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Brief Reports

Split-Screen Video Demonstration of Sonography-Guided Muscle Identification and Injection of Botulinum Toxin

Video

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Abstract: **A standardization of injection procedures for the various botulinum toxin (BoNT) indications has not been achieved to date. One established option to guide the therapist's needle is sonography guidance. It provides real-time visualization of the injection process, which is quick, allows perfect precision, and the procedure as such is painless. To demonstrate these qualities, we have recorded six split-screen video segments that show the handling of the probe and the needle during BoNT injections concurrently with the respective cross-sectional sonography recordings. The video sequences show differentiation of the pollicis longus muscle and individual finger flexor fascicles, needle tracking, and real-time sonography-guided injection of the gastrocnemius, rectus femoris, and iliopsoas muscles. We hope this short presentation will help to encourage a more widespread use of the technique as well as further research on sonography guidance for precise delivery of BoNT injections to various target muscles.** © 2010 Movement Disorder Society

Key words: botulinum toxin; sonography; video

BACKGROUND

Injection of botulinum neurotoxin (BoNT) into muscles is the first-line treatment for focal dystonic and spastic movement disorders and routinely performed uncounted times every day.[1,2] Although accurate injection of the toxin into the desired muscle is crucial for obtaining the best possible clinical result,[3,4] standardization of the injection technique appropriate for the various indications is still lacking. Each therapist has his own individual approach to locate and inject the target muscle(s) (e.g., palpation, electromyography [EMG], electrical stimulation, sonography, computer tomography).

There are several reasons for this variety of injection procedures: First, the muscles targeted for injection greatly differ in size, and deep-seated muscles require a different approach to superficially seated muscles. Second, the approach varies with the underlying disease and different etiologies and the special expertise of the medical department involved. Last but not least, there are far too few studies that investigated the effect of different injection techniques on the clinical outcome in relation to different indications. Although a number of studies were concerned with dosing and BoNT preparations,[5–10] only a few addressed variations of the injection technique.[11–16] However, the application of BoNT with insufficient precision may result in a decreased quality of medical care.[6,17,18]

With this communication we want to demonstrate how sonography can help to identify muscles and guide injections. This technique is widely applied in neuropediatric care[19] and has become increasingly known by neurologists and therapists in neurorehabili-

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

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tation of adults for treating spasticity and other movement disorders.

METHODS

Sonography Equipment and Technical Requirements

A standard ultrasound system meets all requirements for muscle identification and injection. A linear sonar transducer is necessary to display the anatomy without distortion. The frequency of the machine should be set to 5 MHz for deep-seated muscles and at least to 7.5 MHz for superficial structures like the forearm muscles. In the experience of the authors acquired during thousands of injections performed since 2000,[20] the use of probe desinfection wipes and regular bacteriostatic sonography gel in conjunction with skin disinfection reliably prevents infections.

The sonographic images shown here were obtained with technically current equipment (Philips iU 22 ultrasound system, L12-5 50-mm linear array transducer).

Video Recording

Videos were recorded with a regular DV camera and synchronized during recording with the signal from the ultrasound system with an additional standard DV recording machine. Formal editing was done with a standard video-processing software (Pinnacle Studio 12, Pinnacle Systems, Mountain View, CA, USA).

Patients

The patients participating in the videos or their parents or caregivers gave their written informed consent and approved the use of the video material for educational purposes.

RESULTS

We show six video segments that demonstrate muscle identification, the injection technique, needle tracking, and injection of BoNT in one healthy person and in three children with spastic cerebral palsy (CP) (Supporting Information video).

DISCUSSION

Insufficient accuracy of palpation, especially for deep-seated and small muscles was observed in adults as well as in children.[11–13] Sonography helps to identify muscles by showing contour lines of individual muscles, each with a characteristic appearance, and by concurrent oscillations of the intramuscular echo produced by passive movement or tendon stretch. Sonography visualizes bones, blood vessels, and nerves and differentiates between the target muscle and neighboring structures. Distribution of the injected fluid can be observed in real time.

