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Short report

Gilles de la Tourette's syndrome in monozygotic twins

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SUMMARY Concordance is reported of Gilles de la Tourette syndrome in a male twin pair in whom phenotyping revealed a >98·7% probability that they were monozygotic. The development and extent of the illness differed markedly in the two subjects. Our findings are compatible with the view that there is a genetic form of Gilles de la Tourette syndrome.

Gilles de la Tourette's syndrome is a condition of unknown aetiology which is characterised by motor and vocal tics developing in childhood.[1] Coprolalia is the most distinctive feature and occurs in approximately 50% of subjects.[2] Both environmentally linked and hereditary forms are believed to occur[1] though some authors have questioned the significance of genetic factors.[3] Few reports are available on Gilles de la Tourette syndrome in twins.[1 2 4–6] We report on the concordance of the syndrome in a monozygotic twin pair in whom the development and progress of the disorder differed markedly in the two subjects.

Clinical data and methods

The patients were male, of non-Jewish background, who were reared together. Collateral information was obtained from the parents. Obstetric records were personally examined. The mother was a full term primagravida. Pregnancy was unremarkable. The placenta was single and monochorionic. The twins were identical for the following blood group antigens:

A	B;	Cc	D	Ee;	Jk^a;	P;	Le^a;	M;	N	Fy^aFy^b	s	S	K	k
–	–	++	+	–+	–	–	–	+	+	–	+	+	–	+

The total finger ridge count differed by 17. The probability of dizygosity was calculated as 0·013.[7] In addition the boys were similar in the appearance of their irises (blue, lacy), hair (brown, wavy, one clockwise whorl), ear lobes (attached), teeth, and general gestalt. These results indicated a more than 98·7% probability that the twins were monozygous.

At the age of 7 years, CV would suddenly get off his chair in the classroom, spin around, and go back to his seat (table 1). He then developed head-tossing, and, over the next two years, the tics spread to involve the shoulders (shrugging), face (grimacing), trunk and limbs (jerking). At age 9, vocal tics appeared (throat-clearing, grunting, squealing, screaming). At age 12, coprolalia ("shit", "fuck", and "bitch") developed. Later, phrases such as "goddam whore" were verbalised. At school he was a "straight A" student. His condition progressively worsened and at age 17 a diagnosis of Gilles de la Tourette syndrome was made. At this time he had coprolalia and occasional echolalia. Clinically, he displayed most of the tics on the Initial Symptom List of Shapiro *et al*,[2] as well as stretching, kicking the ground, tapping the back of his head and teeth grinding. He had never received psychotropic medication.

DV was "bluish" at birth. He was given respiratory assistance and placed in an incubator for one week. At age 4 years he had a short attention span, high activity level, and inability to sit still. When 5, he tossed his head. Over the next year, he made hooting and barking noises and skipped in steps while walking. At age 6 a diagnosis of "hyperactivity" was made and methylphenidate started. At low doses (1 tablet twice daily, exact dose unknown), his activity level and concentration improved. Within weeks, the tics worsened. By age 7, his movements and vocalisations became even more marked, with severe head tossing, shoulder shrugging, hooting and barking. Methylphenidate was gradually increased. At age 8, his head tossing and body contortions were described as "violent", at which time the patient was taking methylphenidate in amounts four to five times greater than the initial dose. At age 12–13, while still on methylphenidate he appeared to have "outgrown his condition". Accordingly, methylphenidate was phased out. The tics continued to abate, so that by age 16 they manifested only when he was exceptionally stressed or tired. Under these conditions he would nod and tug his hair. This situation persisted to the present time. When examined by us, no tics were observed. DV never showed coprolalia. Aside from methylphenidate, he received no psychotropic medication.

Apart from tics (CV), clinical examination was normal in

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Table 1 *Clinical data*

Item	*CV*	*DV*
Birth order	1st	2nd
Delivery	normal, low forceps	normal
Presentation	cephalic	breech-footling
Condition at birth	"pink, healthy"	"bluish"
Birth weight	5 lbs., 8 oz.	4 lbs., 11 oz.
Developmental milestones	normal	normal
Childhood illnesses	chicken pox, age 8 tonsillectomy, age 10½	chicken pox, age 8 tonsillectomy, age 4
Motor tics	onset age 7	onset age 5
Vocal tics	onset age 9	onset age 5½
Coprolalia	onset age 12	absent
Course of tics	waxing and waning but progressively worse	waxing and waning, progressively worse until age 11–12. Improvement age 13, continuing until virtual disappearance age 16.††
Verbal IQ*†	118	120
Nonverbal IQ*†	123	123
Full scale IQ*†	122	123
Memory quotient*†	129	118
Reitan battery*	minor tactile-perceptual anomalies‡	minor tactile-perceptual anomalies‡
Physical examination	normal, aside from tics	normal, minor simple tics only when stressed
Height§	1·8 m	1·75 m
Weight§	79·4 Kg‖	65·7 Kg
Handedness	right	left
EEG	"minimal intermittent non-specific disturbances of cerebral activity in both frontal regions"	"minimal non-specific disturbance of cerebral activity in both frontal regions"
CT scan	normal**	normal

*psychologic testing performed at age 18.
†Wechsler Scales.
‡possibly indicative of minimal soft signs of bilateral anterior parietal dysfunction; however, no hard test findings for cortical dysfunction were present.
§current.
‖gained approx. 9 Kg since lifting weights for 3 yr.
**some movement artifacts present.
††treated with methylphenidate; see text.

