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Article abstract—A 40-year-old man with severe Gilles de la Tourette's syndrome characterized by forceful self-injurious motor tics, coprolalia, and obsessive-compulsive disorder had bilateral anterior cingulotomies and bilateral infrathalamic lesions placed stereotactically during two neurosurgical procedures. During the second procedure, the patient acutely developed a marked dysarthria. Postoperatively, he manifested a severe gait disturbance with postural instability, bradykinesia, axial rigidity, micrographia, and a profound swallowing disorder. MRI showed asymmetric (left > right) low-density areas in an infrathalamic region as well as low-density areas bilaterally in the anterior cingulate gyri. Although the patient's tic and obsessive-compulsive symptoms improved, the self-injurious motor tics along with other motor and phonic tics have recurred. The patient's speech remains largely unintelligible 8 months following the last surgical procedure, and the other neurologic deficits remain unchanged.

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Gilles de la Tourette's syndrome (TS) is a chronic familial disorder of childhood onset characterized by motor and phonic tics and a broad range of asso-

ciated behaviors including some forms of obsessive-compulsive disorder (OCD) and attention-deficit hyperactivity disorder.¹⁻³ The neurobiologic sub-

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strates for TS are unknown but likely include corticostriatohalamocortical (CSTC) circuits and monoaminergic pathways that modulate the activity of the CSTC circuits.^{4,5} We report a patient with severe TS and OCD whose tic and obsessive-compulsive symptoms showed improvement following bilateral anterior cingulotomies and lesions in the infrathalamic region and whose course was complicated by an extrapyramidal syndrome with gait disturbance, postural instability, bradykinesia, axial rigidity, micrographia, and a profound speech and swallowing disorder.

Case report. This 40-year-old, right-handed man had a severe life-long course of TS beginning at age 3 with facial, head, and shoulder tics. Vocal tics developed at age 11 and included loud noises, coprolalia, echolalia, and blocking. During adolescence, his tic symptoms improved, and by age 20 they had largely disappeared. He first presented at the Tic Disorders Clinic at Yale at 29 years of age. At this time, he reported that his tics had gradually reappeared and that they had become increasingly severe during the previous 4 years.

Examination revealed frequent forceful motor and phonic tics that occurred in bouts either singly or in complex orchestrated patterns (hitting the left side of his face with his right fist, kissing or biting his hand, and grunting in rapid succession). Other motor tics included face, head, shoulder, arm, and abdominal movements. Other phonic symptoms included various noises and sounds, coprolalia, echolalia, and palilalia. Associated symptoms included compulsive behaviors (touching objects, checking, and cleaning) and a history of attention-deficit hyperactivity disorder as well as episodes of major depression. His family history was positive for both tic disorders (father and sister) and obsessive-compulsive disorder (father).

During the ensuing 10 years, a number of medication trials were undertaken in an effort to control his tic (haloperidol, pimozide, clonidine, naltrexone, nifedipine), obsessive-compulsive (fluoxetine), and depressive (desipramine) symptoms. Despite initial success with some of these agents, severe self-injurious tic behaviors continued to complicate his course. Eventually, the patient detached his left retina and developed a traumatic cataract in his left eye. A variety of diagnostic procedures were performed during this interval including EEG, MRI, and CSF studies, all of which were normal.

In 1990, the patient was withdrawn from neuroleptic medications in order to participate in a dose-response study of spiradoline. Subsequently, he declined to resume neuroleptic treatment because of the cognitive blunting he had experienced from these agents. In April of 1990, his tic symptoms were "severe" to "extremely severe," with scores on the Yale Global Tic Severity Scale (YGTSS)⁶ of 23 for motor tics, 15 for phonic tics, and a global severity score of 78. His obsessive-compulsive symptoms were in the "moderate" to "marked" range with subtotals for obsessions and compulsions of 12 and 12, yielding a total score on the Yale-Brown Obsessive Compulsive Scale (YBOCS)⁷ of 24. Apart from his tic symptoms, a complete neurologic examination was unremarkable except for blindness in the left eye.

In early 1991, the patient heard about a neurosurgical procedure that had benefitted a woman with severe TS. He contacted the neurosurgeon at the Tulane Medical

Center and arranged for an evaluation. Prior to his departure, the patient was reexamined in May of 1991 and his tic and obsessive compulsive symptoms were virtually unchanged (YGTSS: motor tic score of 22, phonic tic score of 20, global severity score of 90; YBOCS: obsession subtotal of 11, compulsion subtotal of 11, and a total score of 22).

