BOOKS: NEUROSCIENCE

What Makes One Tic?

Julio Licinio

The universe is not an idea of mine.
It is my idea of the universe that is an idea of mine.
The night does not fall through my eyes.
It is my idea of the night that falls through my eyes.
Besides my thinking and there being any thoughts
The night falls concretely
And the shining of the stars exists as if it has weight.

F. Pessoa, 10–1–1917 (*1*)

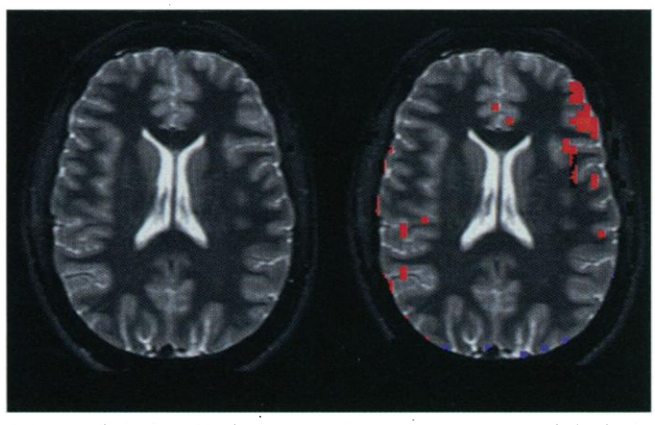
Part of what makes us human is our persistent need to understand things. To this end, we develop hypotheses, attribute causes, and classify events into various categories. As time passes, our knowledge develops and our belief systems evolve, changing the hypotheses we entertain, the causes we accept, and the classification systems we use. In *A Cursing Brain?* Howard I. Kushner describes the evolution of our understanding of Tourette's syndrome. He demonstrates that despite repeated changes in the description, diagnosis, and treatment of the syndrome over the 175 years since it was first described, throughout this period patients who exhibit the syndrome's classical symptoms—ticcing (making involuntary motor movements), grunting, and cursing—have existed.

A Cursing Brain?
The Histories of Tourette Syndrome
by Howard I. Kushner
Harvard University Press, Cambridge, MA, 1999. 319 pp. $29.95. ISBN 0-674-18022-4.

Kushner, a professor of the history of medicine at San Diego State University, focuses on an important, but not very common, disease. His descriptions bring to life clinical presentations that most of us do not see on a day-to-day basis. He develops his book along two parallel tracks: *A Cursing Brain?* is both a detailed clinical description of Tourette's and a narrative of 19th- and 20th-century ideas about the syndrome. The radical shifts in the views of this condition in the last two centuries highlight the making of medical knowledge and humble us enough to question the validity of our current beliefs.

The syndrome itself consists of a remarkable constellation of physical and behavioral symptoms. It may develop in childhood, adolescence, or adulthood. Individuals can exhibit tics, blinking, barks, grunts, yelps, sexual gestures or displays, imitation of others' behaviors, and vocalizations that range from quiet muttering to loud cursing. Not all individuals exhibit all of these symptoms. The severity of Tourette's can vary considerably among patients and over the course of time for individuals. The syndrome was formerly considered rare, but diagnoses have been increasing rapidly; it is now thought to affect 2.9 to 5.3 people per 10,000 in North America.

The clinical picture is fascinating but puzzling. Equally remarkable are the changing medical views of the syndrome, the author's focus through most of the book. "The history of Gilles de la Tourette syndrome," Kushner writes, "is both a history of medicine and a history of the production and (re)interpretation of case histories." He exhaustively documents the variety of hypotheses and theories that have been offered since Jean Itard's 1825 description of the tics and cursing that afflicted the Marquise de Dampierre. In 1885, the neurologist George Gilles de la Tourette selected this case as the first example of the illness that was soon renamed in his honor. He and his mentor, Jean-Martin Charcot, insisted that the disease was progressive and believed they had identified a hereditary degenerative cause.



A trace of ticcing. Nuclear magnetic resonance images of the brain while a patient consciously suppresses (**left**) and then expresses (**right**) ticcing behavior.

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Psychoanalytic views of Tourette's syndrome, introduced in the 1920s and 1930s, interpreted the tics as stereotyped equivalents of masturbation (Sandor Ferenczi), enabled by repressed childhood sexual conflict (Curt Boenheim), and "an attempt to express a sexual wish or idea" (Oliver English and Gerald Pearson). In the 1940s, Margaret Mahler attributed the symptoms to infantilization, parental overindulgence, and overprotection, as well as eroticized verbalizations and "subterranean penis envy." Serge Lebovici, who emerged as the leading French child psychoanalyst during the 1950s and 1960s, was certain that neurotic mothers were the vehicle of transmission of ticcing behaviors to their children. Other psychoanalytic formulations are in direct conflict with one another: some, for example, explain the symptoms as due to excessive masturbation while others blame the suppression of masturbation.

Alternative theoretical interpretations of Tourette's syndrome include a post-infectious event that was treated with removal of infected sinuses (Laurence Selling in the 1920s) and a structural defect that was treated by lobotomy (James Watts in the 1950s). Sedatives, stimulants, and carbon dioxide inhalations have all been tried for therapy. In many cases, psychotropic drugs can ameliorate the symptoms of Tourette's, but these drugs can have severe side effects that some patients find worse than their original condition. The normal waxing and waning course of the syndrome confounds any type of follow-up study.

Over the past two decades, the Tourette Syndrome Association has effectively promoted the clinical awareness of the condition and research into its causes. Kushner describes the creation and evolution of this patient-support group and the important roles Drs. Arthur and Elaine Shapiro played in its efforts. Particularly interesting sections of the book depict the different trajectories followed by the clinical and theoretical constructs of Tourette's in the United States and France. While organic explanations triumphed in North America, the psychoanalytic frame for the syndrome remained resilient in France.

