Risks of Inappropriate Secretion of Antidiuretic Hormone in Multiple System Atrophy

Multiple system atrophy (MSA) affects the hypothalamus, similar to other neurological diseases.[1] Hypothalamic cells synthesize antidiuretic hormone (ADH), which increases water reuptake in the kidney. Hypothalamic disturbances can lead to the syndrome of inappropriate antidiuretic hormone secretion (SIADH) and resultant hyponatremia. ADH levels usually increase in SIADH. However, normal ADH levels are occasionally seen, but they are inappropriate in the presence of abnormally decreased osmolarity (<280 mOsm/kg), a condition thought to suppress physiological ADH secretion.[2] To date, 6 patients with MSA had SIADH (Table 1).[3] We describe the first MSA patient with extreme hyponatremia (99 mEq/L) and the highest reported ADH concentration. We also measured ADH in 14 severely disabled patients with MSA, but not symptomatic SIADH.

Patient

A 61-year-old woman with a 9-year history of MSA (cerebellar type [MSA-C] with subsequent extrapyramidal and autonomic disturbances) became comatose and was urgently admitted to our hospital. A local hospital had prescribed 400 mg L-dopa, 100 mg amantadine, 300 mg entacapone, 1 mg ropinirole, and 30 mg domperidone daily. She had received only alimentary nutrition containing 1.9 g/day sodium chloride via a gastrostomy tube for >1 year. Despite treatment, she remained bedridden. Three days before admission, a fever developed. An extra 1050 mL/day of water given by a family member disturbed her consciousness.

Laboratory data at admission for our and 6 similar patients are summarized in Table 1. All antiparkinson drugs were temporarily suspended, but resumed later without apparent ADH changes. A chest radiograph showed left-sided pneumonia. A brain magnetic resonance imaging (MRI) scan supported MSA.[4] Because of pneumonia and coma, the patient was artificially ventilated through a tracheal tube. Sodium was slowly corrected, and she regained consciousness, without apparent cerebral demyelination. However, artificial ventilation was continued because of central apnea. ADH concentrations remained high (8.5 pg/mL) after pneumonia resolved.

In contrast to our patient, patient 7, with the second lowest sodium concentration, had a successful outcome of SIADH.[3] This 58-year-old woman had a 6-year history of MSA with predominant parkinsonism (MSA-P). SIADH associated with clinical agitation developed after pyelonephritis-related fever. Saline infusion resolved SIADH, which recurred 2 weeks later and responded to water restriction.

Serum ADH and sodium concentrations were measured in 14 patients with MSA (age 66 ± 8 years [mean ± SD], men/women = 8/6, disease duration = 7.1 ± 2.7 years [mean ± SD], MSA-P/MSA-C = 4/10) and 13 with other diagnoses, such as amyotrophic lateral sclerosis and myopathy (age 60 ± 14 years, men/women = 10/3). All subjects had a modified-Rankin-scale score of 4 or 5, with no evidence of hypothyroidism, adrenal insufficiency, inflammation, or symptomatic SIADH. Blood was drawn in the morning >30 minutes after the patients rested in a supine position. Patients with MSA had significantly higher ADH concentrations (9.9 ± 9.6 pg/mL, [mean ± SD], normal 0.3–3.5) than the disease controls (3.1 ± 2.0 pg/mL, $P < .05$, Mann Whitney U test), with equivalent sodium concentrations.

Discussion

Our patient had MSA and extreme hyponatremia, potentially caused by SIADH, a low sodium chloride intake, and a suddenly increased water load. Our findings suggest that SIADH was attributed to MSA and pneumonia, but not to antiparkinson drugs.

Hypothalamic neurons that synthesize ADH are preserved in MSA, whereas the medullo-hypothalamic tract, transmitting stimulation possibly related to orthostatic ADH release, undergoes degeneration.[5] Orthostatic increases in ADH are consistently impaired.[6] Our workup showed increased basal ADH secretion. The mechanism underlying these results might involve lack of stimulation from the brainstem to hypothalamic ADH neurons, making them hypersensitive and causing ADH to be secreted inappropriately.[7]

As shown in Table 1, symptoms of hyponatremia associated with SIADH vary considerably, ranging from fatigue to disturbed consciousness, and generally respond well to treatment. However, our patient became ventilator dependent, possibly because of extremely severe hyponatremia. Clinicians and caregivers should thus be aware that patients with MSA carry a risk of SIADH, sometimes initially accompanied by subtle symptoms, and should carefully regulate salt and water intake to avoid further disability and potentially fatal outcomes.

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Table 1. Clinical and laboratory information of patients with MSA and SIADH

	Patient #						
	1	2	3	4	5	6	7
Age (y)	61	52	67	52	76	62	58
Sex	F	M	M	M	M	F	F
Duration (y)	9	4	11	10	1.5	8	6
mRS before SIADH	5	nd	3	4	nd	nd	4–5
Symptom of SIADH	Coma	Cons. dist.	Unsteady gait	Fatigue	Cons. dist.	Seizure	Agitation
Na (mEq/L)	99	127	124	120	118	118	116
K (mEq/L)	3.7	4.2	5.5	nd	4	nd	nd
Cl (mEq/L)	66	96	89	nd	84	66	nd
ADH (pg/mL)	25.5	3.5	1.48[a]	2.1	3.5[b]	12	11.7[c]
Urine osmolarity (mOsm/kg H_2O)	474	319	420	381	304	nd	722
Serum osmolarity (mOsm/kg H_2O)	205	262	255	246	244	254	nd
Concomitant diseases	Pneumonia	nd	Pacemaker	Fever	nd	Apnea	Pyelonephritis
Antiparkinson drugs	+	+	+	+	nd	nd	+
MSA type	C	P	P	C	P	C	P
References[d]	a	b	c	d	e	f	g

