

Letters to the Editor Related to New Topics

Catonia during Deep Brain Stimulator Implantation Complicated by Intracranial Hemorrhage

Catonia is a syndrome of motor dysregulation characterized by fluctuating stupor, mutism, negativism, catalepsy, automatic obedience, and stereotypy.¹ Other motor signs include gegenhalten, mitgehen, waxy flexibility, echophenomena, and ambitendency. The diagnosis requires two to four features.²

The pathophysiology of catonia remains unclear but may involve dysfunction of frontal circuitry and motor regulatory brain areas. Catonia is most closely associated with mood disorders but also results from medications (e.g., dopamine blockers and serotonergic agents), metabolic derangement, seizures, or focal structural brain lesions.² We present a patient with Parkinson's disease (PD) who developed catonia during deep brain stimulation (DBS) surgery complicated by intracranial hemorrhage.

The patient was a 60-year-old right-handed woman with levodopa-responsive PD for 12 years. Prior to surgery, she was taking levodopa 800 mg, entacapone 800 mg, and ropinirole 8 mg daily but experienced debilitating motor fluctuations, abrupt "off" periods, and dyskinesias, despite adjustments to her medication regimen. She had a history of nonmelancholic depression treated with citalopram 20 mg daily. During presurgical evaluation, she had no dementia on neuropsychological testing or evidence of an active mood disorder. Off-on Unified Parkinson's Disease Rating Scale (UPDRS) testing demonstrated at least a 32% improvement to her standard morning levodopa dose. She was deemed an appropriate DBS candidate and underwent surgical placement of DBS electrodes into each subthalamic nucleus using microelectrode recordings. The surgery was conducted in the off medication state, over 12 hours after her last dose of PD medication. Mild hypertension during the procedure was controlled with low doses of metoprolol.

Before DBS electrode placement, the patient spoke only when asked questions or to complain of intermittent left arm pain. During right electrode placement, she gradually developed dystonic flexion posturing of the left arm and intermittent flexion of the right arm and left leg. When asked questions or given commands, she was mute. She had gegenhalten in both arms and eyelids upon passive manipulation. She had no motor weakness. Other catatonic features included a protruding grimace (schnauzkrampf), bilateral grasp reflexes, and mitgehen in the right arm.

Differential considerations included a worsening of her parkinsonian "off" state versus catonia. Lorazepam 2 mg



FIG. 1. Postoperative three dimensionally reconstructed image (left) and noncontrast head CT (right). [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

was given intravenously. Her Bush-Francis catonia rating scale³ score was 24 prior to the injection and decreased to 10 after 4 min. Rigidity decreased and her grimace and mitgehen disappeared. She spoke a few words softly and followed simple commands. These symptoms remained unchanged as the left DBS electrode was placed.

Postoperative noncontrast head CT (see Fig. 1) revealed an acute intraparenchymal hematoma in the right frontal lobe measuring 7.0 cm by 2.8 cm. There was a small amount of associated extra-axial blood. There was mild adjacent mass effect with effacement of the cerebral sulci and frontal horn of the right lateral ventricle with subfalcine herniation and associated mild midline shift to the left.

She was transferred to neurosurgical intensive care where her Bush-Francis score 4 hours after surgery was 28. Her features of stupor, rigidity, negativism, grimacing, and mitgehen had returned. She was managed supportively for 10 days without change in her examination. A trial of high dose lorazepam or electroconvulsive therapy (ECT) was not pursued. She was then transferred to a subacute care facility closer to home where her subsequent course is unknown.

We know of no other cases of catonia associated with DBS surgery or treatment. In the intraoperative setting, the main differential consideration was whether her exam represented a worsening of her parkinsonian "off" state. Her rigidity and paucity of spontaneous movements were consistent with this diagnosis. However, the mutism, negativism, gegenhalten, and grimacing were inconsistent with previous "off" examinations. The positive lorazepam challenge supported the diagnosis of catonia.

We cannot infer a specific mechanism for the development of catonia in our patient. Although the frontal lobe hemorrhage is an obvious etiologic candidate, there may have been contributions from multiple factors, including the direct surgical manipulations of basal ganglia regions and the patient's demographic predisposition to catonia. Despite her history of PD and mood disorder, she had never been catatonic prior

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to DBS surgery. There are a number of reports of catatonia secondary to infarct or hemorrhage.⁴ Gelenberg reported a case of catatonia following bilateral surgical lesions of the globus pallidus to relieve symptoms of PD.⁵ Catatonia has also been reported following surgical removal of lesions near the pallidum, hypothalamus,⁶ and cerebellum.⁷

As the field of DBS grows to include treating mood disorders—the leading cause of catatonia—the teams caring for patients should be familiar with this increasingly recognized syndrome and consider including formal assessments for catatonia part of routine care.