One of the book's shortcomings is the absence of consideration of the syndrome's

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history prior to its recognition in the 19th century. But the major weakness of the book is that Kushner systematically cites and highlights infectious events in the case histories he discusses even though he notes that "researchers should remain skeptical about new claims and interventions, even when they appear to work." These events may lead the reader to hypothesize that the syndrome is a post-infectious (that is, possibly inflammatory or immune) disorder. The author fails to mention that although the incidence of post-infectious syndromes, such as Sydenham's chorea, has decreased in the last decades due to better treatment of infections, the incidence of Tourette's appears to be increasing. The human need to explain things is evident in Kushner's own narrative. The sad truth, however, is that all psychiatric disorders are still of unknown cause.

Of the five major pathological mechanisms of disease—neoplasia, infection, inflammation, degeneration, and ischemia—inflammation is the most compatible with the chronic waxing and waning course of disorders such as Tourette's. But inflammatory theories for psychiatric disorders are not new. The only Nobel Prize ever awarded to a psychiatrist was granted in 1927 to Julius Wagner-Jauregg for his work on the beneficial effects on psychiatric symptoms of the body's response to infection, work which led to the amelioration of the neurosyphilis symptoms after malaria inoculation.

More recently, the cloning of cytokines (the body's inflammatory mediators) and their receptors has led to an enormous growth of research on their possible relevance to neurological and psychiatric disorders. Current research has shown that cytokines and their receptors are expressed in the brain and exert their potent central effects through redundant but discrete pathways and mechanisms. Moreover, the central and peripheral cytokine compartments are integrated but differentially regulated. The pathways and mechanisms underlying the effects of inflammatory mediators on brain function can be activated in the context of stress, inflammation, ischemia, neurodegeneration, infection, and autoimmunity. Although considerable progress has been made in basic brain-immune research, it is not yet possible to conclude that inflammatory mediators cause Tourette's syndrome—or any psychiatric disorder.

I highly recommend *A Cursing Brain?* as a brilliant and readable narrative of how, over time, we change our minds when faced with a puzzling and hard-to-treat constellation of socially maladaptive physical, behavioral, and psychological symptoms. Despite the subtle but distinct bias towards currently fashionable theories whose history is not fully provided, Kushner presents superb and meticulously documented descriptions of Tourette's and of our understanding of the syndrome. Also emerging from Kushner's laborious endeavor is that we sometimes violate the Hippocratic oath (to "first do no harm") because of our persistent efforts to deny our ignorance; we attribute cause in the absence of a sophisticated understanding of how a multitude of biological, social, and cultural signals are processed and integrated to generate adaptive or maladaptive responses. This book might have suitably been subtitled "Pride and Prejudice in the Absence of Knowledge." Only the passage of time will reveal the distance between our current ideas of causation and the concrete reality of symptoms that exist as if they have weight.

Reference

1. F. Pessoa, *Seleção Poética* (José Aguilar Editôra, Rio de Janeiro, 1971), p. 178.

PERSPECTIVES: ATMOSPHERIC CHEMISTRY

Unraveling Aircraft Impacts

Randall R. Friedl

As common as contrails are in the sky today, it is easy to imagine that the 10,000 or so jet aircraft operating every day alter the composition of the atmosphere substantially at aircraft cruise altitudes. But do they? And if so, by how much? Two recent campaigns in the North Atlantic region are now providing much-needed observational constraints on the chemical composition of the atmosphere at the relevant altitudes. Such studies are particularly timely as airline industry forecasts are predicting a doubling in the number of operational aircraft over the next 20 years (*1*).

Jet aircraft emit several chemical species that affect atmospheric chemistry and climate, including carbon dioxide (CO_2), water (H_2O), nitrogen oxides (NO_x), sulfur oxides (SO_x), and soot. Over the last decade, NO_x emissions have attracted the most attention because of their role in forming ozone, a potent greenhouse gas throughout the atmosphere and a common air pollutant in the lower troposphere. Considerable research has been focused on low NO_x combustor technologies, and the International Civil Aviation Organization (ICAO) has twice reduced the ceiling on aircraft NO_x emissions during landing and takeoff.

The NO_x emissions from present-day aircraft into the atmosphere are now relatively well quantified at about 0.5 teragrams of N per year. But their impact on ambient atmospheric chemistry is obscured by other NO_x sources such as lightning and surface emissions (see the figure). Surface emissions, in particular, are substantially larger than aircraft emissions. For example, NO_x emissions from fossil fuels and biomass burning amount to about 20 and 10 teragrams of N per year, respectively. However, most of these emissions are thought to be removed from the atmosphere by uptake on cloud drops followed by precipitation, before they can diffuse or be lifted to aircraft cruise altitudes. If this view holds, then the upper troposphere–lower stratosphere (UT-LS) region (at heights of 9 to 13 km), where most aircraft fly, represents a relatively pristine environment that is affected only episodically during weather events that rapidly lift surface air or bring down stratospheric air. Even the small fraction of surface emissions transported to high altitude is similar in magnitude to the aircraft source—although quantifying this fraction is a major challenge for atmospheric scientists. To complicate matters, the same weather events responsible for surface NO_x transport may also be associated with lightning that can produce and inject NO_x directly at the upper altitudes. But detailed understanding of NO_x generation and transport in lightning events is lacking.

The various source contributions to upper tropospheric NO_x concentrations must be quantified to reach an understanding of aircraft impacts on ozone. Atmospheric photochemical models incorporating the best available parameterizations of NO_x sources and atmospheric transport have hitherto provided the only quantitative guidance (*2–4*). These models have predict-

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