The patient was subsequently admitted to the Hotel Dieu in New Orleans where a series of stereotactic neurosurgical procedures were performed in the summer of 1991. On June 14, bilateral anterior cingulotomies for the control of the obsessive-compulsive symptoms and bilateral infrathalamic lesions for the control of tics were performed. Despite improvement in his obsessive-compulsive symptoms and some of his motor tic symptoms, the patient continued to experience severe motor and phonic tics postoperatively. On July 2, the left cingulate and left infrathalamic lesions were repeated. The target points selected for the second infrathalamic lesion extended inferiorly to the "top of the border of the nucleus ruber." The operative report noted that stimulation at this target resulted in "marked tics in the right arm and leg increasing in severity with increased stimulation." The probe then advanced into the red nucleus where stimulation resulted in a "marked increase in symptoms with much less voltage." A thermocoagulation lesion (90 seconds at 60 °C) was made at this point following which the patient's tics were noted to be "markedly reduced." The electrode was then withdrawn into the field of Forel, and stimulation revealed a "marked decrease in stimulatory response." A further lesion was made in this location using the same parameters described above. Immediately following surgery, it was noted that "his muscle twitching and irregular muscular activities seemed to cease"; however, he was also described as being severely dysarthric and had "great difficulty swallowing." His postoperative course was complicated by sepsis of unknown etiology which responded to intravenous antibiotics and a course of corticosteroids.

The patient was reexamined at 4 and 8 months postoperatively. At 4 months, although his motor and phonic tics and his obsessive compulsive symptoms were diminished (YGTSS: motor tic score of 15, phonic tic score of 10, global severity score of 74; YBOCS: obsession subtotal of 5, compulsion subtotal of 7, and a total score of 12), he still exhibited bouts of hitting his head, banging his elbows, and grunting.

The most significant change was in the patient's neurologic status. He presented with a severe dysarthria (characterized by slow, labored movement and restricted range of motion of the lips, tongue, and jaw), which greatly reduced the intelligibility of his speech. He had difficulty with initiation of speech and reported a feeling of weakness during prolonged conversation. The patient also indicated that he experienced severe dysphagia for solids and liquids. He described difficulty initiating swallowing and chewing, closing his mouth when chewing, and could only drink using a straw. In addition, he had developed severe handwriting problems, with difficulty initiating the activity as well as micrographia. He could understand the speech of others, accurately respond to complex commands, and communicate using a typewriter.

On examination, his speech was markedly dysphonic, slowed, and barely intelligible. Articulation was severely abnormal with difficulty initiating speech followed by short bursts of speech and then long pauses. Phonation

