脊髄小脳変性症の立位および歩行障害に対するリハアプローチの取り組み

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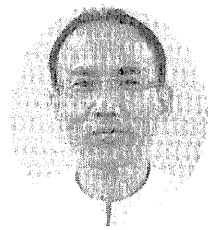

脊髄小脳変性症とリハビリテーション

脊髄小脳変性症(spino-cerebellar degeneration：以下SCD)の立位･歩行障害に対しては、フレンケル体操[1]、重錘や弾性緊迫帯を装着する方法[2]やPNFを用いて体幹・下肢の失調を減じ、それらの改善に繋げるリハビリテーションアプローチ(以下リハアプローチ)が行われています。またSCDのグレードを加味し、筋力低下の予防により立位･歩行能力を維持する[3][4]ことが提唱されています。

SCDの立位では、3 Hz前後の体幹の前後動揺[5]や両足を開いて立ちます。前者では運動感覚の錯覚が起こり[6]、体幹動揺による姿勢の修正は、固有感覚に比べ効率の悪い視覚モニターで補正する[7]ことが難しく、固有感覚入力が増大します。そのために、固有受容器で変換された電気信号である求心性インパルスは増大し、知覚神経が緊張します。後者では股関節内転筋が骨盤の安定性に働き、その支配神経である閉鎖神経は緊張します。その結果、腰方形筋の支配神経が緊張し骨盤が挙上します。骨盤が挙上すると、歩行時の骨盤の上下運動の位置エネルギーが、前への運動エネルギーに変換されず、前に進むことができにくくなります。

神経が緊張するとその可動性が低下し、インパルスの伝導が妨げられます。その結果、感覚情報の減少・歪みや筋緊張低下・亢進が生じます[8]。中枢疾患でも、神経の可動性の改善には、バトラーの神経モビライゼーション[9]が有効である[8]と報告されています。

本稿は、SCDの立位･歩行障害に対し、神経モビライゼーションに準じた方法と、立位･歩行能力の改善に必要なリハアプローチの導入による、本院での取り組みについて紹介します。

対　象

2008年2月～9月まで、磁気治療を目的に神経内科病棟に入院されたSCD患者さん11例中、起立性低血圧によりリハアプローチが困難であった1人を除いた10人を対象としました(表1)。全員、開眼・閉脚（30秒間）は可能でした。

リハアプローチ

先ず立位での体幹の前後動揺の改善を行います。振戦の機序[10]と神経の走行とその髄節支配[11]から、皮膚からの末梢性感覚入力が頻繁となり、緊張した上殿皮神経、外側大腿皮神経からの周期的な感覚性フィードバックにより前後動揺が生じています。それらの神経の伸張により、体幹の前後動揺を改善しました（図1, 2)。

また体幹の前後動揺による視覚的代償と姿勢調節の基本である、頸部を重力に対して正しい方向に保ち、眼球と脊柱起立筋の運動とも連結する、筋紡錘の豊富な後頭下筋群が過剰に働き緊張します。脳は後頭下筋群の緊張をその筋紡錘から読み取り,脊柱

表1　ケース

ケース	性別	年齢	診断名	SCD重症度分類*
1	男性	54	MSA**	Ⅲ度
2	男性	63	MSA	Ⅲ度
3	女性	59	SCA6	Ⅱ度
4	男性	57	MJD***	Ⅲ度
5	女性	47	SCA6	Ⅳ度
6	女性	71	MSA	Ⅳ度
7	女性	75	MSA	Ⅳ度
8	男性	72	SCA16	Ⅱ度
9	女性	63	MSA	Ⅲ度
10	男性	69	遺伝性SCD	Ⅲ度

*厚生省労働省運動失調研究班(下肢機能障害からの分類)
**Multiple System Atrophy　***Machado-Joseph diseas

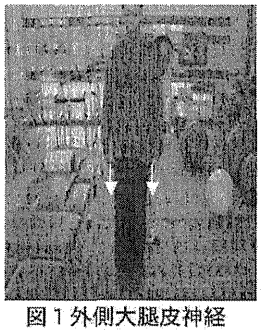
図1 外側大腿皮神経

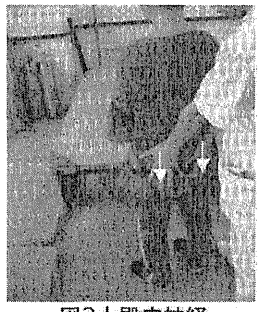
図2上殿皮神経

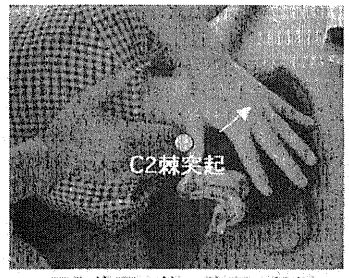

図3 後頭下筋・後頭下神経

図4 ①外側大腿皮神経②閉鎖神経
③伏在神経

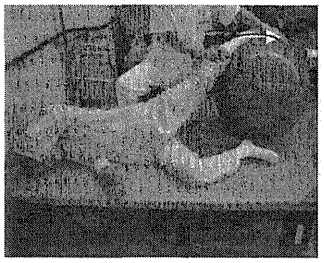
図5 総腓骨神経

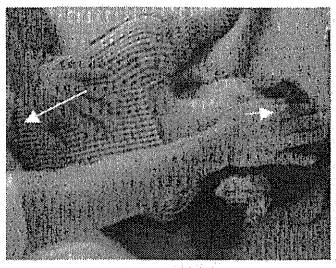
図6 副神経

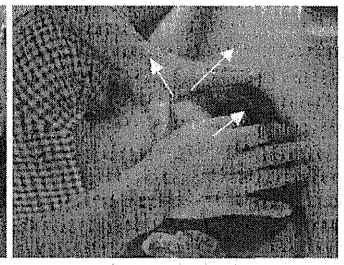
図7 顔面神経

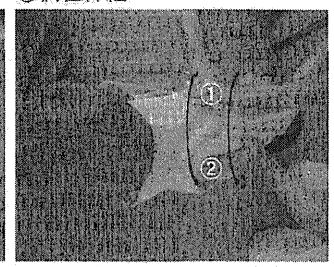

図8 ①肋間神経の外側皮枝
②脊髄神経後枝

起立筋に命令し頸椎以下の全ての脊椎を編成して働かせます。そして頭頸部の後退は根源的な恐れの反応を誘発し、転倒し易くなります[12]。

後頭下筋群の過緊張は、一方の手でC2棘突起を固定し、他方の手で上外方向へ力を加え、それらの筋群のストレッチと後頭下神経の伸張を行いました(図3)。

次に立位·歩行時の開脚位で生じる骨盤挙上は、神経内神経叢[13]から閉鎖神経とその連結の強い坐骨神経(総腓骨神経・脛骨神経)、外側大腿皮神経、大腿神経(伏在神経を含めて)を考慮して神経モビライゼーションし、腰方形筋の支配の脊髄神経の緊張を抑制し、骨盤挙上を改善しました(図4, 5)。

