The Ticcing Link

Many mental disorders and a few crucial genes may tie into Tourette's syndrome

By BRUCE BOWER

In 1902, a Frenchman identified only as "O." bared his soul in print under the title "Les Confessions d'un Ticquer." As a boy, O. wrote, he had felt the urge to imitate any curious gesture, facial expression, phrase or pronunciation he observed in others. In private, he practiced each imitation over and over; in public, the well-rehearsed "tics" would involuntarily reappear for months thereafter.

O. soon developed numerous other vocal and body tics, often driven by irrational, irresistible thoughts. For example, as soon as he placed his pince-nez on his nose, he felt compelled to continually readjust its position, occasionally jerking back his head for a better focus. His gaze wandered back and forth, from the rim of the pince-nez to whatever he was looking at, and he felt uncomfortable when either was not in his line of sight.

"My tics upset my pince-nez, and I have to invent another tic to get it back into place," O. lamented. "The absurdity of this vicious circle does not escape my observation, and I know I am its author, yet that cannot prevent my becoming its victim."

O.'s confession also included the comments of his two physicians. They noted that he consciously suppressed his many tics for an hour or two in the company of others. When the pressure to tic became too great, O. would retreat to an empty room, they wrote, "abandoning himself in his moment of solitude to a veritable debauch of absurd gesticulations, a wild muscular carnival, from which he returns comforted, to resume sedately the thread of the interrupted dialogue."

O.'s strange condition is known as Tourette's syndrome (TS), and it is hardly a turn-of-the-century relic. Although modern clinical descriptions of TS are rarely as penetrating as O.'s confessions, TS today affects a surprisingly large number of people — perhaps 100,000 to 330,000 in the United States alone — and currently receives the close attention of several research teams. Some of those scientists, at last May's meeting of the American Psychiatric Association in New York City, described their efforts to uncover the genetic foundation of TS and decipher the connection of multiple tics to a number of psychiatric disorders and behavior problems.

One research team even proposes that TS is linked to one or a few genes responsible for many impulsive, compulsive, learning and mood disorders. Others contend that the close study of TS will nudge neurologists and psychiatrists toward a much-needed reconsideration of how brain, mind and body interact.

Despite these hopes, TS remains poorly understood and is often stigmatized. Its most infamous feature is the compulsive blurting out of obscenities, but this symptom occurs in only about one-third of TS sufferers and is not a requirement for diagnosis. The syndrome's cardinal signs are motor and vocal tics appearing almost daily for at least a year, beginning before age 21. All manner of jerks, grimaces, noises, imitations and compulsions may occur.

For instance, some Touretters are impelled to court danger by holding their hands as close as possible to open flames or spinning objects such as fans.

As the tide of nervous energy rises, thoughts and mental associations typically become more frenzied. A rapid and tenuously connected stream of ideas pours forth, at times expressed in creative and amusing ways.

TS symptoms wax and wane in the course of a day, and as O. demonstrated, Touretters can control them to some degree. The disorder strikes three to four times as many males as females.

"Most cases of Tourette's syndrome are mild and don't come to medical attention," says neurologist Roger M. Kurlan of the University of Rochester (N.Y.). Kurlan, who has studied nearly 200 members of an extended Canadian family with many TS cases, estimates that one in 2,500 people suffers full-blown Tourette's and one in 700 has a milder form of the disorder.

Careful monitoring of 3,304 elementary school students in southern California indicates that one in 100 boys has some form of TS — a much greater frequency than ever suspected, says geneticist and study director David E. Comings of City of Hope Hospital in Duarte, Calif. In contrast, the disorder affects only one in 759 girls, reports Comings, whose findings will appear in an upcoming JOURNAL OF CLINICAL PSYCHIATRY.

Physicians of O.'s era — including French neurologist Georges Gilles de la Tourette, who described the condition in 1885 — were not versed in epidemiology, but their insightful clinical descriptions stimulated much interest in TS. From the 1920s to the 1950s, psychoanalysts dominated thinking on tics and Tourette's. One influential psychoanalytic theory held that unresolved emotional conflicts might cause some people to return unconsciously to a childlike personality, or "motor ego," in which tics represent muscular expressions of inner aggression. Unfortunately, psychoanalytic psychotherapy offered little relief to TS sufferers.

The emphasis shifted to biology in the 1960s with the discovery that the powerful tranquilizer haloperidol, often used to treat schizophrenia, dramatically reduces many motor tics. Since haloperidol interferes with transmission of dopamine, a chemical messenger in the brain, researchers proposed that Tourette's resulted from an excess of dopamine.