[a]The ADH concentration might have been different when sodium was measured.
[b]Na = l29 at the measurement of ADH;
[c]Na = 117 at the measurement of ADH.
[d]References: a, the present report; b, Clin Neurol 1992;32:177–181 (in Japanese); c, Int Med 1994;33:773–778; d, Shinkeinaika 2002;56:541–544 (in Japanese); e, Tokushima Red Cross Hosp Med J 2003;8:73–77 (in Japanese); f, Shinkeinaika 2006;64:445–446 (in Japanese); g, Mov Disord 2008;23:1325–1326.MSA, multiple system atrophy; SIADH, syndrome of inappropriate antidiuretic hormone secretion; mRS, modified Rankin scale; nd, not described; cons. dist., consciousness disturbances; ADH, antidiuretic hormone secretion; C, cerebellar; P, predominant parkinsonism.

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A Proof-of-Concept Trial of the Whey Protein Alfa-Lactalbumin in Chronic Cortical Myoclonus

Alpha-lactalbumin (ALAC) is a whey protein naturally present in human milk and with a very high tryptophan/large neutral amino acids (Trp/LNAAs) ratio.[1] In a pilot study, ALAC improved seizure control in patients with drug resistant epilepsy.[2] Moreover, recent data indicate that ALAC treatment reduces seizure activity in different rodent epilepsy models, including genetically epilepsy-prone (GEPR)-9 rats.[3] These animals exhibit a severe seizure disorder and explosive myoclonus and there is evidence of an inverse relationship between the level of serotonergic neurotransmission and seizure severity in these rodents.[4] Based on these findings, we

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Additional Supporting Information may be found in the online version of this article.
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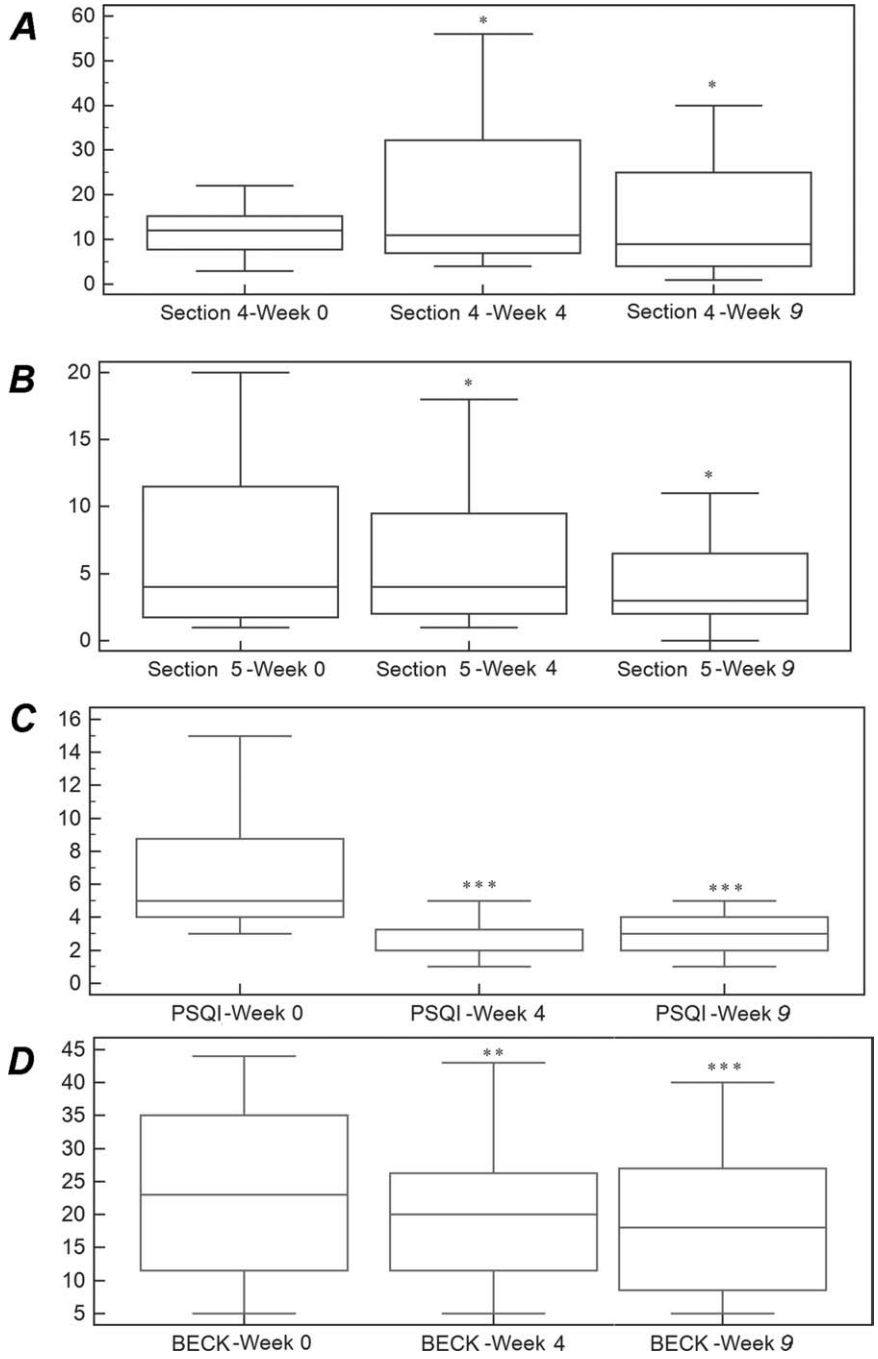