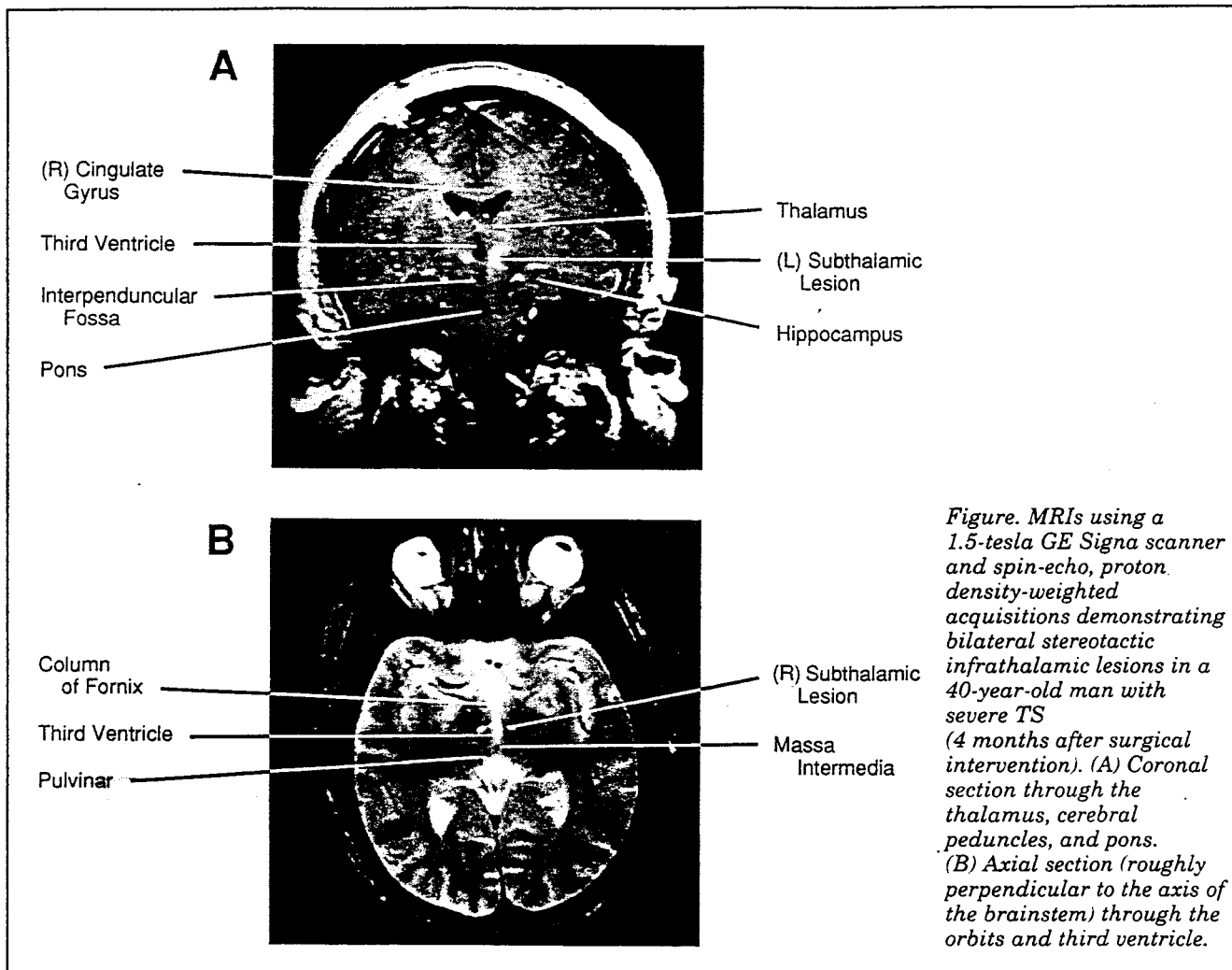


Figure. MRIs using a 1.5-tesla GE Signa scanner and spin-echo, proton density-weighted acquisitions demonstrating bilateral stereotactic infrathalamic lesions in a 40-year-old man with severe TS (4 months after surgical intervention). (A) Coronal section through the thalamus, cerebral peduncles, and pons. (B) Axial section (roughly perpendicular to the axis of the brainstem) through the orbits and third ventricle.

had a strained strangled quality. Cranial nerve examination showed severely abnormal extraocular movements with slowed vertical > horizontal saccades, saccadic pursuit movements, and apraxia of eye opening. Vestibular ocular reflex testing elicited brisk eye movements. His palate and tongue moved very slowly, and his gag reflex was hyperactive. He was bradykinetic with poor dexterity in fine motor control. The patient had increased axial rigidity. Movements of the extremities were slowed and uncoordinated. No tremor was noted. He had a mild right hemiparesis in addition to his generalized motor dysfunction. Reflexes were brisk in the lower extremities with bilateral extensor plantar responses. His balance was markedly abnormal, and he had developed a tendency to fall on turning or moving quickly. His gait was slow, unsteady, and wide-based. He also had marked retropulsion. Overall, the patient's deficits most closely resembled those of a severe progressive supranuclear palsy.

An MRI at 4 months following the last surgical intervention revealed asymmetric (left > right) low-density areas in the infrathalamic regions as well as low-density areas bilaterally in the anterior cingulate gyri (figure, A and B). As visualized in coronal section (figure, A), the extent of the infrathalamic lesions, particularly the lesion on the left side, necessarily involves portions of the basal intralaminar nuclei of the thalamus, the red nucleus, the zona incerta, the H fields of Forel, and the sub-

thalamic nucleus, as well as efferent fibers from mid-brain dopaminergic centers (ventral tegmental area and the pars reticulata of the substantia nigra) and efferent fibers from the cerebellum via the dentatorubrothalamic projections.

At an 8-month follow-up, the patient's condition was unchanged (YGTSS: motor tic score of 15, phonic tic score of 9, global severity score of 69), except that he reported continued improvement in his obsessive-compulsive symptoms (YBOCS: obsession subtotal of 2, compulsion subtotal of 5, and a total score of 7).

A comprehensive evaluation of the patient's speech mechanism was completed at 8 months. On oral motor examination, he had reduced tongue strength (on elevation), a slight deviation of his tongue to the right, and reduced palatal coordination and hyperactive gag reflexes. Palatal movement was present, but complete closure was not consistently achieved on phonemes requiring coarticulation. Posterior lingual sounds produced with the blade or base of the tongue (K, G) were initiated with marked difficulty. Posterior tongue placement frequently triggered laryngeal spasm and coughing. Intermittent episodes of laryngeal spasm were frequent, particularly after prolonged conversation. Difficulty initiating and ceasing each utterance was observed in addition to an inability to control the breath stream during speech production.

Using a Rothenberg mask (coupled with transducers

to measure air pressure and flow from the oral cavity during speech activity and a digital audio recorder), gross abnormalities in the execution of timing events and regulation of airflow as well as initiation and release of specific gestures involving lingual as well as laryngeal coordination with respiratory events were documented. Repetitive productions of utterances demonstrated deterioration of rate, intensity, and range of motion in the upper articulators, which was pronounced during the final phase of each task. Abnormal prolongation of sound and frequency and amplitude distortions resulted from the inability to coordinate these gestures in time.