Compared with other techniques, sonography is especially suited for pediatric patients.[21] It was introduced to pediatric neurology in 2000[15,20,22] and is now widely established and recommended for BoNT treatment in children with CP.[23] In a study with 54 children, Py et al.[17] found that BoNT injections administered with sonographic guidance were clinically more effective than those administered without such guidance. This is supported by other studies in which the precision of injections was carefully controlled resulting in excellent improvements on upper limb function in children with CP.[24,25] Nevertheless, it has to be acknowledged that no prospective, controlled trial on this topic exists.

There are limitations and challenges for sonography-guided injections. Although small laptop devices are available for mobile use, most sonography devices available on-site require separate workspaces, thus demanding for organizational adaptations when the physician wants to use them to guide BoNT injections. The injection of deep-seated muscles in larger extremities, especially in adipose adult patients, cannot be performed with the same visual acuity as in superficially seated muscles. Misaligned extremities will keep the therapist from using the “typical" approach and demand the use of alternative strategies and expert spatial and anatomical knowledge. Chronic spasticity is associated with substantial atrophy of muscle bulk and significant increases of muscle echogenicity, thus rendering the detection of contour lines far more difficult. However, similar limitations are also true for almost all other injection procedures.

To date and to our knowledge, no studies have been published that would correlate the economic burden of traditional, EMG or electrical stimulation, and sonography-guiding techniques in neither children nor adult patients with the clinical benefit. However, if an ultrasound machine already is at hand, the cost per injection will be diminished when compared with EMG or electrical stimulation requiring costly Teflon-coated needles. In our experience, adequate training and routine use has further reduced the time needed for precise muscle identification and injection when compared with traditional injection techniques.

By demonstrating with six split-screen video segments the easiness of muscle identification and of sonography-guided injections, we hope to encourage the use of sonography within the clinical setting and for research purposes. Sonography allows accurate identification of target muscles and precise BoNT injection—essential conditions when addressing important questions regarding the optimization of therapy, such as dosage, dilution, safety, and long-term alteration of the muscle tissue.

LEGENDS TO THE VIDEO

Segment 1: Demonstration of flexor pollicis longus muscle and fascicles of deep finger flexors (0 minute 0 second to 0 minute 48 seconds). Cross section in the middle of the forearm of a 32-year-old healthy man. Medial (ulnar) muscles are located on the left of the sonographic image. Linear transducer with 12 MHz displayed to a depth of 4 cm of the anatomy. First, the distal interphalangeal joint of the thumb is moved by the investigator, thereby inducing concurrent oscillations of the intramuscular echo of the flexor pollicis longus muscle. The same procedure is demonstrated for fingers II–V to display the single fascicles of flexor digitorum profundus II–V. Please note that at the middle of the forearm, the fascicles are lined up parallel to each other.

Segment 2: Injection of the medial gastrocnemius muscle (0 minute 48 seconds to 1 minute 12 seconds). Cross section in the upper third of the lower leg. No change to the display settings compared to Segment 1. From top to bottom the following structures can be differentiated: subdermis, perimysium (displayed as a white line), medial gastrocnemius, and soleus muscle bordering on the tibial bone. Two injections into the gastrocnemius muscles are shown, which are preceded by the placement of the needle. The needle tip of the 27-gauge needle can be located by the movement induced in the surrounding tissue. The injected volume is 0.5 mL each.

Segment 3: Needle tracking in the medial gastrocnemius muscle (1 minute 12 seconds to 1 minute 40 seconds). Similar cross section as in segment 2. The injection is performed along the longitudinal axis of the transducer, thereby allowing the therapist to follow insertion of the needle.

Segment 4: Injection of the iliacus portion of the iliopsoas muscle (1 minute 40 seconds to 2 minutes). Cross section of the left lower trunk below the inguinal ligament at the height of the femoral head. Three muscles can be seen: the iliopsoas muscles, pars iliacus right above the femoral head, the rectus (right/lateral to iliopsoas), and sartorius muscle on top. The injection into iliopsoas muscle is performed at two sites with 0.5 mL each.