FIG. 1. Summary of efficacy data. The different end-points scores: (A) Unified Myoclonus Rating Scale, section 4 (action myoclonus); (B) Unified Myoclonus Rating Scale, section 5 (functional performance); (C) Beck Depression Inventory; (D) Pittsburgh Sleep Quality Index) obtained before (left), after the double-blind phase (middle), and at the end (right) of the trial were compared by using the Wilcoxon signed rank test. Placebo and ALAC treatment did not differ in the effect on myoclonus (A, B) whereas a clear improvement of sleep quality and depressive symptoms was observed (C, D). $^{*}P > .05$; $^{**}P < .05$; $^{***}P < .01$.

conducted a placebo-controlled trial to test the efficacy of ALAC in patients with chronic cortical myoclonus.

Patients and Methods

Thirteen patients (7 men; mean age: 89.2 ± 11.9 years; range, 20–53) participated to the study. Six patients had Unverricht-Lundborg disease, 6 benign adult familial myoclonic epilepsy, and 1 Lafora disease(Suppl. Table 1). Patients signed a written informed consent approved by the ethical committee. The severity of myoclonus was assessed by sections 4 (action myoclonus) and 5 (functional performance) of the Unified Myoclonus Rating Scale (UMRS).[5] We also evaluated depression and sleep quality using the Beck Depression Inventory (BDI) and the Pittsburgh Sleep Quality Index (PSQI) questionnaires.

Patients were randomized to receive 0.75 g ALAC tablets or placebo. ALAC was orally administered at a starting dose

of 1.5 g (2 tablets) per day followed by increments of 1.5 g/day each week up to the target dose of 4.5 g (6 tablets) per day. Dosage of concomitant anticonvulsants remained stable for at least 1 month before the trial. The double-blind phase lasted 3 weeks and was followed by an open-label 4-week follow-up. Full assessment was obtained at weeks 4 and week 9.

Statistical analysis was obtained by the Wilcoxon matched-pairs test and the Student *t* test for categorical data.

Results

All the subjects completed the trial. None of patients experienced subjective change of myoclonus. Six individuals were randomized to receive placebo (Suppl. Table 1). No serious adverse events were recorded. Two subjects on ALAC (15.3%) and 1 subject on placebo (7.6%) reported mild drowsiness.

Placebo and ALAC treatment did not differ in their effect on the UMRS scores (Fig. 1A,B; $P > .05$) whereas a striking improvement of sleep quality and depressive symptoms was evident during ALAC treatment (Fig. 1C,D; $P < .01$). At the end of the trial, 6 patients were withdrawn from ALAC. Seven (53.6%) subjects are still on treatment (mean follow-up: 24 ± 1.5 months) (Suppl. Table 1).

Discussion

This short, proof-of-concept trial failed to demonstrate an antimyoclonic effect of ALAC. However, ALAC showed a tolerability profile comparable to placebo and it was associated to striking improvement of sleep quality and depressive symptoms. Due to these effects, more than one-half of the subjects decided to continue ALAC treatment after the end of the study. As sleep disturbances and depressive symptoms have a significant impact on quality of life and are more than twice as prevalent in people with epilepsy compared with healthy individuals,[6] ALAC may be a valuable therapeutic option for these patients. Randomized, double-blind studies should explore the potential efficacy of ALAC in other seizure types. ■

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Attention to Self in Psychogenic Tremor

Distraction of attention away from the affected limb forms the basis of the majority of clinical tests used to distinguish psychogenic from organic movement disorders, in particular tremor.[1] This implies that psychogenic movement disorders are associated with increased attentional focus toward the affected limb, a hypothesis supported by functional imaging studies in conversion disorder reporting increased activity in areas associated with "self-monitoring."[2,3] We wondered whether the simple observation of patients with psychogenic tremor (PsyT) might reveal excessive attention to their tremoring limbs and to movements of these limbs in general, compared to patients with organic tremor (OrgT).

Videos (see Video, Segments 1 and 2) were sourced from a consecutive series of patients with clinically definite PsyT, according to Fahn-Williams criteria,[4] and OrgT was collected in a standardized manner as part of a separate study. From the 48 videos, which all included recording of the tremor in standard positions and motor tasks, such as assessment of bradykinesia, we selected those where three or more tremor positions and motor tasks were recorded with the patients' eyes clearly included in the video frame. During video recordings, patients had been given no specific instructions regarding where to look. Visual attention, defined as a

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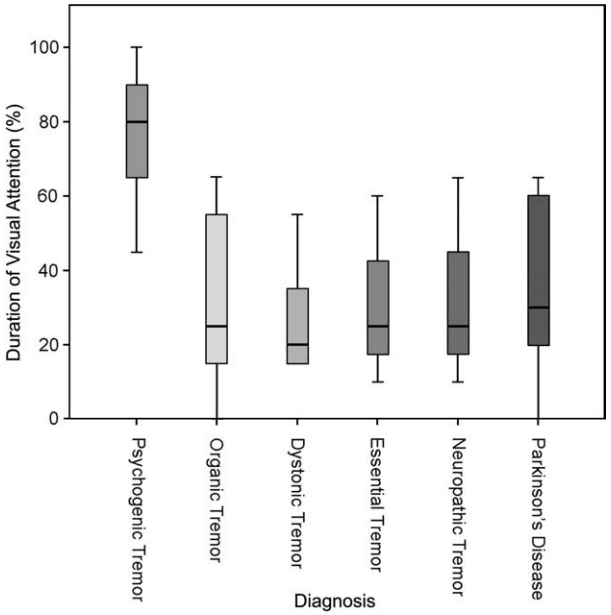

FIG. 1. Mean percentage of visual attention (for definition, see text) for patients with psychogenic tremor and organic tremor (data for all organic tremors combined and different tremor subtypes are shown). Box and whisker plots show median (solid black line), 25th and 75th percentile (top and bottom of the box) and smallest and largest observation (error bars) in each group.

patient looking directly at the moving limb, was timed for each task separately and compared to the total duration of the task's video segment (i.e., approximately 5 seconds). This measure was scored independently by two raters blinded to diagnosis. Interobserver agreement was tested with an intraclass correlation coefficient (ICC).