Laryngeal valving was largely ineffective and poorly coordinated with the movements of upper articulators. This was observed during videostroboscopic examination of the laryngeal and pharyngeal structures using an Olympus flexible fiberoptic endoscope attached to a camera and video monitor during connected speech, rapid repetition of syllables, and sustained phonation. As with the lips, tongue, and jaw, syllable production in the larynx was labored. Abductory and adductory movements were characterized by the same slowed pattern observed in the upper articulators. Phonation was forced (with adduction assisted by the supraglottis including the pharynx and false vocal folds). Easy onset of phonation or relaxed laryngeal posture could not be stimulated. Maximum phonation time was limited to 6 seconds. Vibratory characteristics of the vocal folds were obscured by partial to complete closure of the false vocal folds and supraglottis during phonation. Analysis of acoustic signals specific to vocal fold vibration revealed harmonics-to-noise ratio lower than normal, with frequency and intensity range limited during speech reflected in a monotonic quality. There were measurable perturbations in amplitude and frequency of vocal fold vibration. Laryngeal resistance measures were elevated, likely a result of the constriction in the supraglottis during phonation.

The remainder of his neurologic examination showed no improvement at 8 months, and there was little interval change in the appearance of his lesions on MRI.

Discussion. During the past 30 years, a series of case reports have documented a variety of neurosurgical interventions for individuals with intractable TS. Many of these stereotactic procedures were aimed at disrupting CSTC circuits by lesions of thalamic nuclei (rostral intralaminar, medial, and ventral lateral nuclei)⁸⁻¹³ or by lesions directed against thalamocortical projections¹⁴⁻¹⁶ or cortical lesions (anterior cingulate, frontal cortices).^{16,17} In addition, improvement in tic symptoms has been reported following lesions that interrupt cerebellar input to the thalamic nuclei.¹⁸ Most of the patients are reported to have sustained benefit from these procedures, but caution is warranted given the small sample sizes, limited periods of follow-up, lack of controls, and the potential for serious side effects. Specifically, these reports have mentioned aseptic meningitis,¹⁷ bacterial infections,¹⁴ seizures,¹⁴ obesity,¹⁵ mental confusion and difficulties concentrating,^{9-12,16} personality changes,^{9-11,16} clumsiness and weakness,⁹⁻¹¹ as well as the transient loss of speech¹³ as side effects to these procedures.

Due to the extent of the lesions in this patient, it was difficult to identify which lesions were responsible for the 30 to 45% reduction in motor and phonic tics and which were associated with the numerous unwanted side effects of the surgery. For example, the apparent selective lesions in the dopaminergic projections to the striatum and the pallidum could have accounted for both the emergence of his progressive supranuclear palsy-like extrapyramidal symptoms^{19,20} as well as the reduction in tic symptoms. In addition, the lesions to the intralaminar nuclei of the thalamus⁹⁻¹² and the destruction of red nucleus and the dentatorubrothalamic projections¹⁸ probably contributed to the improvement in his tic symptoms.⁹⁻¹² Finally, it is possible that the lesions in the pallidosubthalamic tract could lead to a disinhibition of the subthalamopallidal and subthalamonigral projections, which in turn would increase the inhibition of thalamocortical projections. This view may be consistent with the working hypothesis advanced by Anderson et al²¹ that TS is due in part to dysfunction of the subthalamic nucleus and reduced glutamatergic input from the subthalamic nucleus to the medial pallidum and the pars reticulata of the substantia nigra.

The neurobiologic basis for this patient's severe unremitting extrapyramidal symptoms was less clear. Aspects of his clinical presentation were similar to progressive supranuclear palsy in which diffuse neuronal degeneration has been noted in the subthalamic nucleus, substantia nigra, pontine tegmentum, periaqueductal gray matter, and the pallidum.^{19,20}

Based on the prevailing models of hyperkinetic movement disorders^{22,23} and a review of the complex neuroanatomy of the lesioned infrathalamic areas, we conclude that lesions in this area have the potential to disinhibit thalamic centers and consequently exacerbate tic symptoms, particularly if the nearby subthalamopallidal, pallidothalamic, and nigrothalamic tracts were disrupted.

Our patient's experience, while heuristically interesting, emphasizes the need for caution in the application of surgical techniques that could damage the neural substrates needed for the normal control of motor function. Caution appears particularly warranted with regard to lesions in the dominant infrathalamic area. This patient's severe neurologic complications, coupled with the reemergence of his self-injurious hitting tics, argue compellingly that his was a negative outcome that compounded the tragedy of his life.

Addendum. Follow-up examination at 16 months revealed no change in his neurologic status. Despite the use of an electronic device to facilitate communication, the patient has become increasingly discouraged over the loss of effective speech.

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