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Sleep Apnea Associated With Floppy Epiglottis in Adult-Onset Alexander Disease: A Case report

Alexander disease is a rare leukoencephalopathy, caused by dominant mutations in the gene encoding glial fibrillary acidic protein (GFAP).¹ A recent study reported that patients with adult-onset Alexander disease might develop sleep-disordered breathing (SDB), a condition characterized by repeated episodes of apnea and hypopnea during sleep,²

although the mechanism of airway obstruction in this disease has not been clarified. Here we report a patient with adult-onset Alexander disease presenting with SDB associated with floppy epiglottis.

A 40-year-old man with a 10 year history of slowly progressive ataxic gait was admitted to our hospital because of nocturnal inspiratory stridor. He was diagnosed having adult-onset Alexander disease on the basis of DNA analysis of the *GFAP* gene, which revealed a heterozygous substitution of T for C at nucleotide 302, leading to conversion of Leu 101 to Pro, as reported previously.³ Examination on admission revealed that his height, weight, and body mass index were 169.5 cm, 69.5 kg, and 24.2, respectively. Neurological examination revealed truncal and limb ataxia, dysphagia, dysarthria, spastic weakness, palatal myoclonus, urinary incontinence, and mild cognitive impairment. His only medication was urapidil (30 mg daily) for his neurogenic bladder.

The patient also presented with inspiratory stridor during sleep. His Epworth sleepiness score (ESS) was nine (<10: normal). Polysomnography, performed according to the recommendations of the American Academy of Sleep Medicine (AASM) Task Force in 1999,⁴ revealed severe SDB (apnea index, 67.0/h; apnea–hypopnea index, 67.1/h; maximal apnea duration, 67 s; and arousal index, 34.3/h). Of the 479 apneic episodes, 53.0% were obstructive, 37.8% were mixed, and 9.2% were central. Although the saturation during the awake status was 96 to 97%, oxygen desaturation was severe (%sleep time with SpO₂ below 90%, 58.6%; mean oxygen saturation, 89.0%; and minimal oxygen saturation, 75%). His desaturation was observed regardless of the sleep stage, although oxygen saturation was comparatively lower during non-REM stages (SpO₂ = 85%) than during REM stage (SpO₂ = 89%). Frequency of rapid eye movement (REM) sleep were normal (%stage REM = 21%), and latency of REM sleep were slightly short for his age (REM latency = 66 minutes).

Fiberoptic laryngoscopy during wakefulness revealed no apparent sites of upper airway obstruction, but under propofol-induced anesthesia⁵ it revealed that the epiglottis was sucked into the glottis during inspiration (Fig. 1). To determine whether continuous positive airway pressure (CPAP) treatment can improve SDB associated with floppy epiglottis, we examined the effect of the treatment on airway obstruction and oxygen saturation. We found that positive pressure >6 cm H₂O exacerbated upper airway obstruction by further promoting the downward displacement of the epiglottis into the laryngeal inlet. In addition, CPAP treatment >10 cm H₂O worsened oxygen desaturation from 94 to 86%. We decided to abandon treatment using CPAP or noninvasive positive pressure ventilation (NPPV), because there was a possibility that positive pressure ventilation might cause worsening of upper airway obstruction. Instead, we proposed treating the patient's SDB with tracheostomy; however, he did not choose tracheostomy but wanted to continue rehabilitation for his dysphagia.

In this report, we present several novel findings in the patient with SDB and adult-onset Alexander disease. First, patients with this disease can develop inspiratory stridor and obstructive sleep apnea associated with floppy epiglottis. Floppy epiglottis is a condition in which the epiglottis is sucked into the glottis during inspiration and is a common cause of laryngeal stridor in infants, which is caused

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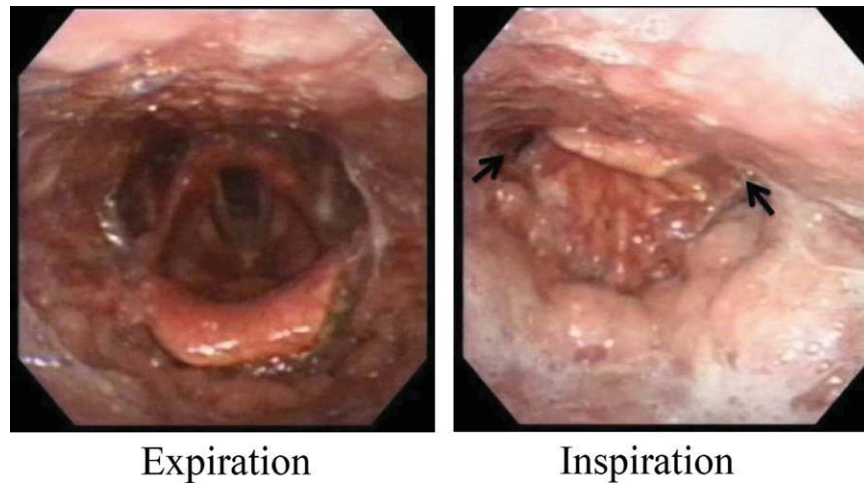