Thirty videos were useable, 13 patients with PsyT (7 females) and 17 patients with OrgT (5 with dystonic tremor, 4 with essential tremor, 3 with neuropathic tremor, and 5 with PD; 6 females). In total, we scored 6.3 minutes of patients with PsyT and 8.0 minutes of patients with OrgT. The number of tremor positions/tasks assessed did not significantly differ between PsyT and OrgT. There was significantly greater visual attention to limbs in patients with PsyT (66%), compared with OrgT (32%): $t = -3.68$; $P = 0.001$ (see Video). There was no significant difference in attention between different types of OrgT (see Fig. 1). Interobserver reliability was excellent (ICC = 0.93). The area under a receiver operating characteristic (ROC) curve plotted from the data was 0.81, consistent with a "good" level of discrimination of this test between PsyT and OrgT, and with a cut-off of 60% visual attention, sensitivity of 77%, and specificity of 88% to differentiate organic from psychogenic tremor were found.

We demonstrate excessive visual attention toward the limb in patients with PsyT. Visual attention to the limb may be a marker of explicit control of movement, usually seen during the performance of novel tasks, proceeding to nonattentive implicit movement control when the task was learned.[5] It is a common experience that explicit concentration on the components of normal movement (e.g., driving a manual car) impairs performance, whereas an external locus of attention is generally beneficial.[6] This may be why it is common to find additional movement abnormalities not complained of by the patient, such as abnormally slow finger taps or give-way weakness, when subjects with psychogenic disorders are asked explicitly to perform such movements during examination. Although the level of a patient's attention to their limb during examination is clearly not diagnostic of PsyT, it may add to the overall clinical impression that guides the differentiation of organic from psychogenic tremors and also underlines the importance of abnormal attentional focus in the pathophysiology of psychogenic movement disorders.

Legend to the Video

Segment 1 shows video from 2 patients with psychogenic tremor who both demonstrate prolonged visual attention to the limb that is tremoring and during performance of finger taps (which are performed abnormally slowly). Segment 2 shows a patient with essential tremor who has very little visual attention to the limbs during tremor or motor tasks.

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Local Field Potential Oscillations of the Globus Pallidus in Huntington's Disease

Deep brain stimulation (DBS) of the internal globus pallidus (GPi) can dramatically improve chorea in Huntington's disease (HD).[1] Local field potential (LFP) oscillations of the GP have not been investigated in HD, so far. A 65-year-old female patient with genetically confirmed symptomatic HD with medically refractory hyperkinesia underwent bilateral DBS of the GP. The target was determined by fusion of stereotactic CT and preoperative 3 Tesla MRI. Intraoperatively, multiunit activity (MUA) and LFPs were recorded simultaneously with 5 combined micro-macroelectrodes in steps of 0.5 to 1 mm, starting 10 mm above the target point, using the Inomed ISIS microelectrode recording system (Vers.2.4beta; inomed Medizintechnik GmbH, Teningen, Germany) in the unanesthesized patient. Postoperative offline LFP analysis of the trajectories, which were chosen for chronic stimulation, was carried out using BrainVision Analyzer software (Vers.1.05; Brain Products GmbH, Munich, Germany). Electrode impedances were 1 kOhm. Signals were amplified by the factor of 2,000, sampled at 2.5 kHz and down-sampled to 512 Hz, band-passed between 0.5 and 160 Hz, and notch-filtered at 50 Hz. The fast Fourier transform (FFT) was applied over the recorded segment of 60 seconds, with an FFT window of 0.5 seconds and 50% overlap, leading to a resolution of the spectra of 1.2 Hz. Informed consent was signed by the patient, and data acquisition was performed in accord with the declaration of Helsinki.

Postoperative stereotactic cranial CT (2-mm slice thickness) fused with the preoperative MRI showed correct electrode placement in the GP. The border between GPe and GPi was defined by MUA at 7 mm and maximal neuronal activity was recorded at 3 to 4 mm above the calculated target, respectively. Spectral analysis revealed peaks in the theta/alpha-, beta-, and low gamma band. Within one frequency band, power increase was found only in the 4 to 12 Hz theta/alpha and 35 to 45 Hz low gamma band in the GPi at approximately 3.5 mm above and just around the target point, respectively. No other power increase within a frequency band was found in the spectral analysis up to 100 Hz (Fig. 1). Theta/alpha activity was the dominant frequency band in respect to power and matched the spatial distribution of MUA. Both hemispheres showed a similar distribution of LFPs and MUAs.

In the motor cortex, the 40-Hz piper rhythm is supposed to represent the physiological cortical motor drive and increases with voluntary movements.[2,3] This oscillatory low gamma activity might be imposed from elsewhere, because it is also found in the intrathalamic network and cerebellothalamocortical projections.[4] In the GPi of patients with generalized dystonia, synchronized gamma activity to both voluntary and involuntary movements has been described.[5] We found low gamma activity in our patient at the pallidal base, which contains important pallidal output fibers.[6] Hence, this low gamma activity might be a feature in HD, reflecting pathological exaggeration of the motor drive, comparable to those found in the motor cortex of patients with cortical myoclonus.[7] Interestingly, we did not find high gamma activity in our patient's GPi, although movement has been described to affect high gamma band activity, too.