Table 2 *Gilles de la Tourette's syndrome in twins*

Twin pairs	*Gender*	*Zygosity*	*Criteria for zygosity*	*Concordance*	*Ref*
1	M	Monozygotic	Not given	Discordant*	(4)
1†	M	Unstated	Single placenta‡	Concordant	(5)
2	M/F	Dizygotic		Discordant	(2)
1	M	Monozygotic	Serologically identical§	Concordant	(2)
1	?	Monozygotic	Unstated	Concordant	(1)‖
1	M	Monozygotic	Single placenta‡ Identical appearance	Concordant	(6)

*Unaffected twin not examined.
†Diagnosis unclear; neurological and clinical findings in addition to those characteristic of Tourette's syndrome present.
‡Unstated or unknown whether monochorionic or dichorionic.
§Nature of serological tests used not stated; physical appearance dissimilar.
‖Personal communication by Cohen, T to Eldridge *et al*, 1979(1); no details given.

both twins. Mental state examination revealed bright, personable, and well-adjusted boys with no manifest psychopathology. Neuro-ophthalmological assessment (including slit-lamp examination for Kayser-Fleischer rings) revealed no abnormality. Serum calcium, phosphorous and other routine laboratory investigations were normal in both patients. There was no clear evidence of organic signs on the modified Reitan battery. There was no family history of Gilles de la Tourette syndrome or any tic disorder. A paternal first cousin had Down's Syndrome.

Discussion

Genetic factors are believed to play a role in Gilles de la Tourette syndrome.[1] Evidence for this view, derived from familial aggregation studies has, however, been questioned.[3] Few reports are available on Gilles de la Tourette syndrome in twins (table 2). Unfortunately, establishment of zygosity by rigorous criteria in these twin studies is wanting. In our patients there was

>98·7% probability that they were monozygotic.

In CV the age of onset, the presence of vocal tics, motor tics, and coprolalia together with the absence of other physical symptoms, laboratory abnormalities or history of drug exposure make the diagnosis of Gilles de la Tourette syndrome fairly certain. DV was initially diagnosed as "hyperactive". Further, treatment of hyperactive behavioural disorders with methylphenidate may induce Gilles de la Tourette syndrome.[8–10] Hence the concordance of diagnosis in our twin pair may be questioned. However, signs and symptoms of the hyperactive syndrome (minimal brain dysfunction) are not uncommonly found in Gilles de la Tourette syndrome patients.[2 11] Also, vocal tics which are characteristic of Gilles de la Tourette syndrome are not a feature of minimal brain dysfunction. Though DV has never exhibited coprolalia, this symptom only occurs in 50% of Gilles de la Tourette syndrome patients.[1] The motor and vocal tics antedated drug therapy so that DV's condition cannot be considered a consequence of methylphenidate therapy. Our diagnosis of DV is Gilles de la Tourette syndrome.

Our observations support the view of Eldridge *et al*[1] that there is a genetic form of Gilles de la Tourette syndrome. Even though our twin pair was concordant for the syndrome, the onset and development differed significantly in the two subjects. Similar variation in outcome in a monozygotic twin pair who were identical serologically (but dissimilar in appearance) has been noted by Shapiro *et al*.[2] In our twin pair the twins were similar in appearance but the older twin, the one with the active Gilles de la Tourette syndrome, was 1½ inches taller.

An enhancement of central catecholaminergic mechanisms is believed to underlie the pathophysiology of Gilles de la Tourette syndrome.[10] Methylphenidate increases the availability of neurotransmitter at postsynaptic catecholaminergic receptor sites and in this manner is believed to account for the precipitation[10] or worsening of established Gilles de la Tourette syndrome.[8 12] In keeping with the foregoing observations, methylphenidate also worsened the tic behaviour in DV, at least for the first several years. The subsequent abatement of Gilles de la Tourette syndrome in DV despite continued administration of methylphenidate may have been an idiosyncratic and independent event unrelated to methylphenidate. On the other hand we can speculate that the improvement that ensued with continuous methylphenidate therapy resulted from progressive desensitisation of catecholamine receptor sites in the presence of chronic neurotransmitter excess.[13]

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