The Prevalence of Gilles de la Tourette’s Syndrome in Children and Adolescents with Autism

Simon Baron-Cohen
University of Cambridge, U.K.

Catherine Mortimore and John Moriarty
Institute of Neurology, University of London, U.K.

Jon Izaguirre
Children’s Centre, Southport, U.K.

Mary Robertson
Institute of Neurology, University of London and University College London, U.K.

Thirty-seven pupils attending a special school for children and adolescents with autism were observed for the presence of motor and vocal tics. Subsequent family interviews confirmed the diagnosis of comorbid Gilles de la Tourette’s Syndrome (GTS) in three children with autism, giving a minimum prevalence rate of 8.1%. Family history data also suggested this was heritable. The presence of GTS was not associated with superior intellectual, language, or social development. Results suggest that the rate of GTS in autism may exceed that expected by chance. The limited sample size constrains this conclusion. A large-scale epidemiological study testing this association study would appear merited.

Keywords: Autism, Tourette syndrome, comorbidity, pervasive developmental disorder.

Abbreviations: GTS: Gilles de la Tourette’s Syndrome; PDD: pervasive developmental disorder; TROG: Test for Reception of Grammar.

Introduction

Gilles de la Tourette’s Syndrome (GTS) is a neurodevelopmental disorder defined by the presence of chronic, multiple motor and vocal tics of childhood onset (DSM-IV: American Psychiatric Association, 1994). Typically, tics develop at 6–7 years of age, show a fluctuating course, and decrease in severity during adulthood. The precise aetiology of GTS is unknown. In most cases, GTS appears to be genetically transmitted (Curtis, Robertson, & Gurling, 1992; Eapen, Pauls, & Robertson, 1993). Implicated neurological abnormalities include functional abnormalities of the basal ganglia and prefrontal cortex (reviewed in Chase, Geoffrey, Gillespie, & Burrows, 1986), and biochemical abnormalities of the dopamine and serotonin neurotransmitter systems (reviewed in Baker, Chokka, & Bornstein, 1986). GTS is often accompanied by obsessive-compulsive behaviours (Frankel et al., 1986), which may be an alternative expression of the putative GTS gene(s) (Pauls, Towbin, Leckman, Zahner, & Cohen, 1986).

Autism is also a neurodevelopmental disorder, itself defined by abnormal social and communication development, with a pattern of restricted and repetitive interests and activities (DSM-IV: American Psychiatric Association, 1994). Autism has an earlier age of onset than GTS, and shows a chronic and unfluctuating course. The aetiology of autism is unknown, although possible factors include genetic (Bailey et al., 1995; Folstein & Rutter, 1977), neurobiological (Bauman & Kemper, 1994), and cognitive (Baron-Cohen, 1995; Frith, 1989) abnormalities.

Although distinct disorders, autism and GTS share several behavioural features. Here we list some of these shared features, whilst pointing out how these may differ in the two syndromes: (1) Echolalia and palilalia are common in both GTS and autism, although in autism, unlike GTS, these behaviours may be appropriate to the level of speech development. (2) Types of obsessive-compulsive behaviours are frequently seen in both autism and GTS, although in autism these may be better described as rigid and ritualistic behaviour, such as an insistence upon sameness and resistance to change. (3) Like GTS, autism is associated with abnormal motor behaviours, although in autism these often take the form of stereotypies, such as spinning, rocking, and hand flapping.
Recently, a growing number of case reports have documented the co-occurrence of autism and GTS in the same individuals. Early reports described the development of motor and vocal tics in adults with autism following withdrawal from long-term neuroleptic treatment (Mueller & Aminoff, 1982; Stahl, 1980). Owing to the adult onset, Stahl interpreted the development of tics as secondary to neuroleptic withdrawal, although Mueller and Aminoff also discussed the possibility that long-term neuroleptic use may have masked or delayed the appearance of tics that may otherwise have developed spontaneously. Later case reports of childhood-onset motor and vocal tics in autism or Asperger syndrome have also interpreted their development as secondary to neuroleptic withdrawal (Littlejohns, Clarke, & Corbett, 1990; Perry, Nobler, & Campbell, 1989).