Segment 5: Injection of the rectus femoris muscle (2 min 0 seconds—2 min 31 seconds). Cross section of the anterior thigh with the rectus femoris muscle superficially displayed under the skin and subcutaneous fat tissue. The probe is moved from proximal to distal and back to demonstrate the dimension of the muscle bulk. Correct needle position within the rectus femoris again is ascertained by oscillating movements. The injected volume is 0.3 mL and can be seen as echogenic reflex on the monitor screen.

Segment 6: Injection of the semitendinosus muscle (2 min 31 seconds—2 min 58 seconds). Cross section of the dorsal thigh with the medial hamstrings (semimembranosus and semitendinosus muscle) to the left, and biceps femoris to the right. The semitendinosus is located by passively stretching the tendon through pressure near its insertion. The position of the needle within the semitendinosus is ascertained by making small oscillating movements. The injected volume is 0.5 mL.

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A Comparison of Two Brief Screening Measures of Cognitive Impairment in Huntington's Disease

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Abstract: **The goal of this study was to explore whether the Montreal Cognitive Assessment (MoCA), a new screening instrument, would be more sensitive to mild to moderate cognitive impairment in Huntington's disease (HD) than an established screening measure, the Mini Mental State Exam (MMSE). Our reasoning for this query is that the MoCA includes a broader range of test items and an additional assessment of executive functioning and attention compared with the MMSE. Using the receiver operating characteristic (ROC) analysis to examine performance of HD and control groups on both tests on overall scores and scores from various subdomains (i.e., visuospatial abilities) revealed that the MoCA achieved higher sensitivity without sacrificing specificity in many domains relative to the MMSE.** © 2010 Movement Disorder Society

Key words: Huntington's disease; Mini Mental State Exam; Montreal Cognitive Assessment; executive function; visuospatial; language

Neuropsychological test batteries can be useful tools for discriminating between levels of cognitive impairment in individuals with neurologic diseases. However, a complete neuropsychological assessment is unsuitable for most medical visits, when clinicians require rapid assessment of global cognitive functioning. Consequently, brief screening instruments are a means to summarize, and concisely communicate, information about a patient's overall level of cognitive functioning. A number of brief screening measures have been developed, such as the Folstein Mini Mental State Exam (MMSE),[1] 7-Minute Screen,[2] Blessed Information Memory Concentration test,[3] and Alzheimer's Disease Assessment Scale.[4] These vary greatly in sensitivity and specificity depending on test length and target population (for review see Cullen et al.).[5]

The MMSE, the most commonly used brief screening instrument for cognitive impairment,[5] effectively distinguishes individuals without significant cognitive impairment from those with dementia. Although it is an accurate indicator of probable AD,[6–8] it is subject to ceiling effects in individuals with intact abilities or in patient groups with more subtle cognitive deficits. In addition, the MMSE relies heavily on intact verbal rather than visuospatial skills and it lacks items to assess executive functions and complex attention. These limitations may be more apparent in assessment of individuals with Huntington's disease (HD) since the cognitive profile is often characterized by deficits in executive functioning, visuospatial abilities, and attention,[9,10] rather than memory or language. Recently, an alternative screening measure, the Montreal Cognitive Assessment (MoCA),[11] was developed to capture performance deficits in a wider array of cognitive domains using items with a greater range of difficulty relative to the MMSE. Because of its inclusion of executive function/attention and visuospatial items, we hypothesized that the MoCA would be more sensitive than the MMSE to impairments seen in mild to moderate HD.