But according to Comings, the best evidence now suggests that the basic problem in TS is a genetically caused scarcity of another brain messenger, serotonin. Normally, serotonin applies a chemical brake to activity in many parts of the brain. Comings theorizes that people with TS inherit from both parents a gene that limits serotonin availability. This, in turn, would interfere with communication between the limbic system (which controls emotions and initiates behavioral responses to external and internal sensations) and the frontal lobes

(which integrate sensory information, knit thoughts together and allow for planning and foresight).

Comings and his co-workers have analyzed the medical histories of 130 TS patients and 1,851 of their relatives, as well as 25 healthy controls and 541 of their relatives. Both distant relatives and immediate family participated in the study. A slew of psychiatric and behavioral problems turned up in the relatives of people with TS: dyslexia, depression, excessive anxiety, obsessive-compulsive disorder, alcoholism, illicit drug abuse, obesity, eating disorders, exhibitionism and other sexual disorders, persistent aggressive and violent behavior, and hyperactivity combined with severe attention deficits. About 30 percent of the TS relatives had some type of behavioral disorder, compared with 6 percent of the control relatives, Comings says.

All of the above problems have previously been linked to abnormalities in serotonin metabolism, he asserts. Comings and his associates have turned up further support for the serotonin link in blood samples from a group of 1,440 individuals including TS sufferers, their relatives and healthy controls. Average blood levels of serotonin and its chemical precursor were significantly lower in Touretters and their parents, the researchers found.

Apparently, many people with TS have inherited two genes – one from each parent – predisposing them to the syndrome, Comings asserts in *Tourette Syndrome and Human Behavior* (1990, Hope Press, Duarte, Calif.). In his view, a serotonin shortage allows a broad spectrum of behavioral and psychological conditions to surface in people with a double dose of the gene, and to a lesser extent in relatives with one TS gene. On the basis of their studies, Comings and his colleagues estimate that at least half of all cases of hyperactivity with attention problems relate to a family history of Tourette's.

Moreover, they suggest that approximately 15 percent of the population carries at least one of the proposed TS genes, and that half of these carriers have an addictive, compulsive, mood or learning problem.

Scientists in the United States and England are now attempting to track common genetic changes in families with many cases of TS. The location of a shared genetic "mutation" in family members with TS would reveal a small section of DNA containing a potential predisposition gene. So far, no such genetic links to TS have been found.

Comings' contention that a wide spectrum of mental and behavioral disorders springs from one or a few common genes contradicts the still widespread view that these conditions are, for the most part, learned or generated by childhood traumas. "The human psyche is quite resilient to many environmental stresses unless it is destabilized by the effects of these [proposed] genes," he argues.

Although nearly all TS investigators expect the eventual discovery of a genetic basis for Tourette's, many disagree with Comings' expansive theory. Psychiatrist Mary M. Robertson of Middlesex Hospital in London, England, argues that TS sufferers with additional behavioral problems, such as hyperactivity, more often seek help at treatment centers, thus creating a false impression that TS usually goes hand in hand with many other disorders.

A generally accepted view among TS researchers is that of geneticist David L. Pauls of Yale University. Pauls says a common gene probably accounts only for Tourette's syndrome, obsessive-compulsive disorder and isolated motor or vocal tics that fall short of full-fledged TS. Over the past 10 years, Pauls and his colleagues have interviewed 86 people with TS and 338 of their siblings and parents. Among the relatives they find substantially elevated rates only of TS, isolated chronic tics and obsessive-compulsive disorder. Pauls notes that depression, anxiety and other problems noted by Comings may often stem from the social fallout of TS, such as isolation from others and rejection at school and work.

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Stigma indeed attaches to TS, yet the syndrome's trademark tics may remain mild enough to go unnoticed even by those who experience them, says Kurlan. In his study of the extended Canadian family, 16 of 54 people with TS were unaware of their motor and vocal tics. Only 10 of the 54 sought medical help for their symptoms, and most did not receive a TS diagnosis until their interview with Kurlan and his associates.

Although TS appears undoubtedly hereditary, its natural history remains unclear, Kurlan adds. "About 15 percent of normally developing children have mild, temporary tics," he observes. "We don't know the significance of transient tics in the development of Tourette's syndrome."