FIG. 1. Floppy epiglottis revealed by fiberoptic laryngoscopy under propofol-induced anesthesia. (Left) During expiration, patency of the upper airway was maintained, and the vocal cords were visible. (Right) During inspiration, the epiglottis was sucked into the glottis. Complete airway obstruction was avoided by narrow gaps between the epiglottis and glottis walls (arrows). [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

by a congenital abnormality in laryngeal cartilage.⁶ Although floppy epiglottis of adult onset is a very rare condition, it has been reported in patients after a head injury⁷ or a cerebrovascular accident.⁸ We recently reported that patients with multiple system atrophy develop floppy epiglottis, which causes inspiratory nocturnal stridor and obstructive sleep apnea.⁵ Because it has been speculated that floppy epiglottis is caused by the loss of laryngeal motor tone associated with the degeneration of the nucleus ambiguus,⁹ floppy epiglottis in the present patient might be related to brainstem lesions associated with Alexander disease.

Second, this study reported that patients with adult-onset Alexander disease can develop sleep apnea of central origin, though central apnea was not frequent (9.2%). Future studies should be performed to investigate whether adult-onset Alexander disease can develop central apnea, because patients with this disease have prominent atrophy of the lower brainstem, where the respiratory center is located. When patients with adult-onset Alexander disease develop SDB, it is important to determine the mechanism of sleep apnea.

Finally, we show that CPAP treatment can exacerbate floppy epiglottis-associated SDB. In addition, a recent study showed that CPAP treatment exacerbated the airway patency of congenital floppy epiglottis.¹⁰ It is important to note that CPAP treatment can exacerbate SDB in patients with floppy epiglottis.

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Propriospinal Myoclonus Due to Cord Compression in the Absence of Myelopathy

Video



A 43-year-old woman presented with 3 year history of involuntary rapid flexion of the trunk and proximal legs, inconsistently preceded by a sensation of tightness in the posterior thigh muscles. These myoclonic jerks could only be suppressed for a few seconds and they could be triggered by sensory stimulation (such as rubbing her back). The movements were exacerbated by prolonged standing and by flexion or rotation of her neck. She worked in a bakery, where negative myoclonus (asterixis) of the legs would cause her to stumble while carrying trays of baked goods. For one year before the onset of myoclonus, she had been experiencing a burning discomfort in both thighs after prolonged sitting. These symptoms were ameliorated by ropinirole 2 mg QHS, but this was discontinued as the myoclonus became the predominant source of disability. Myoclonus did not improve with valproic acid, clonazepam, or levetiracetam despite slow titration to doses sufficient to cause side effects. There was no family history of myoclonus or dystonia. She denied leg weakness or numbness, bowel, bladder, or sexual dysfunction. Examination showed spontaneous and stimulus-sensitive axial and appendicular myoclonus (see Video Segment 1). There was a right crossed adductor response. All laboratory tests, including complete blood count, human T-cell lymphotropic virus I and II antibodies, antitransglutaminase immunoglobulins, and iron studies, were normal. Somatosensory evoked potentials had normal amplitudes and latencies.

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EEG with back-averaging did not show any cortical onset of the myoclonus. MRI of the brain was normal. MRI of the cervical spine (Fig. 1) showed a herniated intervertebral disc at C5 to six contacting the anterior spinal cord without cord deformity or signal change. After consultation with three separate spine surgeons, the patient underwent anterior cervical discectomy with fusion. Postoperatively there was initial exacerbation of the myoclonus for the first 2 weeks. The myoclonus gradually improved over the ensuing 2 months, and virtually resolved once the cervical collar was removed (see Video Segment 2). Less than once per day, a single jerk does still occur. The patient experienced benefit for persistent restless legs symptoms after having resumed ropinirole.

DISCUSSION

Propriospinal myoclonus involves a shock-like flexion of the trunk or proximal extremities due to caudal and rostral conduction along propriospinal pathways from a spinal generator site.¹ The movements can be triggered by external stimulation, such as tapping of bicep or patellar tendons, but not by startle. Various premonitory sensations were reported by 6 of 10 subjects in a recent case series of propriospinal myoclonus.² Electromyography can be useful to support a diagnosis of propriospinal myoclonus³ and might have been helpful in our case. We were able to exclude psychogenic myoclonus or myoclonic tics by demonstrating the absence of event-related cortical potentials during EEG. A spinal cord origin was implicated by the asymmetric reflexes and MRI findings.