また臥床時間が長い場合や脳幹の萎縮が生じると、姿勢調整に重要な頸部の屈曲・伸展・回旋を担う胸鎖乳突筋の支配神経である副神経が緊張し、その筋機能が悪くなります。副神経の走行に照らし合わせてモビライゼーションしました(図6)。そして副神経と関連のある顔面神経も図7のように行いました。また後頭部・後頸部・肩甲帯周辺の知覚を支配する皮神経群(大後頭神経、小後頭神経、頸横神経、大耳介神経、鎖骨上神経)から、末梢性感覚入力により胸鎖乳突筋を緊張させている神経は、神経の走行に照らし合わせ皮膚を伸張し改善しました。

体幹の姿勢調整に重要な脊柱起立筋、肋間筋は、側臥位で胸郭の皮膚を前後から水平方向に動かし、脊髄神経後枝と肋間神経の外側皮枝を伸張することで対処しました(図8)。腹筋群は神経のアプローチと共に、筋膜の緊張による姿勢不良を呈しているケースでは、筋膜連結間[12]で伸張しました(図9)。

更に立位·歩行能力の向上のため、以下のリハアプローチを行いました。

歩行を獲得するには,脊髄中枢パターン発生器[spinal central pattern generator(CPG)]を賦活する必要があります。そのCPGは第2腰髄レベルに存在し、ステップトレーニングにより脊髄損傷者での歩行獲得が報告されています14)。CPGの賦活を得るため、立位でのステップトレーニングを、体幹の揺れが起らないように行いました。

またSCDでは腰椎前弯が減少します。腰椎の前弯の獲得により、ニホンザルが二足歩行を獲得でき[15]、歩幅の拡大と足が高く上がり[16]転倒しにくくなります。前弯獲得には,後部筋膜を棘突起の方に短縮するように動かしました[12]。また腰椎前弯の減少は脊髄の動力学[17]も悪くします。その改善には、長坐位でL4腰髄を中心に上下から脊柱を近づけ対処しました(図10)。

SCDでは足関節を底屈位にした膝立ち位が困難で、その肢位での体幹前後動揺と回旋を含めてコントロールし、立位·歩行獲得に繋げました(図11)。

SCDでは下腿三頭筋の伸張反射の抑制が失われることが、立位保持障害の起序[18]となります。その伸張反射のコントロールと、足底の皮・圧感覚からの感覚情報の導入による立位·歩行能力の改善のため、バランスパッド上で閉眼・タンデム立位を取り、外側大腿皮神経で姿勢をコントロールしました(図12)。

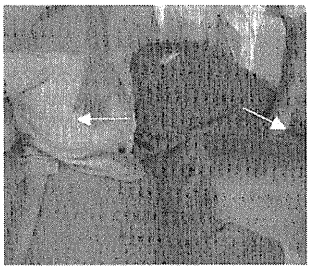
図9 腹直筋と大腿直筋

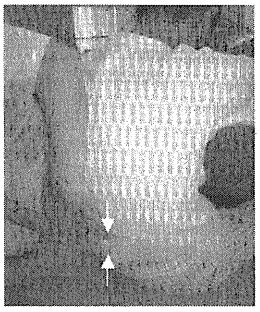
図10

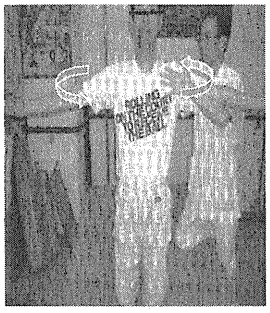
図11 膝立ち位

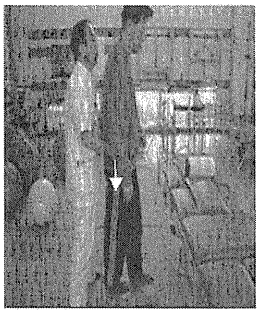
図12 タンデム立位

多系統萎縮症でパーキンソン症状のある場合は、頭部を前方に変移した姿勢の要因となる、筋緊張の亢進した筋群[19]を支配する神経群（副神経・肋間神経・長胸神経・胸背神経）の緊張を抑制することが大切です。

施行時間は40分/1回、施行回数は入院期間中の10回としました。

リハアプローチ前後の検討

リハアプローチの効果については、International-co-operative ataxia rating scale(ICARS)[20]の姿勢および歩行項目、10m自立歩行可能者数、最大歩行速度、ケーデンス、歩行時のBalance efficacy scale (BES)、Berg balance scale(BBS)[21]、閉眼・閉脚(30秒間）可能者数について、リハアプローチ施行前後で比較検討しました。

結　果

ICARSの姿勢および歩行項目、10m自立歩行可能者数、10m最大歩行速度、ケーデンス、歩行時のBES、BBSにおいて、リハアプローチ施行後で有意に改善しました。閉眼・閉脚可能者数については、差は認められませんでした(表２)。

考　察

今回のリハアプローチにより、ICARSの姿勢および歩行項目の改善、全症例の10m自立歩行の獲得、歩行速度のスピードアップ、ケーデンスの正常値化傾向、歩行時の恐怖心の指標であるBESの減少、バランス指標であるBBSのスコア向上による転倒リスク減少の効果がありました。磁気治療との相乗効果もありますが、本院でのリハアプローチは、SCDの立位･歩行障害の改善に有益であったと言えます。