Realmuto and Main (1982) were the first to report the development of GTS in a drug-naïve child with autism. These authors interpreted this co-occurrence as a chance association, as did a subsequent report of childhood-onset GTS in autism (Barabas & Matthews, 1983). However, Barabas and Matthews also discussed the possibility of a common neurochemical abnormality.

A number of case reports of GTS comorbid with autism or Asperger syndrome have since been published. Most of these later reports have speculated on possible aetiological relationships between autism spectrum disorders and GTS, including common chromosomal and genetic abnormalities (Hebebrand et al., 1994; Kerbeshian, Burd, & Martsof, 1984a, b; Sverd, Montero, & Gurevich, 1993). This recent discussion of common aetiological factors implies a higher rate of comorbid autism and GTS than would be expected by chance. However, although the growing number of case reports suggests this higher rate, there have been few studies of the prevalence of comorbid autism and GTS.

The estimated general population prevalence of autism is 2.5 per 10,000 (DSM-IV: American Psychiatric Association, 1994). The estimated general population prevalence of GTS is 2 per 10,000 (Robertson, 1994). Hence, if autism and GTS are truly independent, the rate of co-occurrence expected by chance would be roughly 5 per 100 million.

A few studies have documented the prevalence of GTS in populations of individuals with autism spectrum disorders. Kerbeshian and Burd (1986) reported a clinical series of six individuals with Asperger Syndrome, of whom three (50%) had comorbid GTS. The same group (Burd, Fisher, Kerbeshian, & Arnold, 1987) reported a rate of 20.3% of GTS in an ascertained sample of 59 individuals meeting DSM-III criteria for infantile autism or pervasive developmental disorder (PDD). Of the 12 children with comorbid GTS, 10 had an atypical PDD, whereas only 2 had autism. Kano’s group (Kano, Ohta, & Nagai, 1987; Kano, Ohta, Nagai, Yokota, & Shimizu, 1988) described 2 children with autism and GTS, drawn from a sample of 76 children with autism, suggesting a much lower prevalence rate of 2.6%.

Autism spectrum disorders may be considerably more common than autism itself. Ehlers and Gilberg (1993) estimate their prevalence to be as high as 0.74%. Fewer studies have documented the rate of autism spectrum disorders in populations of individuals with GTS. Comings and Comings (1991) reported 16 individuals with autism, Asperger syndrome, or PDD, among a clinical series of 1400 children and adults with GTS, suggesting a rate of 1.1% of autism spectrum disorders in GTS. Berthier’s group (Berthier, Bayes, & Tolosa, 1993) reported 9 individuals with Asperger Syndrome among a clinical series of 100 patients with GTS, giving a prevalence rate of 9.0%.

We are not aware of any studies reporting the rate of comorbid autism and GTS in the general population. However, Sverd (1991) reported 10 children with autism or PDD and comorbid GTS. Given the population statistics for the geographical regions from which these children were clinically ascertained, Sverd argues that these children represent a rate of comorbidity exceeding that of chance.

It is clear that all reported prevalence rates exceed that expected by chance. However, two inconsistencies in the research to date require explanation. First, reported rates of GTS in autism spectrum disorders (2.6%, 20.3%, 50.0%) tend (with the exception of Kano and colleagues’ statistic of 2.6%) to exceed, by far, reported rates of autism spectrum disorders in GTS (1.1%, 9.0%). These results suggest a sampling bias. One source of bias may be that studies reporting the rate of autism spectrum disorders in GTS have sampled clinic outpatient attenders. The difficulties of most children with autism are likely to be identified during the preschool years, and these children are likely to attend special schools. Unusual behaviours that develop subsequently will tend to be considered in the context of the child’s autism, and as the key management of these children’s needs will be met in special school placements, the need for further assessment for a subset of unusual behaviours is unlikely to be recognised or felt. Hence, outpatient samples of children with tic disorders probably under-represent children with autism, and staff at special schools for children with autism are unlikely to look for the presence of tics.

