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SUPPRESSION OF EXTRAPYRAMIDAL SIDE EFFECTS OF DOXEPIN BY THALAMIC DEEP BRAIN STIMULATION FOR TOURETTE SYNDROME

Thalamic deep brain stimulation (DBS) has been shown to improve tics in patients with Tourette syndrome (TS). However, problems with psychosocial adaptation and comorbid depression can complicate treatment and necessitate concomitant antidepressant therapy. Here, we describe the occurrence of an acute movement disorder including dystonia caused by the tricyclic antidepressant doxepin that interfered with the otherwise effective DBS treatment of a malignant motor tic in a patient with TS.

Case report. A right-handed 31-year-old man with TS (Diagnostic and Statistical Manual of Mental Disorders, 4th edition) had compulsory left-hand pounding of the chin leading to chronic ulceration of the skin, loss of teeth, and mandibular fractures (video 1, segment 1, on the Neurology® Web site at www.neurology.org). This left-sided violent tic was accompanied by bilateral milder motor tics (e.g., touching the lips, his nose, or his glasses with the left or right hand or twisting his ankle) and grunting as a single vocal tic (Yale Global Tic Severity Score [YGTSS] 77). Obsessive and compulsive symptoms (OCS) presented as compulsive ranging, counting, and touching, as well as intrusive thoughts (Yale-Brown Obsessive Compulsive Scale [Y-BOCS] 24). Disability and social isolation were associated with recurrent depression and 2 suicide attempts. Treatment with typical and atypical antipsychotics, clonidine, benzodiazepines, pergolide, and tetrabenazine and 3 years of psychotherapy was not effective. Therefore, with approval by the local ethics committee and after obtaining informed consent of the patient, stimulation leads were stereotactically implanted bilaterally in the associative-limbic part of the centromedian-parafascicular complex of the thalamus (thalamus_cm/pf, 4 mm posterior and 5 mm lateral to the midcommissural point). An immediate microlesioning effect with complete suppression of tics and relief from OCS was observed for 3 days. The initiation of DBS (left: 0, 130 Hz, 60 µs, 5.0 V; right: 4, 130 Hz, 60 µs, 4.0 V) yielded an immediate and complete suppression of the violent left-hand tic, the bilateral milder tics, feet movements, and the vocal tic (video 1, segment 2) as well as the obsessions and compulsions (YGTSS 15/100; Y-BOCS 0). After 13 months of successful treatment of TS, the patient received doxepin (200 mg) for the treatment of recurrent depression. Within 14 days the patient felt restless, and an acute onset of involuntary nonsuppressible phasic movements independent of his previous tic repertoire was observed. An increase of stimulation intensity (right: 8.0 V; left: 6.0 V) yielded a transient improvement. Tentative reduction of the left side stimulation intensity (video 2, segment 1) to 4.0 V was followed by an exacerbation of abnormal movements, implying akathisia with restlessness slightly pronounced on the contralateral (right) leg. Involuntary nonsuppressible phasic movements and tonic postures indicative of dystonia with slow repetitive twisting movements leading to abnormal posture of trunk and neck exacerbated below 4.0 V amplitude (video 2, segment 1; the position of the left arm is voluntary to place the telemetry head of the DBS programmer). After further reduction to 2.0 V the patient exhibited additional involuntary stereotyped movements of the right arm, which imply akathisia and exaggerated tics with poking the right eye. A similar reduction of the amplitude of the right electrode (video 2, segment 2) led to akathisia-exaggerated tics and additional phasic dystonia that differed from tics in respect to sustained and abnormal posture due to simultaneous activation of opposing muscles. Adapting stimulation parameters up to 7.0 V allowed dose-dependent contralateral suppression of these symptoms. Based on reports of acute dystonic reactions after doxepin intake, this medication was tapered down in 1 week, and the abnormal movements resolved completely. Two years after surgery, reassessment documented a permanent elimination of the violent tic, the other symptoms of TS occurring only occasionally and being mild (YGTSS 13 of 100). OCS remained completely resolved.

Discussion. This case 1) documents that DBS treatment of TS can occasionally be challenged by the occurrence of extrapyramidal side effects of antidepressant medication, 2) demonstrates that stimulation to the thalamus_cm/pf can ameliorate pharmacologically induced extrapyramidal symptoms, and 3) provides additional evidence for the
persistent relief from TS with violent tics and OCS by thalamic DBS. It has to be considered, though, that the classification of the abnormal movements presented upon doxepin treatment remains difficult because they included features of akathisia, akathisia-exaggerated tics, and additional dystonia. However, clinicians should be aware of this rare but severe adverse reaction to antidepressive medication, particularly in the context of DBS.

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