立位･歩行障害の改善した理由として、脳神経、末梢神経の神経モビライゼーションと求心性神経である皮神経の伸張で、正確な情報の提供と反応が引き出され、体幹動揺や両足を開いた姿勢が改善し、立位･歩行能力の向上が得られたと言えます。また立位と歩行能力の向上を考慮したアプローチにより、立位・歩行バランス能力の向上と歩行に必要なCPGの賦活が得られたと言えます。

閉眼・閉脚の可能者数の有意な改善が得られなかったのは、閉眼での体幹の揺れの増大により下オリーブ核から登上線維への複雑スパイクの発生頻度が多くなります[22]。閉眼による平行線維からのスパイクの頻度も多くなり、それらの入力が同期して起こる機会が増え、平行線維とプルキンエ細胞間の伝達効率は減弱(長期抑圧[23]）します。そのために、適度なプルキンエ細胞の発火が得られず、閉眼・閉脚の改善度が難しかったのではと考えます。リハアプローチとしては、刺激の量と入力のタイミングを考慮する必要があったと思われます。

今後は症例を増やし、神経モビライゼーションに基づいたリハアプローチの方法の確立を目指したいと思います。

表２　結果

評価項目	リハ施行前	リハ施行後
Ⅰ．ICARS：姿勢および歩行項目（点）	17.6±6.8	10.1±3.8**
Ⅱ．10m自立歩行者数(n)	5	10*
Ⅲ．最大歩行速度(秒)	14.1±4.4	11.5±4.9*
Ⅳ．ケイデンス（歩数/分）	108.9±17.6	118.1±9.7*
Ⅴ．歩行時のBES（mm）	67.8±23.3	25.6±20.4**
Ⅵ．BBS（点）	28.5±11.5	40.5±8.6**
Ⅶ．閉眼・閉脚立位可能者数(n)	2	5

mean±SD　*:p<0.05 **:p<0.01

最後に

SCDの立位･歩行障害に対しては、非常に多くの事柄を考慮する必要があり、リハアプローチに確立されたものが無いことが頷けます。そのために、SCDのリハを求めて

来られた患者さんやご家族が病院を訪れられた時に、「私共の病院ではSCDのリハは行っていません。」と、いうような事態がある事も事実です。そのような状況の改善に、少しでもお役に立てれば嬉しく思います。

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Clinical Medicine Insights: Case Reports

CASE REPORT

Abnormal Cystatin C Levels in Two Patients with Bardet-Biedl Syndrome

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Abstract: Bardet-Biedl syndrome (BBS) is an autosomal recessive disorder characterized by central obesity, mental impairment, rod-cone dystrophy, polydactyly, hypogonadism in males, and renal abnormalities. The causative genes have been identified as BBS1-14. In the Western countries, the prevalence of this disease ranges from 1/13,500 to 1/160,000, while only a few Japanese patients have been reported in the English-language literature. The incidence of renal dysfunction or anomalies in previous reports varies considerably ranging from ~20% to universal occurrence. We here report that two Japanese patients who had BBS with normal BUN and creatinine levels had elevated levels of cystatin C, a sensitive marker of glomerular filtration rate. A urine albumin level increased only in the elder patient. Thus, cystatin C may be useful for detecting renal abnormalities in patients with an apparent normal renal function. Because this disease is diagnosed by accumulation of symptoms, such a sensitive marker might help early diagnosis of BBS.

Keywords: mental impairment, obesity, cystatin C, renal abnormality, retinitis pigmentosum

Clinical Medicine Insights: Case Reports 2011:4 17–20

doi: 10.4137/CCRep.S6622

This article is available from http://www.la-press.com.

Introduction

Bardet-Biedl syndrome (BBS) is an autosomal recessive disorder characterized by central obesity, mental impairment, rod-cone dystrophy, polydactyly, hypogonadism in males, and renal abnormalities.[1,2] The causative genes have been identified as BBS1-14 genes that encode proteins possibly linked to cilia function, but more than 20% of patients have no mutations found.[3] The diagnosis is made only by the clinical phenotype with the presence of at least three major symptoms, however, it is often difficult partly because of age-dependent development of some symptoms. In the Western countries, the prevalence of this disease ranges from 1/13,500 to 1/160,000.[3] By contrast, only a few Japanese patients have been reported in the English-language literature.[4–6]

Renal fibrosis is one of the most devastating symptoms, ultimately leading to chronic renal failure requiring hemodialysis.[7] The incidence of renal dysfunction or anomalies in previous reports varies considerably ranging from ~20% to universal occurrence.[2,7] An early detection of such abnormalities may be important for patients and guardians to prepare them. It may also be useful for prompt correct diagnosis of BBS, since the diagnosis of this disease is based on the accumulation of major symptoms as described above. We now report that two Japanese patients with BBS had normal BUN and creatinine level but elevated levels of cystatin C, a sensitive marker of glomerular filtration rate (GFR).

Patients

A 20-year-old man (patient 1) had mental retardation (minimental state examination 23; normal > 24), rod-cone dystrophy, central obesity (height 158 cm, weight 63 kg, and BMI 25.2) and hypogonadism since the age of 5 years. His waist circumference was 83.5 cm. His blood pressure was 131/85 mmHg, and his heart rate was 61 beats/min. He had normal heart sounds with clear breath sounds. A 16-year-old boy (patient 2), the younger brother of patient 1, had polydactyly in addition to the symptoms described above (height 165 cm, weight 93 kg, and BMI 34.2). His waist circumference was 107 cm. His blood pressure was 128/61 mmHg, and his heart rate was 77 beats/min. He had normal heart sounds with clear breath sounds. Their non-consanguineous parents were apparently healthy. The symptoms of patients and probable autosomal recessive inheritance fulfilled the diagnostic criteria for BBS5. After obtaining informed consent, a DNA chip study was performed at Asper Biotech Ltd. (Tartu, Estonia). The DNA chip (version 5) covered 305 mutations from 14 genes causative for BBS and related diseases (BBS1, BBS2, BBS3, BBS4, BBS5, BBS6, BBS7, BBS8, BBS9, BBS10, BBS12, PHF6, ALMS1, and GNAS1), but identified no pathological alterations. Nevertheless, because about one fifth of patients with clinically definite BBS have no identifiable mutations as described above and because the chip covered only mutations previously reported to be pathogenic, these results could not rule out the possibility of a diagnosis of BBS in our family.