Second, the rate of Asperger syndrome in GTS appears to exceed by far that of autism in GTS (9.0% vs. 1.1%), and the rate of GTS in Asperger syndrome appears to exceed by far the rate of GTS in autism (50.0% vs. 2.6%–20.3%). (Note that Comings and Comings’ figure of 1.1% includes individuals with Asperger syndrome and PDD, and that Burd and colleagues’ figure of 20.3% includes individuals with atypical PDD.) This may again reflect a sampling bias. Children with Asperger syndrome, or high-functioning forms of autism, are more likely than children with autism to receive a late diagnosis and to receive mainstream schooling, and these factors may render the identification of tics, and so referral to outpatient GTS clinics, more likely.

This is important as Kerbeshian and Burd’s group (Burd et al., 1987; Kerbeshian et al., 1984a, b) has suggested that the development of GTS in children with autism is a marker for improved developmental outcome. In their study (Burd et al., 1987), the comorbid group had a higher mean IQ (70.4 vs. 45.5), and superior receptive and expressive language skills, than the group with infantile autism or PDD alone. Similarly, Sverd (1988) reported two children with GTS comorbid with a mild form of PDD, and suggested that in some cases of PDD, the co-occurrence of GTS may be an indication of a less
severe variant of PDD. Contrary to these reports, Kano and colleagues (Kano et al., 1987, 1988) have reported two young adults with comorbid autism and GTS, followed since early childhood, neither of whom showed improved intellectual, language, or social functioning following the development of GTS.

The study presented here aimed to establish the rate of GTS in a special school population of children and adolescents with autism. This population was chosen in order to avoid possible sampling biases created by relying solely on outpatient clinics. In addition, the present study employed a prospective, multi-stage design, using both direct observation and family interview methods.

Method

Participants

All pupils attending a special school for children and adolescents with autism were invited to take part in the study. The total school population was 61 pupils, with a mean age of 14:2 (years:months; range 10:10 to 18:9), and a sex ratio of 3:7:1 (male:female). The parents of 41 (67.2%) children responded. Of responders, the parents of 39 (95.1%) children consented and the parents of 2 (4.9%) children declined to take part in the study. Two children for whom parental consent was given were unavailable for observation at the time of the study. Hence, the total number of children participating was 37, with a mean age of 14:2 (range 10:10 to 18:9), and a sex ratio of 4:3:1 (male:female).

Procedure

Stage 1: Case-note identification. The case-notes of all participating children were reviewed to identify any children who had previously been assessed for a tic disorder, or had previously received a diagnosis of GTS.

Stage 2: Teacher identification. The symptoms of GTS were discussed with teaching staff with the aid of a video showing motor and vocal tics in a child and adult with GTS. Teachers were subsequently asked to identify any child who had ever displayed similar behaviours at school.

Stage 3: Observation. Two observers (CM & JM) carried out independent observations of all participating children during a 2-day period. Both observers are experienced in the assessment and diagnosis of GTS. Children were observed at school, in their classrooms, and during their usual school activities. An attempt was made for each child to be observed at different times of the day (morning and afternoon) by the two observers, although this was not possible for all children. Each child was observed for at least 20 minutes (10 minutes by each observer), using a time-interval sampling observational procedure. The presence of motor and vocal tics, and of other abnormal movements, was recorded. Each child was subsequently classified by each observer independently as having motor tics, vocal tics, motor and vocal tics, or not tics, on observation. Children classified as having motor and vocal tics, when both observers’ observations were pooled, were entered directly into Stage 5. Children classified as having only motor or vocal tics, when both observers’ observations were pooled, were entered into Stage 4.