SUBJECTS AND METHODS

Subjects

Thirty-nine subjects with mild to moderate HD were recruited from the University of California, San Diego (UCSD) HD Society of America Center of Excellence (COE) and examined by a senior neurologist. Inclusion criteria included a definitive diagnosis of HD with family history and/or expanded cytosin, adenine, and guanine (CAG) repeat over 39 and overt motor signs (e.g., chorea). The Unified Huntington's Disease Rating Scale (UHDRS)[12] was administered to quantify neurologic and functional deficits. The UHDRS Total Motor Score can range from 0 (no motor symptoms) to 124 (severe, bilateral deficits in all categories). Patients with HD with dysgraphia or dysarthria severe enough to impede administration of test items were excluded from

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TABLE 1. *Means and standard deviations for group demographics and test information*

	HD, n = 39	CC, n = 73	Test statistic	*P* value
Age (yr)	50.7 ± 10.8	51.1 ± 11.3	$t = -0.17$	0.869
Gender (male/female)	14/25	37/36	$\chi^2 = 0.89$	0.345
Education (yr)	14.1 ± 2.3	14.8 ± 2.2	$t = -1.58$	0.117
MoCA[a] total points (range)	20.1 ± 4.5 (11–29)	27.4 ± 1.9 (21–30)	$U = 175.50$	<0.001
MMSE total points (range)	24.9 ± 2.8 (19–30)	29.0 ± 1.0 (26–30)	$U = 276.00$	<0.001

[a]Scores before education adjustment.

Abbreviations: HD, Huntington's disease; CC, community controls; *t*, Student's *t*-test; χ^2, chi-square statistic; MoCA, Montreal Cognitive Assessment; MMSE, Mini Mental State Examination; *U*, Mann-Whitney U statistic.

the study. In addition, subjects were assessed on the UHDRS Functional Capacity Scale, which quantifies competence for activities of daily living on a scale of 0 to 13, with higher scores indicating better functioning.

Seventy-three community control (CC) subjects were recruited from ongoing studies at the UCSD HD COE and screened for any condition that might impair cognition (i.e., head injury, neurologic disease, and substance abuse). Control subjects matched the HD group on mean age and years of education. Human subjects' approval was obtained from the UCSD Institutional Review Board. Subjects were administered the MMSE and MoCA on the same day following standard procedures in counterbalanced order.

Measures

The MoCA and MMSE assess a range of cognitive skills on a scale of 0 to 30 points with higher scores indicating better performance and a suggested impairment cutoff of 25 or fewer points. An item-by-item comparison is beyond the scope of this study, as the tests include items that vary by type and level of difficulty, and identical items receive differential weighting. As an alternative, we grouped individual items into four widely used cognitive domains (visuospatial, language, memory, and orientation) based on previous research[13] to compare their relative utility in distinguishing controls from patients with HD. The visual-spatial items included design copy (both tests) and figure drawing to command (MoCA only). The language items included object naming, phrase/sentence repetition (both tests), verbal commands, and reading comprehension (MMSE). The verbal memory items included recall of either five (MoCA) or three (MMSE) previously presented words. The MoCA also includes a fifth executive function/attention domain comprised of items for phonemic fluency, visuospatial sequencing/alternation based on Trail Making B Test, verbal abstraction, auditory span, and target detection using auditory vigilance for the letter "A." To permit more direct comparisons between measures, we excluded scores from the serial subtraction items from both tests because of differential weighting, consequently the MMSE does not have an executive function/attention analysis.

Statistical Analysis

The raw data were examined for outliers and parametric distribution requirements. Between-group comparisons of demographic characteristics were conducted using Student's two-group *t*-tests (or χ^2 for nominal data). Because of significantly non-normal distributions, we used nonparametric Mann-Whitney U to illustrate between-group differences, and Wilcoxon rank sum test to illustrate within-group performance on MoCA and MMSE point totals. Using the receiver operating characteristic (ROC) analyses, we examined the ability of the two instruments to differentiate between HD and CC subjects using the total number of points (excluding MoCA education correction), and using groupings of test items representing cognitive domains. The ROC analysis yields sensitivity and specificity statistics, and a graphical representation of how well each test or domain classifies patients with HD and controls beyond a chance (50%) level.[14]

RESULTS

There were no significant differences between the groups on age, education, or gender variables (see Table 1). In the HD sample, mean CAG repeat number was 44.6 (SD = 3.6; range: 40–57). The UHDRS mean motor score was 36.9 (SD = 17.7; range: 10–76). Mean Functional Capacity Score (FCS) for the HD group was 6.6 (SD = 1.9; range: 2–11 points).