Tests for Renal Morphology and Function, and Other Laboratory Tests

To detect morphological renal abnormalities, the patients underwent abdominal CT scans and abdominal sonography, with no apparent anomalies. Blood and urine tests routinely performed in Japan failed to identify any obvious abnormalities (Table 1, upper rows). Other laboratory data of the elder and younger patients included normal blood sugar levels (78 mg/dl and 81 mg/dl, respectively), normal total cholesterol levels (144 mg/dl and 131 mg/dl, normal 120–220 mg/dl), unelevated triglyceride levels (28 mg/dl and 72 mg/dl, normal 30–150 mg/dl), negative serum CRP, and negative urine occult blood or glucose. Creatinine was measured by an enzymatic method. Serum cystatin C

Table 1. Results of sensitive renal function tests.

Patient #	1	2
BUN (mg/dl)	7	9
Cre (mg/dl)	0.6	0.8
Urine protein	− ~ ±	−
Urine albumin (with cre correction normal = <10)	248*	5.2
Cystation C (0.63–0.95 mg/l)	0.96*	0.97*

Note: *Abnormal values.

and urine albumin were then examined. Cystatin C was measured by a colloidal gold agglutination method. The results showed elevated cystatin C concentrations in both patients and microalbuminuria in the elder patient (Table 1, lower rows). Cystatin C levels of the age- and sex-matched controls were also examined, the result of which showed 0.86 mg/L for an elder control and 0.91 mg/L for a younger control.

Discussion

We describe abnormal levels of serum cystatin C in two patients with BBS (Table 1). Cystatin C is a plasma protein with a molecular weight of 13.4 kDa and belongs to the cysteine protease inhibitors.[8] It is constantly synthesized in all types of cells, excreted into plasma, and filtered completely by the glomeruli. Consequently, increasing serum levels of this marker indicate decreasing GFR. Measurement of cystatin C more sensitively detects mild GFR abnormalities than that of creatinine, a more common but less sensitive marker of GFR,[8] probably because the lower molecular weight of creatinine (113 Da) facilitates its easier filtration in the glomeruli. In addition to the sensitivity, cystatin C is a more reliable marker than creatinine for detection of chronic renal disease, since creatinine levels are affected by many extrarenal patient-related factors such as muscle mass and consumption of cooked meat that is a source of creatinine.[8] Our patients had only mild increases in cystatin C. Nevertheless, because cystatin C levels age-dependently increase with decreasing GFR, the values of our young patients seem sufficiently high for their ages.[8]

A urine albumin level increased only in the elder patient. Patients with BBS occasionally manifest proteinuria,[7] suggesting that patients had not only decreased GFR but also increased protein leakage. Urine albumin is used to detect early phases of diabetic or hypertensive nephropathy.[9] Because neither of our patients showed apparent proteinuria, the elder patient may be in an early phase of protein leakage. In diabetes mellitus, timely treatment with an angiotensin-converting enzyme inhibitor, independently of rise in arterial blood pressure, is considered if improvement of glycaemic control and moderate decrease of dietary protein intake for 6–12 months have failed to reduce the albumin excretion rate.[9] Screening programs for microalbuminuria and early intervention can substantially modify the natural history of diabetic renal involvement and disease and possibly reduce the incidence of end-stage renal failure.[9] In BBS, although such intervention has not been tested yet, we may consider similar protective methods for renal dysfunction.

In conclusion, patients who have BBS with apparently normal kidney functions may have abnormal levels of cystatin C, facilitating an early detection of kidney dysfunctions that might be helpful for prompt correct diagnosis of BBS. However, because our study is based on the results of the small number of patients, conclusion must await further studies.

Acknowledgment

This study was partly supported by the Health and Labour Science Research Grants (Research in intractable diseases) to Drs Hirano, Yamashita, Ikuno, Iwahashi, Ohishi, Mano, and Ishihara.

Disclosure

This manuscript has been read and approved by all authors. This paper is unique and is not under consideration by any other publication and has not been published elsewhere. The authors and peer reviewers of this paper report no conflicts of interest. The authors confirm that they have permission to reproduce any copyrighted material.

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Journal of the Neurological Sciences 309 (2011) 9–11

Contents lists available at ScienceDirect

Journal of the Neurological Sciences

journal homepage: www.elsevier.com/locate/jns

A novel mutation in the calcium channel gene in a family with hypokalemic periodic paralysis

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ARTICLE INFO

Article history:
Received 10 June 2011
Received in revised form 23 July 2011
Accepted 26 July 2011
Available online 19 August 2011

Keywords:
Hypokalemic periodic paralysis
Hyperkalemia
Calcium channel
Voltage sensor
Diagnostic difficulty
Increased CK

ABSTRACT

Hypokalemic periodic paralysis (HypoPP) type 1 is an autosomal dominant disease caused by mutations in the Ca(V)1.1 calcium channel encoded by the *CACNA1S* gene. Only seven mutations have been found since the discovery of the causative gene in 1994. We describe a patient with HypoPP who had a high serum potassium concentration after recovery from a recent paralysis, which complicated the correct diagnosis. This patient and other affected family members had a novel mutation, p.Arg900Gly, in the *CACNA1S* gene.

1. Introduction

Hypokalemic periodic paralysis (HypoPP) is an autosomal dominant disease caused by mutations in either the Ca(V)1.1 calcium channel encoded by the *CACNA1S* gene (HypoPP type 1) or the Na(V)1.4 sodium channel encoded by the *SCN4A* gene (HypoPP type 2) [1]. HypoPP type 1 is more common than HypoPP type 2 (1:5–8). In HypoPP type 1, only seven mutations have been found since the discovery of the causative gene in 1994 [2]. However, the prevalence of HypoPP is not extremely low (1:100,000), suggesting that a few common mutations affect many families [3]. The Ca(V)1.1 channel consists of four domains, and each domain has S1 to S6 transmembrane segments. All mutations but one rare one (p.Val876Glu) [4] are involved in arginine residues in the S4 segments of the calcium channel [2,3,5–7]. A recent study proposed a gating pore cation leak current caused by loss of a positive charge of arginine in S4 voltage sensors as a common pathomechanism of HypoPP [1,8].

We describe a patient with HypoPP who had a high serum potassium concentration after recovery from paralysis, which complicated the correct diagnosis. This patient had a novel mutation, p.Arg900Gly, in the *CACNA1S* gene.

