit clinic.<sup>37</sup> Given the heterogeneous spectrum around tics, TS by its nature is a condition of the borderland and not surprisingly some cases breach the man-made DSM-V boundary. Many are probably truly 'of it' but do not have a clinically relevant biological marker in individual patients.

#### Age

Tics presenting over the age of 18 years, too late for DSM V, are the best explored edge of the syndrome, though the literature is small given the number of patients referred. The onset can be particularly explosive, leading to testing of serum antibasal ganglia antibodies and brain imaging that is almost always normal. It often amounts to an unexpected relapse of a milder tic disorder from childhood although some cases do appear to be genuinely new adult onset cases in the 20s and 30s, or occasionally even later. The phenomenology may show some clinical distinctions, for instance (personal anecdote), a lack of premonitory sensations with often a severe disorder, commonly with coprolalia.<sup>38 39</sup> There have been various provoking factors such as drugs or trauma, documented as single cases, which are hard to interpret. Late-onset severe cases tend to settle down over time, leaving a milder disorder that may respond usefully to drugs. The phenotype is unmistakable for florid TS, and therefore, we may presume that these patients have the neurodevelopmental substrate and genetic vulnerability (perhaps suggested by family history); new comorbidity such as obsessive-compulsive disorder can present concurrently. It is unclear why the condition was not expressed earlier in life.

#### Apparently isolated tic syndromes

Isolated blinking, throat clearing, coughing or sniffing tics in adults are relatively common; such people may have other unobserved tics, now or previously. Some other examples can be harder to categorise when they seem unusual and of late onset (online supplementary video 2). For example, a woman in her 50s with depression and psychological trauma who recently started to make a prominent and intrusive snorting noise, suggesting more a tic than stereotypy; she apparently had no tics in earlier life but had an obsessional father with frequent throat clearing and a son with transient facial tics when young. Treatment with standard drugs in this situation is admittedly particularly unreliable but can sometimes help.

### Odd behaviours with the odd tic: is it Tourette's?

Community studies have shown that clinically insignificant tics can be a marker of a wider syndrome, where comorbidities like attention-deficit hyperactivity disorder are the more important features. This is common but some patients are referred because mild tics have been spotted in the context of harder-to-explain neuropsychiatric symptoms or antisocial behaviours. Tics are not the clinical problem here but could potentially signify a vulnerability to a comorbid presenting disorder. Sometimes this may be another diagnosable condition, for example, the DSM-V diagnosis 'intermittent explosive disorder', causing violent outbursts. In other cases, there may be complex mechanisms at play, for example, a man concerned about excessive swearing in front of children. Coprolalic tics do not normally occur with only mild TS and his swearing was driven by obsessional thoughts. These situations appear more psychiatric than neurological, depending on opinion, but can require a neurologist to reduce focus on the tics to allow the real problem to be treated as appropriate.

### Do patients with TS also have psychogenic tics?

Analogous to non-epileptic seizures in patients with epilepsy, some people with TS have functional tics. Given their nature, psychogenic and conventional involuntary mechanisms could be more intimately entwined with tics than with epilepsy, and potentially harder to separate clinically. One patient said, 'The best thing about Tourette's is being able to stick two fingers up at a policeman.' However, as in other functional disorders, this is not a discussion about malingering, although it is difficult to analyse individual cases, given how the internal and external environment influence tics. Good examples are children's 'tic fits' at bed time<sup>40</sup>—probably with a psychological

mechanism similar to panic attacks—or adult attacks that contain elements more resembling a dissociative seizure than a storm of tics (see online supplementary video 4). It is difficult to draw a dividing line between a behavioural symptom and a behavioural influence on tic expression, but it is appropriate to try behavioural management. The question spills into the literature on primarily functional tics, which cites diagnostic associations features such as lack of family history, inability to suppress tics, lack of rostrocaudal distribution, absence of echolalia, late onset or poor response to medication.<sup>41</sup> All these features can individually occur with convincing TS, and so an operational definition is challenging. Anecdotally, there have been a small handful of cases that I felt had a florid onset of psychogenic-looking tics; these have often settled over time, leaving at least a few simple tics, which are tempting to classify as an underlying tic disorder.

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### Key points

- ▶ Tourette's syndrome affects 1% of children and is generally less intrusive in adulthood; patients' tics have a very wide range of severity.
- ▶ There are commonly comorbidities, such as obsessive-compulsive disorder, attention-deficit hyperactivity disorder and depression, which impact on quality of life and may require psychiatric input.
- ▶ The syndrome is often familial and has a complex genetics currently being investigated in international consortia.
- ▶ Tics can be treated with specialised behavioural interventions (hard to access) or drugs such as neuroleptics (aripiprazole) or noradrenergic agents (clonidine), with a rather variable response.
- ▶ Some people with Tourette's syndrome have an atypical history or features that go beyond diagnostic criteria, including apparent adult onset.



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