As expected, the HD group scored significantly lower than the CC group on the MOCA and MMSE total scores (see Table 1). In addition, within-group comparisons indicated that both the HD (Wilcoxon $z = -5.3$; $P < 0.001$) and CC groups (Wilcoxon $z = -5.9$; $P < 0.001$) had lower total scores on the MoCA relative to the MMSE.

TABLE 2. *ROC analysis for MoCA and MMSE scores per group*

	Test	AUC	S.E.	*P*	Sensitivity (%)	Specificity (%)
Total score	MoCA	0.938	0.025	<0.01	97.4	30.1
	MMSE	0.903	0.033	<0.01	84.6	31.5
Visual spatial	MoCA	0.745	0.052	<0.01	69.2	30.1
	MMSE	0.595	0.059	0.10	23.0	4.1
Language	MoCA	0.669	0.056	<0.01	59.0	28.8
	MMSE	0.57	0.059	0.23	23.1	9.6
Memory	MoCA	0.825	0.043	<0.01	82.1	32.9
	MMSE	0.713	0.052	<0.01	71.8	32.9
Orientation	MoCA	0.603	0.059	0.08	20.5	0
	MMSE	0.713	0.056	<0.01	46.2	0
Exe Func Attention	MoCA	0.833	0.0485	<0.01	69.2	13.7

ROC, receiver operating characteristic; MoCA, Montreal Cognitive Assessment; MMSE, Mini Mental State Examination; AUC, area under the curve; SE, standard error; *P* probability value

Using ROC analysis, we examined performance of both groups on all test domains (see Table 2 for sensitivity and specificity percentages and Fig. 1). The area under the curve (AUC) values demonstrate that both tests significantly discriminated HD from CC subjects on total scores; however, the MoCA score yielded higher sensitivity while maintaining a comparable level of specificity relative to the MMSE. A similar pattern was found in the memory domain, with both tests accomplishing successful group discrimination; the