Stage 4: Re-observation. All children classified as having motor or vocal tics (but not motor and vocal tics) at Stage 3 were re-observed at their school by one observer (CM), for a further 20 minutes each, 4 weeks later. Children for whom both motor and vocal tics had been observed, when all observations (Stages 3 and 4) were pooled, were also entered into Stage 5.

Stage 5: Family interviews. The parents of the children classified as showing both motor and vocal tics on observation were invited to discuss their child’s possible GTS. Interviews were conducted at the children’s school, by a neuropsychiatrist (MMR) and psychologist (SBC) experienced in the specialist assessment and diagnosis of GTS and autism, respectively.

DSM-III-R (American Psychiatric Association, 1987) criteria for GTS were used in preference to DSM-IV (American Psychiatric Association, 1994) criteria, as DSM-IV requires the additional criterion that tic symptoms must cause marked distress or significant impairment. The adoption of this subjective criterion is inappropriate for many research purposes (Comings, 1995; Erenberg & Fahn, 1996; Freeman, Fast, & Kent, 1995). Particular issues for this study are that personal distress may not be experienced by young children, and may be difficult to establish in children with limited communication and in some children with learning disability. The interviewers also observed each (Stage 5) child on the same day as the family interviews, either as part of the interview, or during the child’s usual school activities.

Subsequently, previously obtained results on the Test for Reception of Grammar (TROG) measure of vocabulary and syntax comprehension (Bishop, 1983) were made available to the research team for each Stage 5 child.

Results

The numbers of children identified at each stage of the study are shown in Table 1.

At Stage 2, the teachers of 29 of the 37 participating children were available for discussion at the time of the study. Nine of these 29 children (31.0%) were identified by their teachers as having shown a history of tic-like behaviours. This information was not used to classify children, as teachers reported some difficulty in differentiating between voluntary and involuntary movements and noises. (However, five of the nine teacher-identified children were also identified by the trained observers as showing motor and/or vocal tics, and two of these nine were later diagnosed with GTS.)

Four children entered Stage 5 of the study. The parents of one child declined to be interviewed. For the remaining three children, at least one parent was interviewed. For two of the children, a second parent or other relatives also took part in the interview. The diagnosis of GTS was confirmed after family interview for all three children. Family history data confirmed a family history of GTS in all three cases. A brief description of each diagnosed child is given below.

### Table 1

| Numbers of Children Identified at Each Stage of the Study |
|---------------|---------------|---------------|----------------|
|               | Motor tics only | Vocal tics only | Motor and vocal tics |
| Stage 1       | 0              | 0              | 0               |
| Stage 2       | 4              | 1              | 4               |
| Stage 3\(^a\) | 8              | 0              | 2               |
| Stage 4\(^b\) | 6              | 2              | (8)             |
| Stage 5\(^c\) | 0              | 3              | (3)             |

\(^a\) Non-cumulative.  
\(^b\) When both observers’ data were pooled.  
\(^c\) When all observations (Stages 3 and 4) were pooled.
Child 1
Child 1 was aged 16:6 at the start of the study. He displayed multiple motor and vocal tics on observation. Simple motor tics included blinking, mouth movements, head-jerking, finger-flexing, and arm extensions. Simple vocal tics included throat-clearing and high-pitched noises. More complex motor tics included lip-smacking, face-rubbing, body-tapping, head-clasping, clapping, stamping, and whole-body jumping. Complex vocal tics included exaggerated laughing and bird-like noises. Echolalia and palilalia were also observed. He did not show any other abnormal movements, such as stereotypies, on observation.

The following history was obtained on family interview. Child 1 was born by forceps delivery, and was mildly jaundiced. He had developed tics between the ages of 7 and 12 years old, and had a wide repertoire of simple and complex motor and vocal tics. He had a positive history of both echolalia and palilalia, but a negative history of coprophenomena, echopraxia, and palipraxia. His tics had shown a fluctuating course, were exacerbated in crowds, and had decreased in severity with age. The tics did not appear to cause any distress. He also showed obsessive-compulsive behaviours, including checking and forced-touching. He had a history of mild self-injurious behaviour, in the form of hand-biting. He had a positive maternal family history of both motor and vocal tics, and a positive paternal family history of tics. He fulfilled DSM-III-R criteria for GTS, of moderate severity.