Resolution of spinal segmental myoclonus⁴ or propriospinal myoclonus⁵ after surgery for associated radiculopathy has been previously reported. We suggest that radiculopathy or, as in our patient, compression or vascular embarrassment of motor tracts in the spinal cord, can lead to myoclonus by disrupting afferent signals originating distal to propriospinal pathways. Disruption of this afferent information would be expected to disrupt inhibitory motor loops. Our case demonstrates that propriospinal myoclonus can be caused by compressive spinal cord lesions even in the absence of other signs of myelopathy and can be relieved by decompressive surgery.

LEGENDS TO THE VIDEO

Segment 1. Patient had stimulus-sensitive axial and appendicular myoclonus while seated, and asterixis of proximal lower extremities with weight bearing.

Segment 2. Myoclonus virtually resolved after cervical spine surgery.

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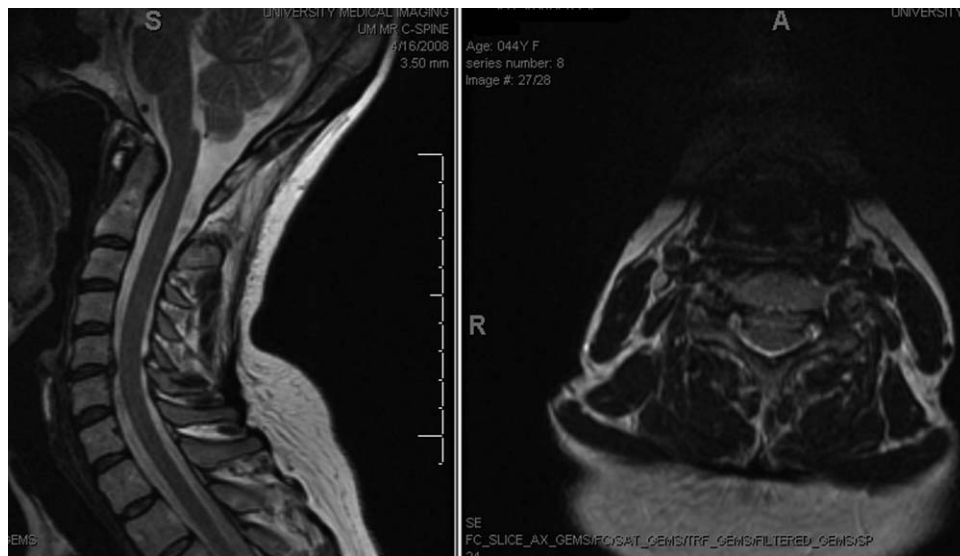


FIG. 1. C-Spine MRI shows C5 to 6 posterior disc bulge with minimal narrowing of the spinal canal.

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Chorea in Adults Following Pulmonary Endarterectomy

Video 

Pulmonary endarterectomy (PEA) is performed in patients with chronic thromboembolic pulmonary hypertension with surgically accessible thrombi.¹ In our hospital, 5 patients developed chorea in the post operative phase. We have previously reported on the occurrence of chorea following PEA with deep hypothermia and circulatory arrest in a smaller patient population.² The aim of this article is to present the patient’s videos and to discuss the probable pathogenesis of chorea in adults.

Five out of 106 consecutive adult patients who underwent PEA in our hospital developed chorea. Nine patients died during or shortly after surgery without having regained consciousness and were excluded from the analysis. PEA was performed as previously reported.³

The records of all patients were assessed for surgical characteristics. The data of patients with chorea ($n = 5$; 3 women; age $45.5 \pm \text{SD } 12.3$ years) were compared with the data of patients without chorea ($n = 92$; 57 women; 54.7 ± 13.9 years) using Mann-Whitney U test.

In chorea patients, the total circulation arrest time was longer ($63 \text{ minutes} \pm 9$ vs. $44 \text{ minutes} \pm 17$; $P < 0.01$), and they were rewarmed quicker ($0.18^\circ\text{C}/\text{minutes} \pm 0.03$ vs. $0.14^\circ\text{C}/\text{minutes} \pm 0.02$; $P < 0.0001$; see Fig. 1) as compared to nonchorea patients. Mean bypass time was longer in chorea patients as compared to nonchorea patients (137 minutes