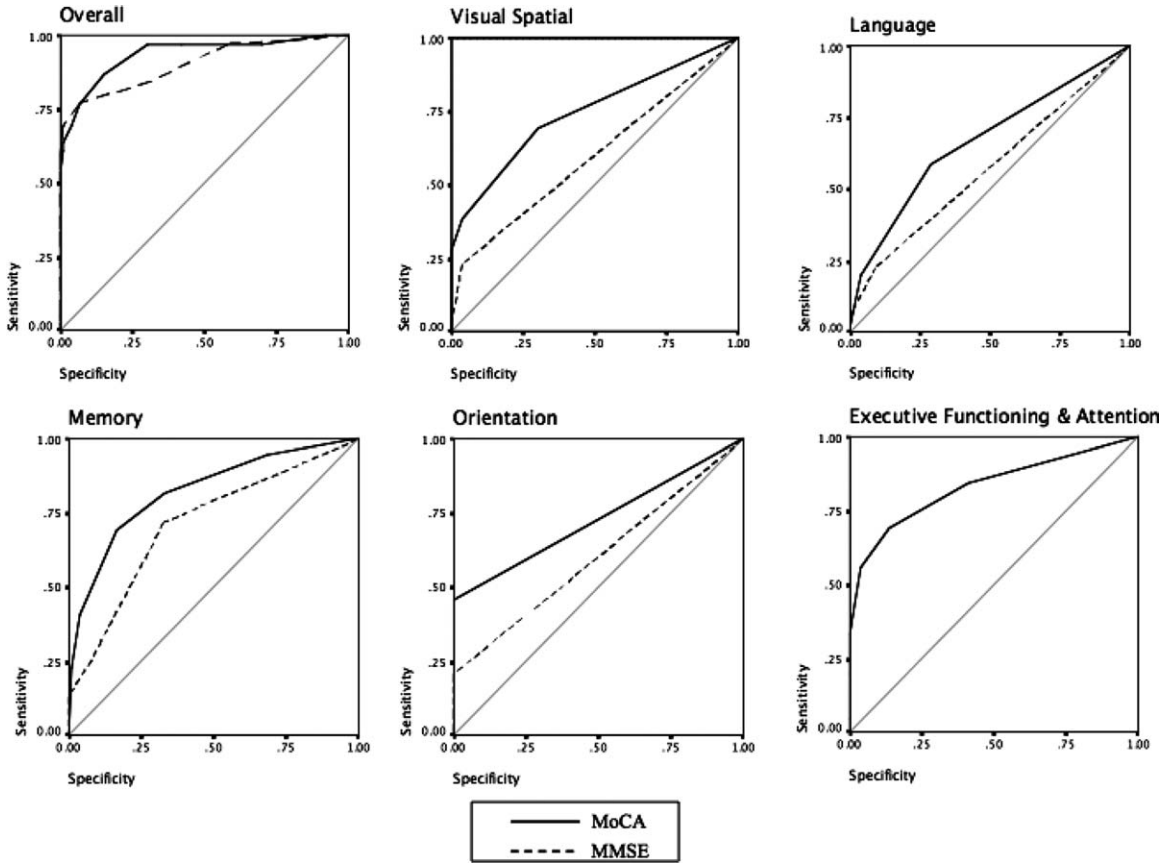

FIG. 1. Receiver operating characteristic curves for showing MoCA and MMSE discriminatory capability in HD and CC for total scores (upper left), visual spatial ability (upper middle), language (upper right), memory (lower left), orientation (lower middle), and executive functions (MoCA only).

MoCA, however, yielded higher sensitivity and comparable specificity. In contrast, only the MoCA, and not the MMSE, yielded significant AUC values for visuospatial and language scores, with higher sensitivity and specificity relative to the comparable MMSE domains. The MMSE showed superior discrimination on orientation. Finally, the MoCA executive function/attention score yielded a significant AUC for group discrimination.

DISCUSSION

To determine whether the MoCA would be more sensitive to HD-related cognitive impairment than the more widely used MMSE, we evaluated the performance of patients with HD and matched CCs on these two measures. Our expectation that the MoCA's expanded assessment of executive function/attention and visuospatial skills would improve discrimination between groups was confirmed. The HD group had significantly lower total scores on both the MoCA and the MMSE relative to controls. More importantly, the MoCA yielded a broader range of scores than the MMSE in both groups, suggesting better identification of within-group differences in deficits in the patients with mildly to moderately impaired HD. Although our primary focus was a within-subjects comparison for the HD group, we noted that the MoCA's range of scores for the control group was more than twice that of the MMSE, again suggesting improved sensitivity to cognitive differences.

The ROC analyses also showed that the MoCA achieved higher sensitivity without sacrificing specificity in many domains relative to the MMSE. For example, the MoCA improved discrimination of spatial abilities by including a visuospatial item (clock drawing) that requires planning abilities. Another somewhat surprising advantage of the MoCA was in the language domain. Despite fewer items relative to the MMSE, the MoCA showed superior discriminability in this HD group with putatively intact language skills. On the other hand, the MMSE was more discriminatory on the orientation domain, likely a result of differential weighting of these items.