Child 1 was assessed on the TROG measure of receptive language (Bishop, 1983) at age 15:0 (18 months preceding entry into the study). He performed with an age equivalent of 5:3, giving a discrepancy of 9:9.

Child 2
Child 2 was aged 14:10 at the start of the study. On observation, he displayed several simple motor tics, such as blinking, arm-extensions and abductions, and whole-body jerking, and a simple vocal tic, in the form of a loud guttural noise. He did not show any complex tics on observation, although his tics were of marked intensity. He did not show any other abnormal movements, such as stereotypies, on observation.

The following history was obtained on family interview. Child 2 had been born by forceps delivery, and had been mildly jaundiced. He had suffered several febrile convulsions between the ages of 5 and 7 years of age. He had developed motor tics at the age of 5 years in the form of blinking, and vocal tics at the age of 9 years. He had a positive history of echopraxia, but a negative history of coprophenomena, paliphenomena, and echolalia. Typically, his tics had shown a fluctuating course, had increased in severity at adolescence, and were exacerbated by excitement and distress. At times, the tics disrupted his activities and caused distress to himself and his family. He also had marked compulsive behaviours, including checking, a concern for objects to be positioned in exactly the “right” place, and forced touching. These compulsive behaviours had warranted a trial of behaviour therapy. He also had a history of self-injurious behaviours, such as smacking himself. He had a positive maternal history of motor and vocal tics. He satisfied DSM-III-R (and DSM-IV) criteria for GTS, of moderate severity. Although he had received a low dose of chlorpromazine for 1 year during adolescence, the onset of tics had preceded this treatment.

Child 2 was assessed on the TROG measure of receptive language (Bishop, 1983) at age 14:5 (5 months preceding entry into the study). He performed with an age equivalent of < 4:0, giving a discrepancy of > 10:5.

Child 3
Child 3 was aged 13:9 at the start of the study. On observation, he showed several simple motor tics, such as blinking, blowing-out, and whole-body jerking, and some simple vocal tics, such as whooping noises. He also displayed palilalia on observation. He showed additional stereotypical behaviours on observation, as well as over-activity, jumping, and a variety of noises which were not considered tic-related.

The following history was obtained on family interview. Child 3 was born by caesarean section, at 10 days post-maturity. He had developed facial grimacing between 3 and 4 years of age, and grunting at 7–8 years, and ticks had shown a fluctuating course. He had a positive history of echolalia and palilalia, but a negative history of coprophenomena, echopraxia, and palipraxia. The tics did not appear to cause any personal distress, although the onset of excessive blinking at age 11 had caused some concern to his family. He also showed compulsive behaviours, such as flicking light switches on and off, and forced touching, including a ritual of touching the corners of objects with his foot before leaving a room. He had a history of self-injurious behaviours, including head-banging. He had a positive maternal family history of vocal tics and obsessive-compulsive behaviours. He satisfied DSM-III-R criteria for GTS, of mild severity. Motor and vocal tics had preceded a small dose of thioridazine at 8 years of age.

Child 3 was assessed on the TROG measure of receptive language (Bishop, 1983) at age 13:4 (5 months preceding entry into the study). He performed with an age equivalent of < 4:0, giving a discrepancy of > 9:4.

Discussion
The observed rate of 8.1% of GTS in this special school population of children with autism far exceeds that expected by chance. This observed rate may currently be the most accurate estimate of the prevalence of GTS in autism, as previous studies have retrospectively assessed the rate of GTS in clinical series of individuals with autism, and have not used prospective multi-stage studies, using combined observational and family interview methods.