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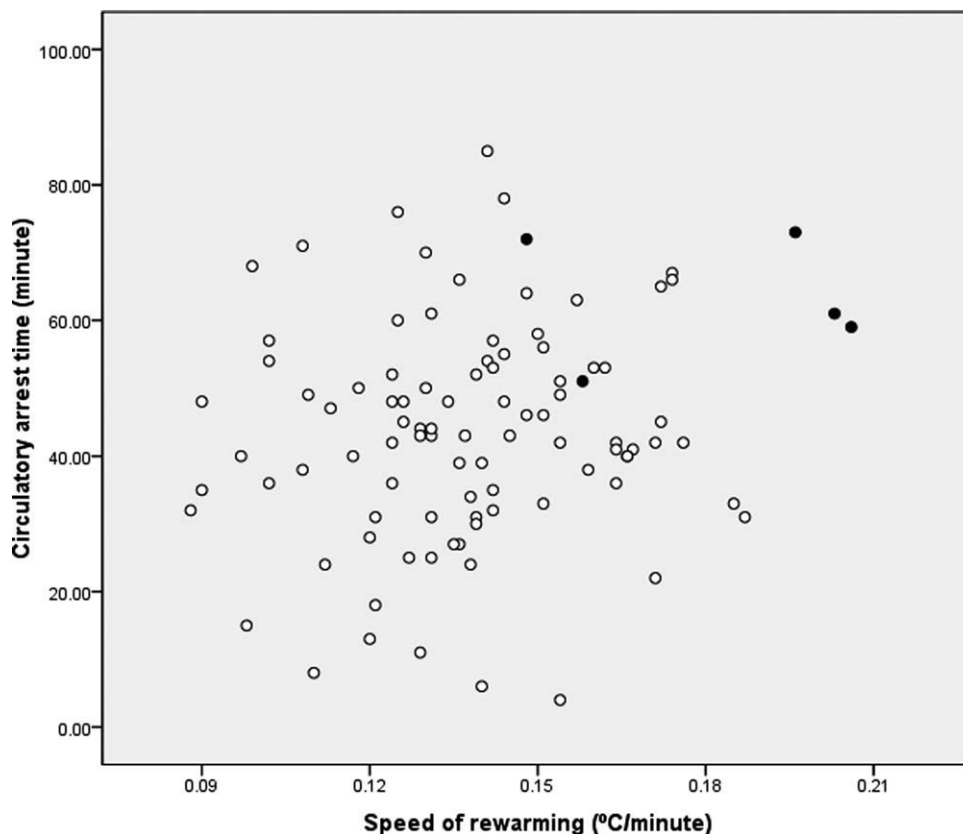


FIG. 1. Scatter plot of total circulatory arrest time versus speed of rewarming. The filled dots indicate patients with chorea ($n = 5$) and the open dots patients without chorea ($n = 92$). The scatter plot shows that patients with chorea had a relatively longer circulatory arrest and were rewarmed faster.

± 26 vs. 110 minutes ± 29 ; $P < 0.05$). Moreover, the chorea patients were offered higher absolute temperatures ($37.8^{\circ}\text{C} \pm 0.5$ vs. $36.9^{\circ}\text{C} \pm 0.7$; $P = 0.002$) during rewarming. There was no difference between patients who developed chorea and those without chorea regarding age, gender, total time on pump, speed of cooling, highest temperature reached, and reperfusion time. All chorea patients underwent formal neuropsychological testing and when possible MRI of the brain (Table 1). The choreatic movements started 3 to 7 days after surgery and gradually faded.

Chorea is well known in children^{4,5} and seems to be associated with prolonged time on pump, duration of circulatory arrest time, deep hypothermia, and hypoxia.⁶⁻⁸ The course of chorea in children appears similar to what we have observed; chorea starting 3 to 7 days postoperatively, gradually fading, and disappearing in the following weeks to months.⁹⁻¹¹

Deep hypothermic circulatory arrest impairs the recovery of both cerebral blood flow (CBF) and cerebral metabolism proportional to the duration of the arrest.¹²⁻¹⁴ In an animal model, however, rapid rewarming after hypothermia during cardiopulmonary bypass surgery causes an increase in the cerebral metabolic rate for oxygen that is temporarily unmatched by CBF.¹⁵ The slower recovery of CBF—as compared to metabolism—may be explained by the following

phenomena: cerebral micro vessels have an initial contractile response to acute increase in temperature¹⁶; hypothermic cerebral micro vessels are less responsive to vasodilatory stimuli¹⁷; and the production of brain vasodilatory substances is determined by brain temperature rather than cerebral metabolism.¹⁸ We hypothesize that the chorea in our patients might be a sequela of brain lesions caused by a mismatch between CBF and brain metabolism induced by faster rewarming. In addition, the longer circulation arrests might have aggravated slower recovery of CBF.

Diffusion weighted imaging in patient D showed bilateral lesions of the globus pallidus. In children with postpump chorea, neuropathological abnormalities involving the external globus pallidus and the pallidusubthalamic pathway have been reported.^{19,20} The globus pallidus and striatum are susceptible for hypoxemia, probably due to differential cellular responses to deprivation of energy substrates and sustained activation of glutamate receptors.²¹

In conclusion, chorea in adults following deep hypothermia with cardiac arrest appears to be related to lengthy circulation arrest and faster rewarming. Although initially the chorea may be incapacitating, the course is rather benign. Clinicians should avoid quick rewarming following hypothermia and if possible shorten the circulation arrest period.