To our knowledge, this is one of the first investigations of the MoCA's ability to assess cognitive deficits in patients with HD. Because our selection of subjects with HD focused on those with mild to moderate symptoms, the range of scores represents a potential limitation for the generalizability of these findings to more severely impaired subjects. Furthermore, without additional neuropsychological testing, it is difficult to estimate appropriate cutoffs for patient groups, and further research will be needed to translate these findings into implications for everyday functioning. Nevertheless, our findings are consistent with other studies that examined the ability of these instruments to detect evidence of cognitive impairment in other patient groups (e.g., Parkinson's disease[15] and cerebrovascular disease).[16,17] These findings also support a recent observation by Zadikoff and colleagues[15] that the MMSE fails to adequately sample the executive function/attention domain, with a corresponding loss of sensitivity to disorders like Parkinson's Disease (PD), especially in its early stages. In conclusion, the MoCA may be the preferable screening measure for assessing mild to moderate cognitive impairment in individuals with HD due to its ability to detect subtle deficits in specific cognitive domains associated with the disease.

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Pathological Laughter in Gilles de la Tourette Syndrome: An Unusual Phonic Tic

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Abstract: **Patients with Gilles de la Tourette syndrome (GTS) can display socially inappropriate behaviors as part of their multiform tic phenomenology. Pathological laughter (PL), defined as the presence of episodic and contextually inappropriate outbursts of laughter, has been detailed as a symptom of various psychiatric and neurological conditions. We present a case series of eight subjects diagnosed with GTS who reported PL as part of their tic repertoire. All subjects experienced PL as a simple phonic tic, accompanied by characteristic premonitory urges and significant impairment in social interactions. In addition, all patients presented with multiple tic-related symptoms (mainly self-injurious behaviors and echolalia, n = 7; palilalia, n = 6; coprolalia/mental coprolalia, n = 5), and six patients had comorbid conditions (in particular obsessive-compulsive disorder/behaviors, n = 7; attention-deficit hyperactivity disorder, n = 4). We suggest that the pathophysiological mechanisms underlying the expression of PL as a tic could involve a dissociation between frontostriatal and limbic networks.** © 2010 Movement Disorder Society

Key words: Gilles de la Tourette syndrome; tic phenomenology; pathological laughter; neural correlates

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Tics, the hallmark of Gilles de la Tourette Syndrome (GTS), are highly heterogeneous in character, severity, complexity, and frequency, presenting as sudden involuntary movements (motor tics) and vocalizations (phonic tics).[1] Complex symptoms range from echophenomena to compulsion-like behaviors. Phonic productions illustrate well the phenomenological diversity of tics: brief utterances devoid of linguistic meaning, including throat-clearing and sniffing constitute simple phonic tics, whereas more complex vocalizations including syllables and phrases comprise complex phonic tics.

Nonobscene socially inappropriate behaviors (NOSIB) have also been described in GTS populations.[2] These can take the form of involuntarily insults directed toward individuals, often based on personal aspects such as intelligence and general appearance. Such behaviors are targeted not only, although usually, at a family member or familiar person at home or in a familiar setting such as work or school but also less commonly at a stranger in public settings. It has been suggested that NOSIB are more common in young boys and closely related with attention-deficit hyperactivity disorder and conduct disorder, but not obsessionality.[2] Social impairment is an inevitable byproduct of NOSIB; verbal confrontation, difficulties in schooling and occupation, fistfights, removal from a public place, and legal trouble are noted implications.[1]

It is increasingly recognized that tics in the context of GTS can be unusual in their manifestations, with reports of complex tics characterized by diaphragmatic contractions resulting in pathological air swallowing[3,4] and retching/vomiting.[5] In tabulated form, we report a case series of eight patients diagnosed with GTS who displayed repetitive inappropriate laughter as part of their core clinical presentation. In these instances, the feature of inappropriate laughter represents a previously undocumented simple phonic tic overlapping with the NOSIB spectrum. The lack of reports on laughter as a tic may indicate a rare phenomenon, yet, it may also suggest that this feature of GTS is both unanticipated and underreported by clinicians.