This study supports the use of prospective multi-stage designs, using independent observation and direct family interview methods to assess the prevalence of GTS in children with autism. It is important to use populations of children with autism who are not selected for the presence of GTS. That no participating child had previously received a diagnosis of GTS, or an assessment for a tic...
disorder, supports the suitability of special school populations for future prevalence studies.

In accordance with Kano and colleagues, this study does not lend support to earlier suggestions that the development of GTS in children with autism is a marker for improved developmental outcome, or indicates a less severe variant of PDD. On clinical impression, the three comorbid children did not show superior intellectual, language, or social development to their non-comorbid peers. On the TROG measure of receptive language (Bishop, 1983), our children showed a developmental delay of at least 9–10 years. At the time of the study, expressive speech had not developed in one child (who used sign language), and the remaining two children used largely single words and stereotyped phrases. Given that these children had already reached adolescence, and that the onset of GTS was at 7–12 years, 5 years, and 3–4 years, respectively, these results suggest that these children’s development was not significantly accelerated with the onset of GTS. However, a longitudinal group design using repeated quantitative measures would be necessary to compare accurately the rate of development of children with autism who develop GTS with those who do not.

We consider the rate of 8.1% of GTS in autism as a minimum prevalence estimate for several reasons. First, that a significant proportion of children not identified as having GTS did, however, show motor or vocal tics (but not both) on observation. Children with GTS show a fluctuating course of tic expression, and so it is plausible that those children showing only motor or vocal tics, if observed for a longer period, would have shown both motor and vocal tics, and so entered the final stage of the study. Indeed, this is demonstrated by the two children who were identified as showing both motor and vocal tics only after re-observation at Stage 4. Second, children identified by their teachers as showing tic-like behaviours, but not identified by the researchers as showing motor or vocal tics on observation, may have been identified by the researchers as showing tics if they had been observed at a different time, or for a longer period. For both of these reasons, the observed rate of 8.1% of GTS in children with autism may be an underestimate.

In the final section of this paper we consider some methodological issues important to future research. First, it is possible that children with autism also appeared to show a higher prevalence of alternative tic disorders (such as transient tic disorder, chronic motor tic disorder, and chronic vocal tic disorder). The possibility of an increased rate of other tic disorders in autism has relevance for genetic studies. This merits full investigation.

Second, we should be aware of the possibility that the high observed rate of tics in children with autism may simply reflect the difficulty in distinguishing tics from other abnormal movements and noises in this population. In particular, complex motor tics can be difficult to distinguish from stereotypes in the absence of self-reported subjective experiential information, particularly regarding the volitional nature of behaviour. Such self-report data is not easily available in children with autism. However, tics, in contrast to stereotypes, are typically short-lived, contextually inappropriate, and interrupt the flow of behaviour or speech. Future studies might develop quantitative measures using these observable parameters with which to distinguish tics and other abnormal movements in children with autism.

Third, the method used here was only tested in one (medium-sized) school for children with autism. The sample size is not sufficiently large to enable robust conclusions, but given the apparent link between autism and GTS re-emerging even in a study of this size, we would advocate that a large-scale prevalence study of such comorbidity is merited.

Fourth, there is the possibility that despite the elevated rates found here, the link between these two conditions may not reflect any genetic factor. Rather, the observed elevated rate of GTS in children with autism could simply be due to some other common aetiological factor such as a neurochemical and/or a frontostriatal abnormality. What we can conclude is that the elevated rate of GTS in autism support neither a chance co-occurrence, and nor is it a neuroleptic-induced artefact. Future work addressing the genetic vs. other biological explanations of the link between these two conditions will be important in furthering our understanding of their respective pathogeneses.

Acknowledgements—We are grateful to the staff and pupils of the participating National Autistic Society school for their help with this study, to Patrick Bolton for discussions, and to Michael Trimble for his support and his comments on an earlier draft of this paper. Simon Baron-Cohen was supported by the Tourette Syndrome Association (U.S.A.) and the NHS Anglia and Oxford Region during the period of this work.

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Manuscript accepted 28 April 1998