

13 Tic Disorders

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Introduction and History

Gilles de la Tourette (under the tutelage of Charcot at the Salpêtrière) described the syndrome of tics, echolalia and coprolalia in Paris in 1885, initially in 9 patients (not all of whom he had met). The same syndrome had in fact been previously described by Trousseau 20 years earlier. Interest in this syndrome in Paris was sparked by descriptions of “culture bound” startle syndromes (latah, myriachit and the “Jumping Frenchmen of Maine”). These syndromes were characterised by echolalia, coprolalia and automatic obedience in response to startling stimuli. Tourette noted in his patients that the behaviours occurred in some people in the absence of a clear stimulus. In most of the latter part of the 19th Century and the first 60 years of the 20th Century, psychoanalytical explanations for tics were in vogue. However, in 1961, the first successful treatment of tics with haloperidol was recorded by Seignot and an explosion in biological research into the causes of TS began. The familial/genetic aspects of TS were documented in the ensuing years although a single gene cause for TS looks unlikely. Epidemiological studies have now suggested that TS, as it is currently defined, is common in children, although often mildly expressed. Associated problems with attention, concentration, obsessiveness and mood changes are also commonly described. Finally, research into autoimmune mechanisms, has renewed interest in the relationship between TS and Sydenham’s chorea (St. Vitus’ dance).

Clinical Features

Tics are stereotyped movements which may be jerky or dystonic. They are often experienced with premonitory sensation (an itchy, tense or tight feeling which is experienced around the area of the tic or as a mental phenomenon). They can be suppressed at the expense of internal tension. The movement itself often brings relief of the tension and suppression can lead to a “rebound” phenomenon. Sometimes tic-like movements can be entirely voluntary in order to reduce the premonitory sensations. Tics may be present in motor or phonic domains and can be simple (eye blinks) or complex (squatting, jumping or twirling). Diagnosis of tics in children is more difficult as premonitory sensations are harder to elicit (either they are not experienced or children find them difficult to describe).

Differential Diagnosis

Current classification covers two areas; idiopathic tic disorders and neurological disorders in which tics present as a symptom.

Idiopathic tic disorders are divided into the following categories:

- Transient tic disorders (disorders lasting less than 1 year)
- Chronic multiple tics (motor or phonic but not both)
- Tourette syndrome (onset before 18 years, motor and phonic tics, no other neurological explanation)
- Tic disorder NOS (for example, a syndrome identical to TS but onset over 18 years)

These distinctions do not have a clear basis in epidemiology or pathology, and the categories are open to a number of criticisms. For instance, the category “transient tic disorder” can only be diagnosed when it has ceased, which diminishes its validity. One criticism of the TS category, levelled at other disorders which have been defined by their “idiopathicness”, is that when a cause is found for some people with the syndrome, they automatically cease to have it by definition.

More recent factor analytical studies have suggested reclassification along the following lines;

- TS simplex (just tics)

- TS complex (tics plus echo-, pali- or coprophenomena)
- TS plus (TS plus comorbid conditions such as ADHD or autistic spectrum disorders)

Further advances in brain research will inevitably lead to a reclassification of tic disorders along aetiopathological lines.

Other Conditions with Tics

There are many other disorders of childhood and adulthood which have tics as a symptom. These include neurodegenerative disorders such as Huntington's disease or Wilson's disease, metabolic disorders such as Lesch-Nyhan syndrome and homocysteinuria, neuroacanthocytosis and intoxication with drugs such as amphetamines and cocaine. Tics can appear as a tardive syndrome in those treated with neuroleptic medication and can occur as part of neurodegenerative processes in later life such as cerebrovascular disease. Motor disorder in myoclonus-dystonia can appear tic-like

In the majority of cases, the diagnosis of TS can be made without extensive investigation. Factors in the history or examination which would trigger further investigation would include:

- Intellectual impairment or developmental delay
- Late onset of symptoms
- Presence of myoclonus
- Progressive (rather than "waxing and waning") course
- No "sensory" symptoms
- Fixed dystonias or task-specific dystonias such as writer's cramp
- Other focal neurological signs
- Specific dysmorphic features (e.g. indicating Fragile X or Down syndrome)
- Short lived period of motor disorder with long symptom-free periods (could be drug intoxication)

Tourette Syndrome (TS)

Diagnostic Criteria

The DSM-IV criteria which currently define TS are:

- Multiple motor and one or more phonic tics
- Onset before 18 years of age
- Symptoms present for 1 year at least
- Not due to detectable neurological disorder or substance abuse

The definition includes non-mandatory characteristics:

- Tics occur many times a day in bouts
- Tics tend to "wax and wane", changing in frequency, severity, type and location over time.

There has also been argument about whether to include the idea of "significant impairment of function" into the diagnosis, as there are many people who fulfil the current criteria for diagnosis of TS but don't show any impairment in function. Many clinicians want to include impairment in the diagnostic criteria but researchers (especially geneticists) do not as it may cloud the search for the most appropriate phenotype.