Increase of theta/alpha band activity in the GPi might be a common feature of involuntary movements in general, because it has been described in various pathologies, such as dystonia, PD with levodopa-induced hyperkinesias, myoclonus dystonia, or Tourette's syndrome.[8,9] The spatial correspondence of theta/alpha band and MUA might be the result of similar pathophysiological mechanisms of LFP and MUA. However, similar topography does not necessarily imply causality.

The pallidofugal efferent fibers are anatomically segregated into the dorsal lenticular fasciculus and ventral ansa lenticularis.[6] In PD, DBS of the ventral GPi reduces hyperkinesia and rigidity, but worsens akinesia, whereas DBS of the dorsal GPi improves akinesia and induces dyskinesia, indicating a functional somatotopy within the GPi.[10] Consistently, each pallidofugal output tract could maintain its own oscillatory network, which could at least be partly responsible for the complex motor features in HD consisting of hyper- and bradykinesia, dystonia, ataxia, or even myoclonus.

In conclusion, this report provides new information on oscillatory activity within the GP in a patient with HD and its possible functional significance for the underlying pathophysiological motor network, suggesting different pathophysiological mechanisms leading to the coexistence of hyper- and hypokinesia.

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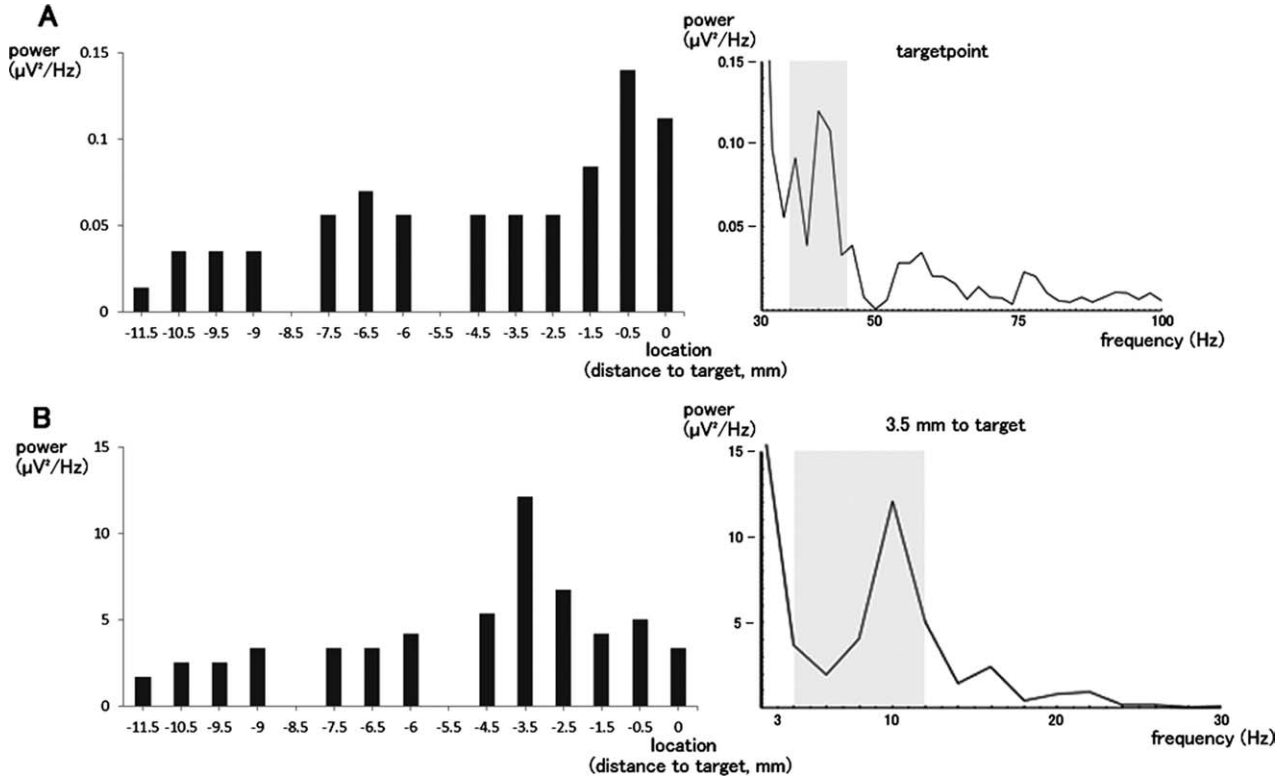

FIG. 1. (A) Spatial distribution of 35 to 45 Hz LFP of the left hemisphere. An exemplary frequency spectrum at the target point shows a 40-Hz peak. (B) Spatial distribution of 4 to 12 Hz LFP of the left hemisphere. An exemplary frequency spectrum 3.5 mm above the target point shows a 10-Hz peak.