TABLE 1. Results of neuropsychological testing and brain imaging of the patients with chorea

Neuropsychological testing	Brain imaging	Choreatic Symptoms
A Day 12; Disinhibition and mild slowness in retrieval of verbal information, no attention deficit	Day 6; MRI showing no abnormalities	She felt as if intoxicated 2 days after PEA and chorea slowly developed. 3 days after PEA she developed generalized chorea with severe dystonia and oculogyric crises (video), hardly noticeable at rest. She could not perform tasks and had difficulty with speaking. The involuntary movements gradually disappeared 4 weeks later. Seven years after PEA, she has no complaints.
B Day 11; Short-term memory impairment, impaired allocation of attention, instability of emotion, and mood disturbances	Day 11; MRI difficult to interpret due to movement artifacts, but no gross abnormalities	She had severe incapacitating generalized chorea with dystonia and oculogyric crises 24 hours after PEA, which was almost absent at rest (video). She could not sit without help. The involuntary movements gradually diminished over the following two months. Six years later she continues to have minor choreatic movements when tired or stressed. She experiences no limitations.
C Day 3; she scored 22 out of 30 on the Mini Mental State Exam, ²² missing 4 points on serial subtraction of 7. No formal neuropsychological examination performed.	Not performed	She displayed dysarthria, ataxia, and mild generalized chorea 3 days after PEA. Next day, the ataxia and chorea were gone. Dysarthria and emotional instability gradually improved over the following days. One week later, she had no neurological symptoms and signs. Seven years later she has no complaints.
D Day 6; Mental slowness, mild word finding difficulties, and disinhibition	Day 8 and day 12; MRI showed bilateral hyperintense lesions of the globus pallidus on diffusion weighted imaging Day 15: IBZM-SPECT scan showed decreased post-synaptic D2-receptor binding	He displayed chorea, dystonia, and oculogyric crises 2 days after PEA. The severe involuntary movements were treated with 5mg haloperidol 3dd1, resulting in gradual fading of the involuntary movements 1 week later. He showed mild generalized chorea till his death three years later, due to a colon carcinoma.
E Day 7; Disinhibition and a dysexecutive syndrome with encoding deficit, divided attention impairment and planning problems.	Day 14: MRI multiple small hyperintense white matter lesions on Flair	He gradually developed chorea 3 days after PEA, which subsided 10 days later. He claimed a lot of attention and was vocally-disinhibited. In 3 weeks time, the behavioural side effects gradually disappeared. He did not display any eye movement abnormalities. 2 years later he has no complaints.

LEGENDS TO THE VIDEO

Transient Chorea Following PEA

Segment 1. The first segment shows patient A 5 days and 15 days after surgery. Five days after surgery, she has a delayed initiation of voluntary actions. When asked a question, there is a delay in answering. When asked to look in a particular direction, there is delayed saccade initiation, and she breaks fixation by blinking (oculomotor apraxia). At the same time, she has chorea-ballism, dystonia, and motor impersistence. In the video, she is asked to take a hand, but she is unable to initiate the movement. She confirms this when asked about it. There is no weakness. Fifteen days after surgery, the chorea has disappeared, though she still seems fidgety.

Segment 2. The second segment shows patient B 4 days, 7 days, 14 days, and 2 months after surgery. Four days after surgery, she has a delayed initiation of voluntary actions. When asked to lift her arms she is unable to initiate the maneuvers. The patient has chorea-ballism, dystonia, and motor impersistence. The video-parts regarding day 7, day 14, and 2 months after surgery show the gradual decline of the chorea.

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Cerebellar Involvement in Progressive Supranuclear Palsy

Among 22 Japanese patients with pathologically proven progressive supranuclear palsy (PSP),¹ 3 patients with unclassified PSP presented with cerebellar ataxia as the initial/principal clinical symptom and had more frequent tau-positive inclusions in the Purkinje cells of cerebellar cortex and more severe involvement of the cerebellar dentate nucleus than other cases. This suggests that “PSP with cerebellar ataxia” is a clinical subtype of PSP. The clinical and pathologic heterogeneity of PSP^{2,3} is illustrated by a personal series of 30 autopsy-proven cases of PSP from Vienna, Austria [18 Richardson syndrome (RS) and 12 PSP-Parkinsonism (PSP-P)]. In none of these patients was cerebellar ataxia reported

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as the initial or principal symptom, whereas two of them (6.7%) developed cerebellar signs in late stages of the disease. This is similar to the frequency in other series.⁴ As in the majority of autopsy series of PSP,^{2,5} the cerebellar dentate nucleus showed considerable involvement, which was more severe in RS than in PSP-P cases,^{3,6,7} whereas in six cases (20%) it was spared. Tau deposits in Purkinje cells were seen in only the two brains from RS cases that had developed late cerebellar signs. As in most Western clinicopathologic PSP series, no case of "unclassified PSP" with cerebellar involvement was observed in our series, which may, at least in part, be related to ethnic and genetic reasons.