2. Patients

The proband (patient 1) was a 41-year-old man who started to have periodic episodes of paralysis, occurring about five times a year, since the age of 21 years. Each episode lasted 12 hours to 2 days. Hard physical exercise seemed to induce paralysis and was therefore avoided. Overeating, but not coldness, also induced paralysis. On a careful, detailed interview, he recalled that he had had a history of hypokalemia at the time of the previous episode of paralysis, but the value was not currently available since the clinic he had visited had permanently closed. He also reported having received potassium supplements at that time, which seemed effective, but were soon discontinued for no apparent reason. A family tree (Fig. 1A) suggested a pattern of autosomal dominant inheritance (Fig. 1A). Two days after a recent episode of paralysis he visited our clinic. Muscle strength was normal, with no muscular atrophy. Laboratory tests showed increased levels of potassium (5.4 mEq/l, normal 3.3–5.0 mEq/l), CK (3233 IU/ml, normal 45–190 IU/ml), AST (104 IU/l, normal 10–40 IU/ml), and ALT (54 IU/ml, normal 5–45 IU/ml). Blood sugar was only slightly decreased to 69 mg/dl (normal 70–139 mg/dl). Other data, including thyroid function, were normal: Na 144 mEq/l, Cl 104 mEq/l, TSH 0.89 mU/ml (normal 0.34–3.88), fT3 3.8 pg/ml (normal 2.1–4.1 pg/ml), and fT4 1.5 ng/ml (normal 1.0–1.7 ng/ml). Electrocardiography and chest radiography showed normal findings. Electromyography showed no myotonic discharges or myogenic changes during non-

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doi:10.1016/j.jns.2011.07.046

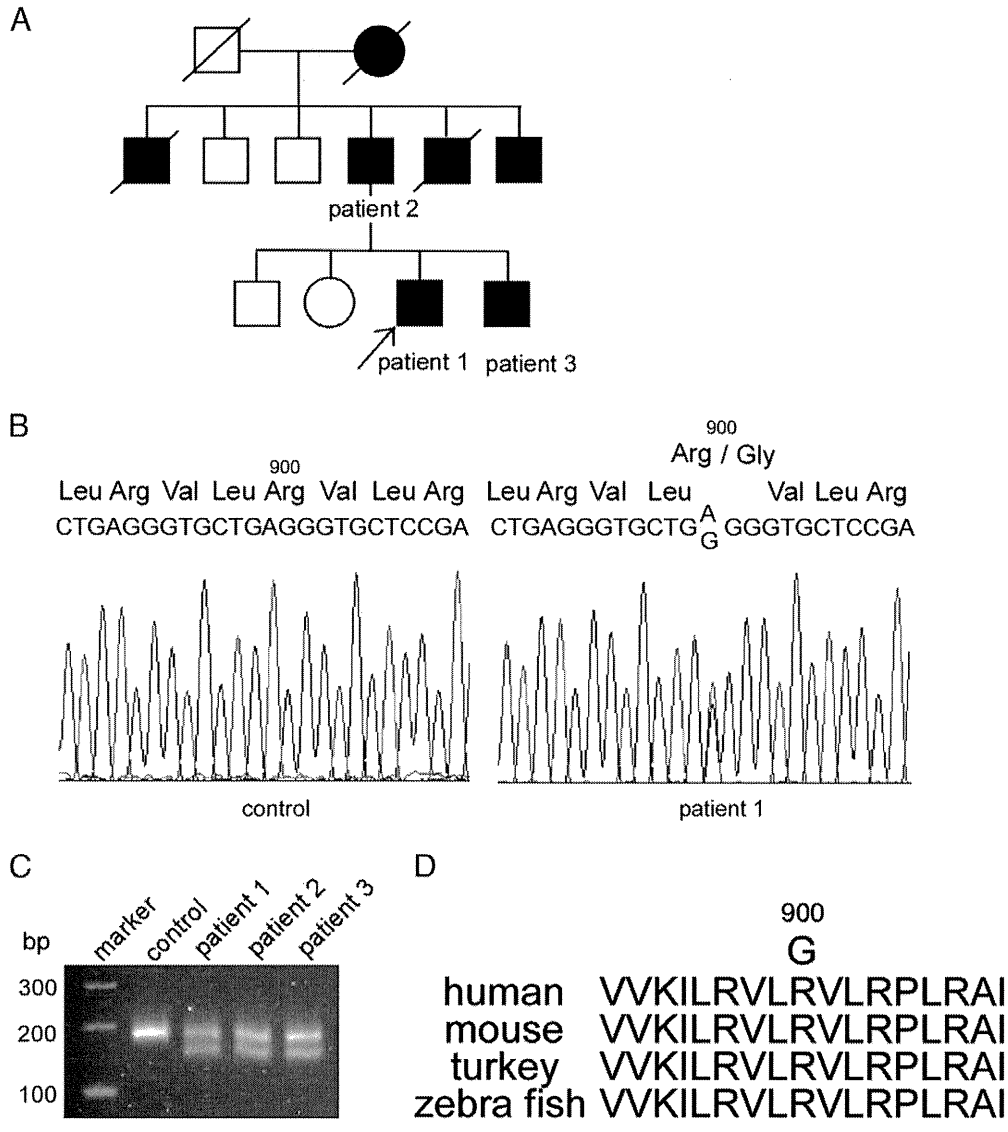

Fig. 1. (A) A family tree of the patient 1 (arrow). This family tree suggests an autosomal dominant pattern of inheritance. (B) The patient had a heterozygous A-to-G transition, resulting in the substitution of Arg by Gly at the 900 residue. (C) PCR-restriction fragment length analyses with a mismatch primer confirmed that Patients 1–3 were heterozygous for the p.Arg900Gly mutation. (D) The Arg at the 900 position is phylogenetically conserved.

paralytic periods. After 19 days, all abnormal blood test values had normalized.

Patient 2 (69 years), the father of the proband, had paralytic attacks since the age of 13 years. Most attacks, occurring 5 times/year, were mild or partial, but severe episodes occurred 10 times over the course of 37 years. Paralysis was induced by hard physical exercise and overeating, but not coldness. He had not been examined in any medical institutions during paralysis. He has had no attacks since the age of 50 years. Patient 3 (35 years), a younger brother of the proband, started to have mild paralytic attacks since the age of 13 years and severe ones since age 15. He also recalled that he had had a history of hypokalemia during paralysis, but the value was not currently available. Recently, he had severe attacks 10 times/year, induced by hard exercise and overeating, but not by coldness.