Researchers have inadequately explored the experience of TS as lived by individuals who suffer from it, and this information, important to understanding the disorder, will never emerge solely from family studies and genetic probes, holds neurologist Oliver W. Sacks of Albert Einstein College of Medicine in New York City.

"There have been persistent efforts in this century to 'physicalize' or 'mentalize' Tourette's, when it is so manifestly both," Sacks argues. Scientific research must be combined with careful listening to and observation of TS patients, he says. In this way, the many forms of ticcing will yield deeper meaning and investigators can learn whether emotions and thoughts precede motor reactions or, as often seems the case, Touretters append mental activity to motor urges and impulses in order to make sense of them.

For example, a jerking of the hand to the face may seem nonsensical to a Touretter at first. However, within days the tic gains meaning when linked to a particular use, such as adjusting the position of one's eyeglasses.

Close attention to the inner experience of TS is also essential for successful treatment, as Sacks notes in an eloquent clinical vignette in *The Man Who Mistook His Wife for a Hat* (1985, Summit, New York). A TS patient who dubbed himself "Witty Ticcy Ray" was very bright but almost incapacitated by frequent, violent muscular tics. Nevertheless, he often produced what he called "ticcy witticisms and witty ticcicisms." In this accomplished part-time jazz drummer, tics and compulsive movements stimulated sudden, wildly creative drum solos.

Sacks prescribed a small daily dose of haloperidol for Ray, but the treatment backfired at first. The drug slowed Ray down, blunted his reflexes and timing, and interfered with his musical creativity. One of his TS behaviors, dodging in and out of revolving doors, resulted in a black eye and a broken nose during his time on haloperidol.

Sacks withdrew the medication and began weekly meetings with Ray to explore the importance of TS in his life, how it affected his personality and how he might get through his days without ticcing. Over three months of personal exploration and soul-searching, Ray recovered a mental reservoir of optimism and a potential for normal functioning that years of TS had largely obscured.

Sacks once again prescribed haloperidol, and Ray's tics departed with few ill-effects. However, he decided to abstain from the drug on weekends so his drum playing could benefit from the flights of fancy inspired by Tourette's.

Two antidepressants that increase serotonin availability in the brain – fluoxetine and clomipramine – also show

promise as TS treatments, says psychiatrist Ruth D. Bruun of Cornell University Medical College in New York City. Clomipramine has proved effective in many cases of obsessive-compulsive disorder (SN: 5/21/88, p.324).

At best, effective TS treatment is "long and arduous," sometimes taking months just to find an effective drug regimen, Bruun says. At worst, as in rare cases of "super-Tourette's" or "Tourette's psychosis," few treatment options exist. People with super-Tourette's are buffeted by a torrent of impulses and constantly shifting mental associations. They are compelled to explore whatever they happen to see – often touching, sniffing, staring, turning objects over, and rattling out questions to no one in particular.

A videotape shown at the American Psychiatric Association meeting features Sacks with a super-Tourette's patient. As the burly, bearded Sacks saunters down the street, the young man darts and twitches around him. He sniffs lampposts, runs back to a fountain that he touches and inspects, and emits a stream of virtually unintelligible comments. Later in the videotape, the young man tells Sacks, "I raise having Tourette's to an art form."

What's more, Sacks notes, the man struggles mightily – as do all super-Touretters – to preserve a sense of his own identify in the midst of constant impulse.

People with super-Tourette's respond poorly to haloperidol and other medications, Bruun says. "Drugs take away an essential part of their personality," she maintains. "A certain joy is associated with super-Tourette's, although it is also quite troubling."

At its ultimate intensity, Tourette's offers insight into "the entire, but normally hidden, inner life of the patient," Sacks writes in *Neurology and Psychiatry: A Meeting of Minds* (1989, Karger, Basel, Switz.). A torrent of external sensations bombards unconscious passions and impulses, which are instantly expressed in motor tics and signs, producing a kind of hyperactive, public dream, he explains.

In one case of super-Tourette's described by Sacks, a woman on a New York City street convulsively and mockingly caricatured the face and figure of nearly 50 passersby in about two minutes. Then the woman ducked into an alley and performed a grotesque, rapid-fire reprise – lasting only about 10 seconds – of all the gestures, postures and expressions she had chosen for mimicry.

High-speed videotaping of such individuals, followed by slow-motion playback, may capture the "dream flashes and ticcy figments . . . to reveal their full character, connection and meaning," Sacks remarks. "Tourette's can make possible a veritable microscopy of mind." □