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Shoulder Pain in Parkinson's Disease: A Case-Control Study

Although pain symptoms related to Parkinson's disease (PD) are described in the literature, an increased risk of shoulder pain in PD compared with a control population has not been established. This study was designed to better define the association between PD and shoulder pain controlling for potential confounders. We hypothesized that shoulder pain is more prevalent in PD patients compared with controls.

A cross-sectional and retrospective study was conducted with PD subjects and normal controls. Subjects were diagnosed with idiopathic PD on the basis of Gelb criteria and

the Hoehn and Yahr scale was determined by a movement disorder specialist.^{1,2} We recruited consecutive patients being seen for routine care in our Movement Disorder clinic, and spouses served as controls. Subjects were asked whether they had shoulder pain, to characterize shoulder pain, if present, and to answer questions related to PD onset, symptoms, medication use, and history of prior injury. Subjects also completed a visual analog scale to assess the severity of pain. Descriptive statistics were used for demographic information. The data was analyzed using multivariate logistic regression, with pain as the outcome variable; and age, gender, Hoehn and Yahr, and history of previous injury as model covariates with statistical significance at $P = 0.05$. The institutional review board approved this study and all subjects signed informed consent.

A total of 25 PD patients and 25 controls were recruited. The average age (mean \pm standard deviation) of the cases was 65.3 ± 12.3 and of controls was 64.6 ± 11.9 . Forty-eight percent of cases were male and 56% of controls were male. Average Hoehn and Yahr stage of cases was 2.2 (standard deviation of ± 0.61). In the PD group, 80% of subjects had pain compared with 40% in the control group. Most of the PD patients described the shoulder pain as dull and aching, with 80% of them experiencing pain in both shoulders, compared with 20% in controls. The pain rating scale in the PD cases ranged from 4/10 to 10/10, when the pain was at its worst. The multivariate regression (Table 1) showed that PD patients have six times the odds of having shoulder pain compared with those without PD. When adjusted for age, gender, and prior injury; PD patients have 21 times the odds of having shoulder pain compared with those without PD. There were no PD cases reporting prior shoulder injury whereas this confounder occurred in many of the controls. There was no association between Hoehn and Yahr stage and presence of pain. In the PD group, 40% reported that PD treatment improved the shoulder pain, 40% reported it was not effective, and 20% were uncertain. The PD treatments reported to help were dopaminergic medications, including carbidopa/levodopa, pramipexole, ropinirole; and deep brain stimulation surgery.

There are several potential explanations for the strong association between shoulder pain and PD. Prior injury has been hypothesized to be related to shoulder pain in PD, but, none of our PD subjects reported previous shoulder injury compared with 70% of the controls. Muscle cramps and tightness occurs in most PD patients³ and the increase in shoulder pain may be related to the rigidity seen in PD. However, in this study the majority of PD subjects suffered from bilateral shoulder pain, despite asymmetry of rigidity on exam. Finally, controls may not have been representative of the general population.

Studies have shown that 30–40% of PD patients complain of pain,^{4,5} which was consistent with our results. A recent study found that PD patients have a lower heat pain threshold compared with controls, with the authors hypothesizing that basal ganglia abnormalities may alter pain coding.⁶ Additionally, PET scans have shown that striatal D2 receptors are involved in central pain pathways and that a decrease in D2 receptors results in an increase in pain perception.⁷ These studies may suggest that pain in PD is related to the underlying pathophysiology of PD rather than motor signs. We did

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TABLE 1. Analysis of shoulder pain adjusted for age, gender, and previous injury

Variable	Cases % (n)	Control % (n)	OR	95% CI	P value
Shoulder pain	80 (20)	40 (10)	6	1.69–21.6	0.006
Adjusted for age and gender			6	1.69–21.3	0.006
Adjusted for previous injury	0 (0)	70 (19)	21.63	4.25–110	0.0002

OR, odds ratio.

not specifically examine whether shoulder pain preceded the original diagnosis of PD and whether shoulder immobility may be a very early potential sign of incipient PD. With the search for preclinical features for neuroprotection and the interest in the overlap between motor and nonmotor features of PD, a detailed study to better define this association in regards to shoulder pain may lead to practical application of these results.