Epidemiology

Epidemiological studies have been hampered by a lack of external validators, a phenotype that is on a spectrum with normal behaviour and by ascertainment bias present in most of the studies on clinic or hospital populations. Rutter's 1970 study of psychiatric disorders in the Isle of Wight indicated a prevalence of tics of around 4% in school aged children but clear diagnostic criteria were not used. A prevalence of 0.1% of TS was found in Israeli army conscripts (some may have grown out of tics by 17 years and others may have disguised them in order to be conscripted). A study in a mainstream school in Essex using observation and clinical examination showed a prevalence of TS of nearly 3%

(5 cases out of 167 pupils). All cases were mild and had not sought medical attention. One of the best community studies of the prevalence of TS performed in North Carolina showed a prevalence of TS in school-aged children of around 0.1% (although this too has been criticised as it may have missed cases of “pure” TS without psychiatric co-morbidity). A number of recent community epidemiological studies (based in Sweden, Taiwan, China and US) have indicated a prevalence of around 1% in school aged children. However, community studies which include an “impairment” criterion give a prevalence of around 0.5%. Thus, in a school of 400 children, around 4 would meet the diagnostic criteria for TS, 2 of whom would have symptoms which impaired function.

Clinical Course

Typical age of onset of TS is between 6 and 8 years with tics starting in the head and neck. Tics tend to wax and wane with symptoms replacing each other over time. The tendency is also for tics to become more complex with time. The average age for the most severe tics is between 12 and 14 years with tics tending to improve in late adolescence or early adulthood. Recent follow-up studies comparing video taped interviews indicate that most people with TS tend to still have tics during adulthood even if they are not aware of having them. There have been few studies looking at the factors that determine whether there is remission or whether the TS symptoms persist into adulthood.

Co-morbidity

Studies of co-morbidity are once again hampered by the problem of ascertainment bias as most are conducted in clinic settings. Obsessive-compulsive behaviours and OCD are very common in TS and share many clinical characteristics with tics. OC behaviours may just be more complex, more goal directed tics. Self-injurious behaviours are seen in a third of clinic patients with TS and it has a compulsive (and sometimes symmetrical) nature. Studies from the veterinary world (especially of horses) show similar patterns of tic-like behaviours and self-injurious behaviours.

Attention deficit problems are very common in TS and may affect around 40% of children attending clinic. However, attentional problems in TS may be caused by tic suppression, obsessional rumination, by medications, depression or anxiety. The recent, community-based epidemiological studies have shown a true co-morbidity with ADHD (not due to ascertainment bias or “pseudo-ADHD”

Both depression and anxiety are considerably higher in people with TS and these syndromes have a multi-factorial aetiology

Aetiology

Tics probably represent a final common pathway of a variety of developmental problems. The aetiology of TS is unknown. Family studies indicate that TS appears to be heritable alongside an early-onset form of obsessive-compulsive disorder but the commonest form of attention deficit hyperactivity disorder (ADHD) does not share genetic factors with TS. The largest genome-wide association study to date showed a linkage to chromosome 2p23.2 with a lod score of 3.8 but this needs replication. One study, identifying the SLITK gene in a family with TS has not been reliably replicated. Imaging studies have shown changes in basal ganglia volumes and symmetries but no clear, reliable abnormality has been reliably demonstrated. Perinatal events appear to confer extra risk but are neither necessary nor sufficient. Recent research using the Sydenham’s chorea model has shown encouraging results (people with TS having a high positive rate for Anti basal ganglia antibodies). However, the average child has 8 streptococcal infections during childhood so demonstrating that this is the pathological agent could be difficult. Some centres are already using prophylactic penicillin and trials are taking place on immune modulating therapies with limited success so far.

Management

Management should be holistic and consider the quality of life of the patient and family at the centre.

Education of the patient and family about the illness is vital. This may include genetic counselling where appropriate. Close liaison with schools is important from the point of view of educating

teachers about TS and monitoring progress. Statements of special educational needs may be necessary.

Treatment should be focussed on the symptoms that most impair quality of life, development or learning. These may not necessarily be tics. Psychological treatments include massed practice or habit reversal. Habit reversal may be useful in people with a small number of disabling tics and a number of recent studies support its efficacy. Randomised controlled trials of pharmaceutical agents support the use of pimozide and risperidone (although pimozide can affect QT interval). There is one case report of a fatality when pimozide was prescribed alongside a macrolide antibiotic and this led to arrhythmia. One RCT supports the use of haloperidol but another demonstrates no difference between haloperidol and placebo. Most of the reports of tardive dyskinesia in TS have been in relation to haloperidol so it is definitely not for first line use. Sulpiride has been extensively used outside the US but there are no RCT's supporting its use (one large open label study). There are small RCT's to support the use of other atypical neuroleptics. Clonidine has been used in children with TS and ADHD but evidence for its efficacy is lacking. Aripiprazole, an newer atypical neuroleptic, has shown initial promise in the treatment of tics.

There has been controversy about whether stimulants used to treat ADHD (such as methylphenidate) have made tics worse. The most recent evidence from the US TS Study group is that stimulants do not make tics worse. This finding needs replication.

For most people, TS is a self-limiting illness and medication should be used sparingly. Side effects can often impair mood, concentration and learning.

Botulinum toxin has been used to good effect in specific tics. Use of botox appears to reduce premonitory sensations in addition to reducing tics. A number of cases have been reported of successful use of botox injections into the laryngeal muscles to minimise coprolalia.

Deep brain stimulation (DBS) has now been reported in around 60 cases of severe TS worldwide. The rationale for its use is sketchy and controlled trials are infrequent. The largest number of cases have electrode implants in the ventro-oralis nucleus of the thalamus but there are around 8 reported cases of successful implantation of GPi (both the "traditional" posterior target and a more anterior "limbic" target in some). In general, results are good with few adverse effects but large controlled trials are urgently needed.

Further Reading

Tourette Syndrome (2006) *Advances in Neurology* Volume 99. (Eds Walkup, Mink, Hollenbeck)

Journal of Psychosomatic Research (2009) Volume 67. This is an invited Special edition dedicated to Tics and Tourette syndrome.