After obtaining written informed consent from Patient 1, a genetic analysis was performed as described previously [2,3,5]. Patients 2 and 3 agreed to genetic testing, but the mother of the proband declined. A novel heterozygous A-to-G transition was identified in the *CACNA1S* gene (c.2698A>G), resulting in a missense change (p.Arg900Gly, Fig. 1B). This mutation was confirmed by PCR-restriction fragment length analyses as follows. The forward primer carried two nucleotide substitutions (ex21mF: 5′-GTGCCATCTCCGTGGTGAAGAcCaT-GAGGGTGCT-3′, lower case letters mean substituted nucleotides) to create the endonuclease *Xcm*I (CCANNNNNNNNTGG) site in a PCR fragment only from a mutant allele. The reverse primer was 5′-GGTCCCAGCCATGGCTGGGCTGA-3′. The PCR-amplified mutant fragment (179 bp) was digested into two fragments (29 and 150 bp), though only the larger fragment was visible. The normal fragment remained undigested. This mutation was present in Patients 1–3, but not in 100 control chromosomes (Fig. 1C). This Arg900 residue is highly conserved among humans, mice, turkeys, and zebra fish (Fig. 1D).

3. Discussion

We found a novel mutation in a patient with HypoPP type 1. This mutation in the S4 segment of the domain III affects the same residue as the previously identified mutation p.Arg900Ser [3]. Similar to previous other mutations involving arginine residues, the positive charge of arginine was abolished by a neutral amino acid, glycine. The Arg900 residue is phylogenetically conserved. Thus, this novel

p.Arg900Gly mutation may cause a gating pore current leak and is most likely causative for HypoPP.

Our patient had a high serum potassium concentration at the visit to our clinic after recovery from paralysis, which complicated the correct diagnosis. However, such hyperkalemia during recovery periods in HypoPP has been described previously, although mutations in either the calcium channel or sodium channel were not specified [9]. To our knowledge, mutations in the *CACNA1S* gene have not previously been associated with hyperkalemic periodic paralysis. Consistent with this, our patient presented with previous episodes of hypokalemia. Although hyperkalemia might have simply been a rebound response to hypokalemia, another possible explanation is that hypokalemia during paralysis may have destabilized muscular membranes, releasing intramuscular potassium into serum. This hypothesis may be supported by the temporal elevation of CK in our patient.

A previous study reported at least one patient with p.Arg900Ser mutation, a mutation occurring in the same residue as ours. The patient had a typical HypoPP phenotype, although detailed clinical information was not provided [3]. Attacks began to occur in the second decade and were associated with low potassium levels or with provocative factors that reduced serum potassium levels. In our patients, disease developed at 13 to 21 years of age and was accompanied by typical HypoPP episodes. Thus, mutations involving the Arg900 residue seem to be associated with a typical phenotype.

In summary, we found a novel mutation in the *CACNA1S* gene, which further supports the gating pore current hypothesis as a pathomechanism of HypoPP. Because this is only the eighth mutation identified over the course of 17 years, further discovery of mutations may provide further insight into voltage-gated channels as well as the pathomechanism of HypoPP.

Acknowledgments

This study was supported partly by Research Grants for Intractable Disease from the Ministry of Health, Labour and Welfare (to MPT).

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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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Funding agencies: This study was partly supported by Health and Labour Science Research Grants (Research in Intractable Diseases) and Grants-in-Aids for Scientific Research from the Ministry of Education, Culture, Sports, Science and Technology of Japan to Dr. Hirano.
Relevant conflicts of interest/financial disclosures: None of the authors have financial support or conflicts of interest related to this study

Published online 10 October 2011 in Wiley Online Library (wileyonlinelibrary.com). DOI: 10.1002/mds.23904

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 = 129 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

Additional Supporting Information may be found in the online version of this article.
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Relevant conflicts of interest/financial disclosures: Dr. Mainardi holds stock in Kolfarma Srl, Genova, Italy, manufacturer of alpha-lactalbumin and Dr. Striano received speaker's or consultancy fees from Eisai, Johnson & Johnson, and UCB Pharma.
Full financial disclosures and author roles may be found in the online version of this article.

Published online 24 October 2011 in Wiley Online Library (wileyonlinelibrary.com). DOI: 10.1002/mds.23908