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Is It a Tic?—Twenty Seconds to Make a Diagnosis

Tics are often classified as a movement disorder. However, their movement kinematics are indistinguishable from normal movements.¹ Also, tics are sometimes preceded by premotor potentials typically present before self-paced voluntary movements² albeit this is not always the case.³ Thus, rather than abnormal movements, tics may be better defined as fluctuating “prewired bits of behavior” misplaced in both context and time.⁴ This implies that it may be difficult to identify a tic in isolation but easier on the basis of its occurrence in time. Therefore, either short (3 seconds) or longer (20 seconds) video clips showing tics of Gilles de la Tourette (GTS) patients or clips showing spontaneous movements of healthy controls were presented to GTS experts with the instruction to decide whether presented movements were tics or not.

Videos of 12 GTS patients (11 men, mean age: 43.1 ± 12.2 years) assessed by MO and MMR were available. GTS was diagnosed according to DSM-IV-TR criteria.⁵ Twelve age and sex matched healthy controls (11 men, mean age: 39 ± 13.3 years) were also filmed. Participants gave informed written consent granting permission for the videos to be used for research purposes.

Video clips were cut from video recordings taken according to the GTS Rush Video protocol⁶ from GTS patients and a standardized video recording from healthy controls with the instruction to wait and to behave normally. Twenty-four tic videos and 24 video sequences from healthy controls showing a spontaneous movement lasting no more than 3 seconds were created from head and shoulder view segments (Table 1).

Another 48 video sequences (24 clips showing GTS patients and 24 clips showing healthy controls) with a duration of 20 seconds were cut from the same video material. Two-blinded GTS experts were asked to review the clips and decide whether the movements were tics or spontaneous movements. First, the 3 second and, after an interval of at least 1 week, the 20-second sequences (with the experts unaware of the 3-second clip rating results) were reviewed.

Frequency of movements in 3-second clips did not differ between groups in any category (Binomial-Tests). In 20-second clips, patients' tic videos showed significantly more tics [mean of 17 (SD 9.4)] than healthy control videos spontaneous movements [mean of 6 (SD 3.4); $df = 1$, $Z = 2.309$, $P < 0.001$; Kolmogorov-Smirnov test; Table 1]. Also, patients'

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TABLE 1. *Movements/tics shown in 3- and 20-second video clips*

Most obvious movements/tics	3-second clips		20-second clips	
	Controls	GTS	Controls	GTS
Eyes	6 (25)	6 (25)	108 (77)	114 (28)
Eyebrow	3 (13)	4 (17)	1 (0.5)	48 (11)
Nose	2 (8)	2 (8)	3 (2)	27 (6)
Mouth	8 (33)	10 (42)	15 (11)	103 (25)**
Jaw	—	—	—	15 (6)
Whole head	5 (21)	2 (8)	12 (8.5)	77 (18)*
Shoulder	—	—	2 (1)	27 (6)
Sum	24	24	141	411**

Numbers are absolute values (% in brackets) of movements/tics shown on respective video clips.

* $P < 0.05$; ** $P < 0.01$ (differences in the frequency of movements occurring in the respective category for 20-second clips).

tic clips showed significantly more mouth ($df = 1$, $Z = 2.107$, $P < 0.001$) and whole head tics ($df = 1$, $Z = 1.656$, $P = 0.009$) than respective movements in healthy controls (Table 1).

Regarding 3-second video clips, expert I categorized 46% videos correctly, and expert II 81% (Inter-rater reliability (IR)—0.59; Cronbach's Alpha). Expert I rated 11 of the 48 short clips incorrectly as showing tics and 14 incorrectly as showing spontaneous movements. Expert II misclassified two videos of spontaneous movements as showing tics and seven tic videos as showing spontaneous movements.

Twenty-second video sequences were classified correctly in 73% by expert I and 96% by expert II (IR 0.71). Expert I incorrectly classified two videos showing spontaneous movements as tics and 11 videos showing tics as spontaneous movements. Expert II misclassified two tic videos as spontaneous movement videos. Except for one video, all misclassified videos of rater II were also incorrectly rated by rater I. Diagnostic accuracy was higher for 20-second clips compared to 3-second clips in rater I ($df = 1$, $\chi = 6.12$, $P = 0.020$; McNemar tests) but not in rater II ($df = 1$, $\chi = 1.3$, $P = 0.300$).

The main finding is that it is more difficult to distinguish a single tic from a single spontaneous movement than a series of tics from a number of spontaneous movements. Thus, tics are probably best described as movements becoming abnormal in time because they deviate from the movement repertoire considered "normal."

Some tics involved certain anatomical regions/muscles more frequently than spontaneous movements, e.g., mouth and whole head tics, but these differences alone do not suffice to explain why diagnostic certainty and inter-rater agreement was so high after only 20 seconds. On 20-second videos GTS patients moved significantly more frequently than healthy controls. This difference, i.e., the "too much" of something normal, was probably the most distinctive element allowing to correctly identify tics. We conclude that longer video clips can capture the nature of tics as "excess" normal movements and aid the diagnosis of a tic disorder.

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