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Reversible Pisa Syndrome in Patients with Parkinson's Disease on Rasagiline Therapy

Pisa syndrome (PS) is clinically defined as the sustained lateral bending of the trunk.[1] Over the years, it has been related to the use of dopamine receptors blockers or cholinesterase inhibitors. In rare instances, idiopathic cases of PS (also termed ''lateral trunk flexion'') have been described in patients with Parkinson's disease (PD).[1,2] In recent years, subacute and reversible PS in PD patients treated with pergolide, entacapone, or other increases of dopaminergic therapy have been reported.[3,4]

We report 4 PD patients who presented reversible PS induced by rasagiline treatment (Table 1). All cases responded favorably to antiparkinsonian treatment; rasagiline was introduced to manage mild motor worsening or wearing-off phenomena. Within 4 weeks after rasagiline 1 mg/day

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Table 1. Clinical features of patients developing reversible PS after introduction of rasagiline 1 mg/day

ID[a]	Sex	Age (y)	Disease duration (y)	Involved side at onset	PS direction	Bending degrees[b]	Therapy at PS onset (mg/day) apart from rasagiline 1 mg/day	PS onset latency after rasagiline introduction (wk)	PS cessation latency after rasagiline withdrawal (wk)
1	M	64	5	L	R	12°	Pramipexole (4.5)	3	4
2	M	73	5	L	L	11°	Levodopa (450)	4	4
3	M	72	7	L	R	21°	Pramipexole (3.0), levodopa (400)	3	2
4	F	67	5	L	R	23°	Levodopa (500)	4	3

M, male; F, female; L, left; R, right; PS, Pisa syndrome.
[a]In all patients, 123I-FP-CIT SPECT showed bilateral reduction of striatal dopamine transporter binding, whereas brain MRI was normal.
[b]Maximal angle of trunk deviation was calculated on the anterior-posterior plane of the spine x-ray by measuring the angle between the line joining right and left posterior superior iliac spines with the reference system defined by spinous processes of the 7th cervical vertebra, the 9th thoracic vertebra, and the sacral prominence.

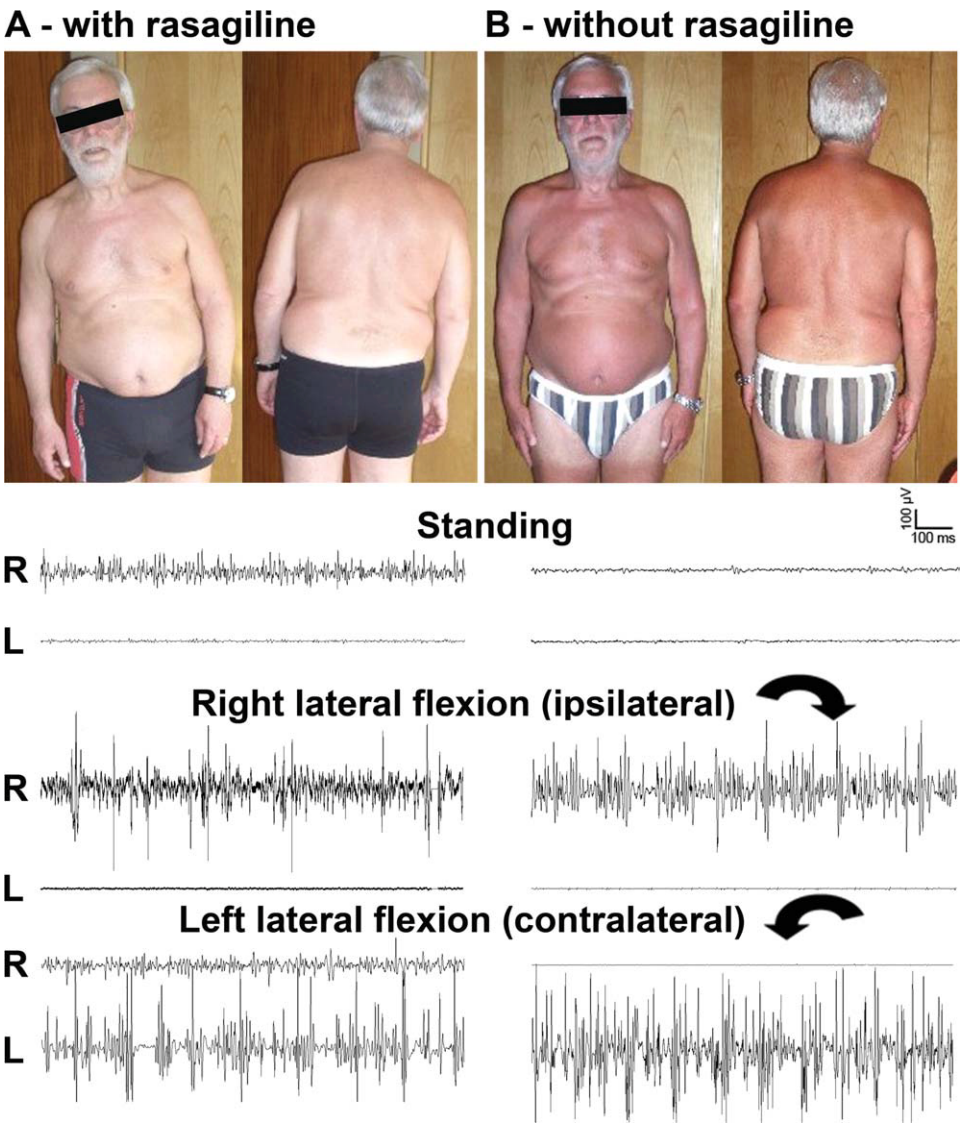

FIG. 1. Case 1's posture along with EMG recordings 3 weeks after the introduction of rasagiline 1 mg/day (**A**) and 1 month following its withdrawal (**B**). EMG of right paravertebral muscles discloses hyperactivity in standing position not ceasing during contralateral flexion (**A**). Complete remission of postural and EMG abnormalities 1 month after rasagilne withdrawal (**B**). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

introduction, the patients developed PS without any awareness of it, which was reported by caregivers in 3 cases but was directly diagnosed by the treating physician in the other case. Withdrawal of rasagiline led to the rapid improvement of posture within 4 weeks in all cases (Table 1). Patients' past medical history was unremarkable; none of them had ever taken neuroleptics, antiemetics, or cholinesterase inhibitors, and laboratory examinations (including serum muscular enzymes and urine tests) were normal. Two patients (cases 1 and 2) underwent EMG with needle electrodes inserted in the paravertebral muscles at the thoracic-lumbar level T12–L1 (longissimus thoracis muscle): it showed no myopathic or neuropathic patterns. In keeping with previously reported methods,[5] EMG was also performed in 4 positions (prone, stance, and during voluntary right and left lateral trunk flexion while standing) and showed hyperactivity of the ipsilateral paraspinal muscle group during standing with bilateral coactivation during contralateral lateral voluntary flexion (Fig. 1A). EMG confirmed the normalization of the traces after the resolution of PS in both patients (Fig. 1B).