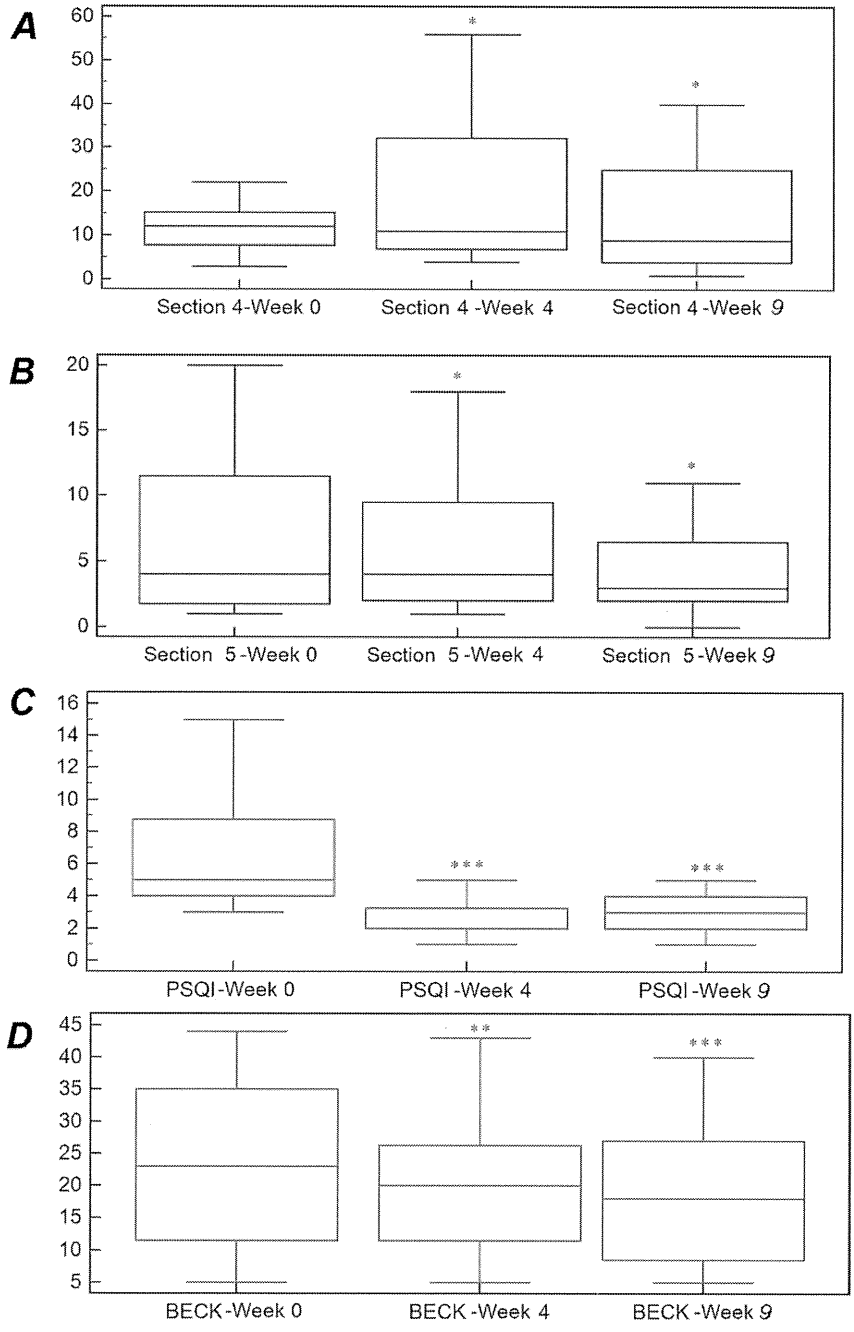

FIG. 1. Summary of efficacy data. The different end-points scores: (A) Unified Myoclonus Rating Scale, section 4 (action myoclonus); (B) Unified Myoclonus Rating Scale, section 5 (functional performance); (C) Beck Depression Inventory; (D) Pittsburgh Sleep Quality Index) obtained before (left), after 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

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

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Funding agencies: D.v.P. was partly supported by an Erasmus Grant. M.E. is supported by a National Institutes of Health Research (NIHR) Clinician Scientist Fellowship. T.S. is supported by an NIHR Research Training Fellowship. This work was performed at UCLH/UCL, who received a proportion of funding from the Department of Health's NIHR Biomedical Research Centers funding scheme.
Relevant conflicts of interest/financial disclosures: Nothing to report.

Published online 24 October 2011 in Wiley Online Library (wileyonlinelibrary.com). DOI: 10.1002/mds.23911

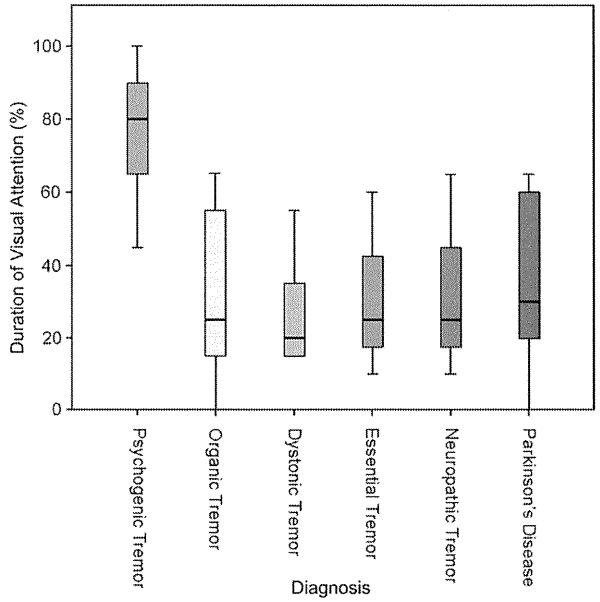

FIG. 1. Mean percentage of visual attention (for definition, see text) for patients with psychogenic tremor and organic tremor (data for all organic tremors combined and different tremor subtypes are shown). Box and whisker plots show median (solid black line), 25th and 75th percentile (top and bottom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

Acknowledgment: We thank Ms. Marika Biernat for her organizational support.

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Funding agencies: Part of this work was supported by research grants from the DFG, BMBF (ERA-Net NEURON, grant 01EW0903), and the Helmholtz Society. S.J.G. is supported by a research fellowship of the Japan Foundation for Neuroscience and Mental Health.
Relevant conflicts of interest/financial disclosures: L.W. and J.V. have received—unrelated to the current project—honoraria in the past from Medtronic, Inc., the company who manufactures the DBS hardware implanted in this patient.

Published online 9 August 2011 in Wiley Online Library (wileyonlinelibrary.com). DOI: 10.1002/mds.23914