Despite the high prevalence and clinical relevance of PS,[1,2,5] its pathophysiology is still poorly known. Although other mechanisms of action—including disease-modifying properties—have been advocated for rasagiline, its clinical effect mainly relies on the inhibition of monoamine oxidase type B, thus leading to the increase of dopamine extracellular levels in striatal synapses. This is in keeping with previous reports of PD patients developing PS soon after therapy adjustments.[3,4] We consistently found activation of muscles ipsilateral to the leaning side at rest, not ceasing during voluntary contralateral trunk flexion, thus indicating the typical cocontraction of agonist and antagonist muscles described in dystonia. In our recently published series of 10 PD patients with PS for a variable amount of time, we were able to show a dystonic mechanism only in 3 cases, thus supporting at least 2 different mechanisms underlying this condition.[5] In fact, because the 4 reversible cases reported here were all examined within a few weeks after PS onset, it could be argued that forms with subacute onset are drug-induced axial dystonias in contrast with chronic forms, whose pathophysiology might partly rely on local changes affecting muscles and bones.[1,5] In these cases EMG features, temporal course and reversibility suggest that PS is triggered by plastic striatal changes induced by a central neurochemical dysregulation. Rasagiline is widely prescribed to PD patients; however, PS might occur more readily in a subset of predisposed subjects. The reason for this individual predisposition is presently unknown and could involve individual factors such as asymmetrical neurochemical changes in the basal ganglia of the 2 hemispheres. Interestingly, in 3 of our 4 cases, PS was directed toward the less affected side, in keeping with previous reports.[5]

In conclusion, the recognition of reversibility of PS during the initial stages of its appearance may be of considerable clinical importance as it may facilitate the rapid withdrawal or reintroduction of dopaminergic treatment, thus avoiding an initial veering toward the chronic irreversible variant. The scarce knowledge about the potential reversibility of PS in the subacute phase might represent one of the more important causes of its evolution into these irreversible forms. In this regard, the relationship between subacute cases and the sporadic description of "idiopathic" PS in PD[1,5] is presently unknown. ■

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Paroxysmal Craniocervical Dyskinesia as Manifestation of Frontal Lobe Epilepsy

Primary paroxysmal movement disorders are a group of rare conditions presenting as recurrent, self-limiting episodes of involuntary movements with preserved consciousness.

Corresponding to their phenomenology, mainly three forms are differentiated.[1]

The brief attacks of paroxysmal kinesigenic dyskinesia (PKD) are characteristically induced by sudden movement.

Additional Supporting Information may be found in the online version of this article.

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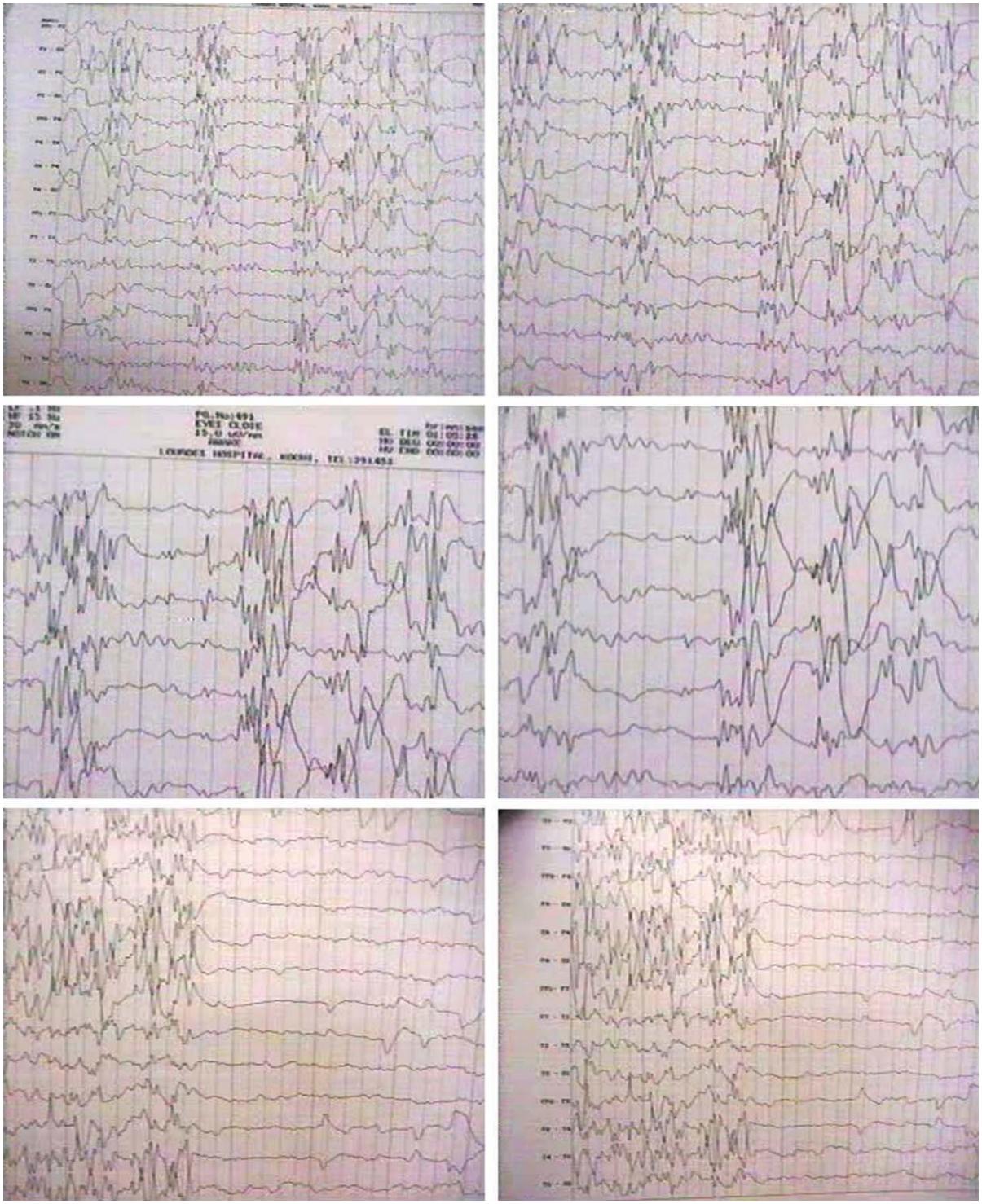

FIG. 1. Ictal surface EEG in longitudinal bipolar montage, covering the right parasagittal, left parasagittal, right temporal, and left temporal region. The EEG shows bursts of bilaterally mesial synchronous spikes, sharp waves, and sharp and slow waves, followed by mild suppression of the background. Additionally, focal spikes in the right frontal region are seen. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

Typically, response to antiepileptic treatment, particularly with carbamazepine, is good.

The more prolonged attacks of paroxysmal nonkinesigenic dyskinesia (PNKD) are precipitated by alcohol, caffeine, or fatigue. In families with autosomal-dominant inheritance, mutations in the myofibrillogenesis regulator- 1 gene have been found.

Bouts of paroxysmal exercise-induced dystonia (PED) are triggered by prolonged exercise and subside with rest. Some of the cases with autosomal-dominant inheritance were shown to be related to mutations in the glucose transporter-1 (GLUT1) gene.

In all the three forms, usually the limbs are affected by dystonic dyskinesias, though more complex movements may be seen.

To date, the underlying pathophysiology has not been understood. There is a debate over whether paroxysmal dyskinesias fall in an interphase between basal ganglia disorder and epilepsy, though no correlates on surface EEG are observed.

Here, we report on the unusual case of an 11-year-old boy with recurrent episodes of a paroxysmal movement disorder affecting mainly his craniocervical region.

Attacks were stereotyped and consisted of dyskinetic-dystonic movements, mainly neck extension and rotating movements of his head, and were accompanied by lip movements and vocalizations in the form of crying, followed by yawning (see video). They would last approximately 3 to 5 minutes and occur many times a day, always with maintained awareness. The patient was able to respond to questions during an attack and even tried to correct the head turning, if asked to do so, but with only partial success. No triggers could be elicited. Clinical examination between the attacks was normal, as were his birth history and developmental milestones, except for mild developmental delay. An EEG done during an attack showed bilateral mesial frontal epileptic discharges, with additional focal spikes in the right frontal region. CT scan and MRI of the brain did not display any pathological findings.

Diagnosed with frontal lobe epilepsy, the patient was started on antiepileptic treatment with carbamazepine (200 mg bid), under which seizures subsided within 2 weeks.

Discussion

In summary, this is a case of frontal lobe epilepsy presenting as a paroxysmal movement disorder affecting the craniocervical region, highlighting the interphase between epilepsy and movement disorders. Typically, surface EEG is normal in paroxysmal movement disorders, such as PKD, PNKD, and PED. However, few studies with depth electrodes have shown discharges in supplemental motor-area spread to the basalganglia.[2] Other shared features of epilepsy and paroxysmal movement disorders are auras preceding attacks and response to treatment with antiepileptic drugs.

Our patient had clear discharges in the frontal lobe. Interestingly, the craniocervical region was affected and attacks occurred only during daytime.

In contrast, complex motor seizures in frontal lobe epilepsy occur more often, sometimes exclusively during sleep. Seizure semiology consists mainly in stereotyped bimanual-bipedal movements (e.g., thrashing movements of the legs) or pelvic thrusting, though retrocollis might be seen. Attacks may have a bizarre quality and may be accompanied by forced laughter, crying, whining, vocalizations, or verbalizations. Consciousness is variably impaired during the relatively brief attacks (10–20 seconds).[3–5] Furthermore, the brief sleep-related attacks of involuntary movement in the previously called hypnogenic paroxysmal dyskinesia (HPD) were shown to be usually a manifestation of frontal lobe epilepsy. Sporadic autosomal dominant familial cases have been reported, and different gene mutations for autosomal dominant nocturnal frontal lobe epilepsy (ADNFLE) have been found.[5]

In conclusion, we wish to draw attention that an EEG should be considered in any patient with stereotyped repetitive attacks involving the craniocervical region, even if attacks are longer lasting, because sometimes they might be caused by frontal lobe epilepsy.

Legend to the Video

The video segment demonstrates a typical attack with dystonic posturing of the neck and face, accompanied by oral automatisms in the form of lip smacking and vocalizations in the form of crying, followed by yawning.

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