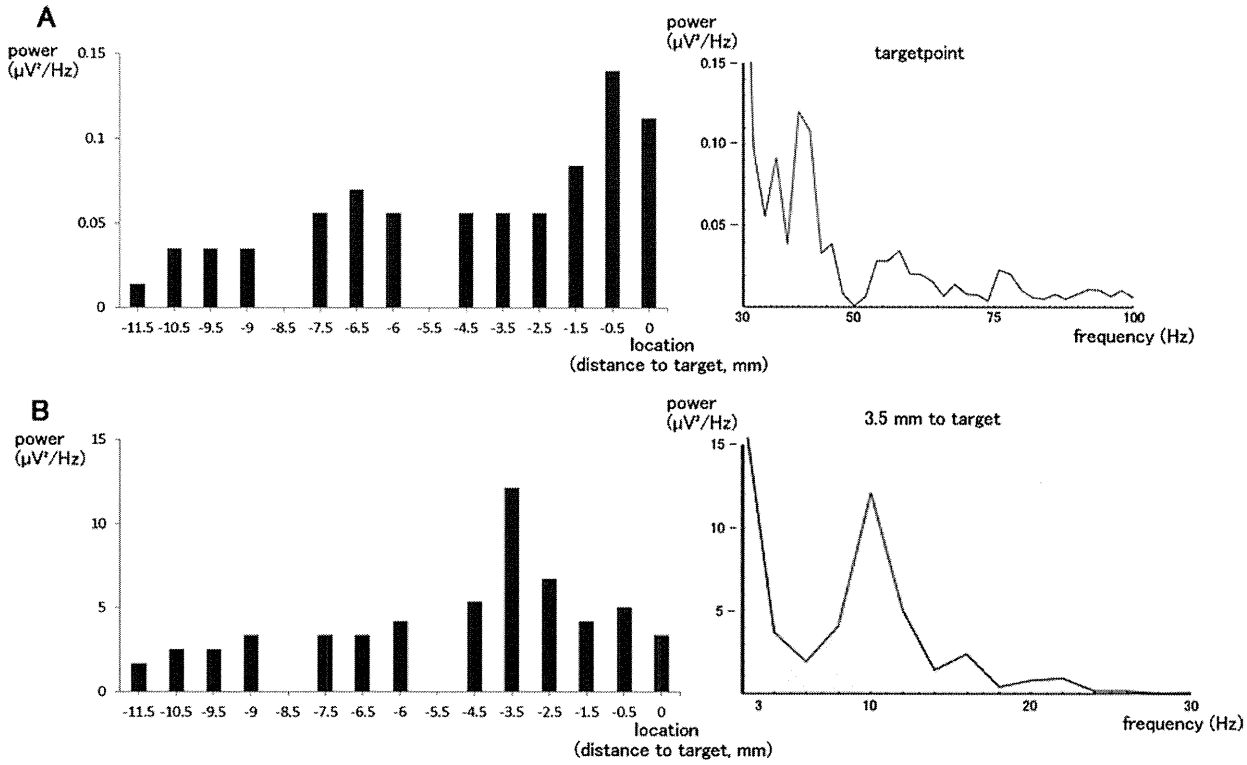

FIG. 1. (A) Spatial distribution of 35 to 45 Hz LFP of the left hemisphere. An exemplary frequency spectrum at the target point shows a 40-Hz peak. (B) Spatial distribution of 4 to 12 Hz LFP of the left hemisphere. An exemplary frequency spectrum 3.5 mm above the target point shows a 10-Hz peak.

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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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Relevant conflicts of interest/financial disclosures: Nothing to report. Full financial disclosures and author roles may be found in the online version of this article.

Published online 24 August 2011 in Wiley Online Library (wileyonlinelibrary.com). DOI: 10.1002/mds.23918

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.

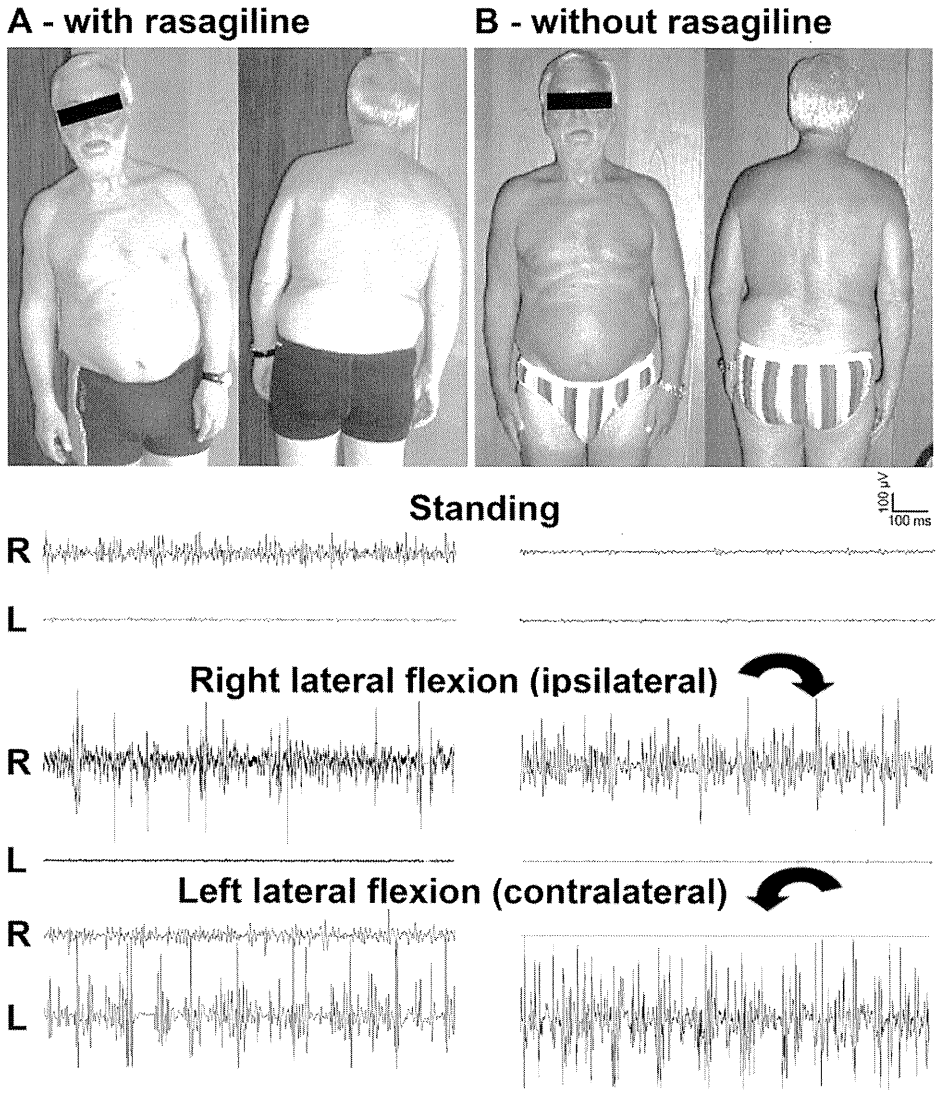

FIG. 1. Case 1's posture along with EMG recordings 3 weeks after the introduction of rasagiline 1 mg/day (**A**) and 1 month following its withdrawal (**B**). EMG of right paravertebral muscles discloses hyperactivity in standing position not ceasing during contralateral flexion (**A**). Complete remission 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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Potential conflicts of interest: Nothing to report.

Published online 1 September 2011 in Wiley Online Library (wileyonlinelibrary.com). DOI: 10.1002/mds.23925