CASE REPORTS

The eight patients described were seen at the Tourette Clinic, National Hospital for Neurology and Neurosurgery, London, United Kingdom (n = 6); the Yale Tic Disorders Clinic, New Haven CT, USA (n = 1), and a demonstration clinic in Cornwall, United Kingdom (n = 1). In each case, a definitive diagnosis of GTS was made through assessment using the National Hospital Interview Schedule (NHIS) for GTS.[6] Diagnosis was made according to DSM-IV-TR criteria[7] and was further corroborated using a specifically designed instrument, the DCI,[8] whilst severity of tic symptoms was assessed using the Yale Global Tic Severity Scale (YGTSS).[9] All patients underwent blood tests (including copper, ceruloplasmin, and acanthocyte titres), structural neuroimaging, and chromosomal analysis for Fragile X to exclude "secondary Tourettism."

Table 1 provides a summary of the clinical characteristics of the eight patients presented. Of note, all patients had tic-related symptoms (full-blown GTS). In addition, 7 of 8 presented with psychiatric comorbidities (GTS-plus).

DISCUSSION

Laughter is a unique vocally communicative behavior that developed before speech; it is an integral constituent of humanity, functioning as a social lubricant, emotional billboard, and arguably holding survival advantage.[10] Physiological laughter involves characteristic facial and respiratory patterns associated with mirth and is elicited by a diversity of stimuli leading to diaphragmatic contractions.[11] On the other hand, pathological laughter (PL) is defined as uncontrolled and unprovoked laughter dissociated from both stimulus and mood, i.e., a dissociation of emotional expression (laughing) from emotional experience (mirth).[12–14]

Various principles have been used to define PL[15,16]; the definition cited most frequently is that of Poeck.[17] According to this definition, PL arises (1) in response to nonspecific stimuli; (2) in the absence of a corresponding change in affect; (3) in the absence of voluntary control of the extent or duration of the episode; and (4) in the absence of a corresponding change in mood lasting beyond the actual laughing.[17] The "laughing tic" may, therefore, be regarded as a form of PL, since it satisfies this set of criteria; however, it is clinically distinct from other neuropathological conditions, discussed below, from which PL classically derives. PL is a clinical phenomenon presenting amidst a range of neuropsychiatric conditions,[18] including epilepsy (gelastic seizures),[19–21] cerebrovascular disease (*fou rire prodromique*),[22–25] brain tumour,[26–29] demyelinating disease,[30,31] and OCD.[32,33]

Broadly, PL may be divided into three categories. In the first, laughter is in keeping with the generally exhilarated state, occurring as part of a global behavior pattern as in mania, schizophrenia, and Alzheimer's disease. Structures in the limbic system and parts of the frontal lobe (i.e., those neuroanatomical structures related to emotional production and regulation) are

TABLE 1. *Clinical characteristics of patients (n = 8) with Gilles de la Tourette syndrome displaying pathological laughter as a tic*

Case (n)	Age (yr)	Sex	DCI (%)	YGTSS (%)	Tic phenomenology (frequency)	Tic phenomenology (character)	Tic phenomenology (complex phenomena and tic-related symptoms)	Laughing-tic characteristics	Comorbid diagnoses	Medications	Treatment response
1	11	M	79	42	39 motor tics 20 vocal tics	Simple motor tics—facial grimacing (frowning; eyebrow raising; blinking; rolling eyes; mouth opening); arm and leg movements (shoulder shrugging) Complex motor phenomena—habitually glancing at watch Simple phonic tics—throat clearing; sniffing; snorting; coughing Complex phonic tics—odd patterns of speech (barely audible muttering; talking to self in different intonations)	Coprolalia, palilalia, echolalia, echopraxia, SIB, OCB	Reflexive—in response to several words (broken glass, crucifixion, all-in-one). Socially inappropriate—deemed to occur in "forbidden" circumstances such as the presence of an injured or distressed individual in the vicinity	ADHD	Haloperidol, Fluoxetine	Fluoxetine controlled reflexive laughing tic, SIB and obsessive-compulsive symptoms
2	14	M	66	57	27 motor tics 8 phonic tics	Simple motor tics—facial grimacing (pursing lips; head nodding) Simple phonic tics—sniffing; making a clicking sound with tongue	Echolalia, echopraxia, SIB	Involuntary noise—preceded by premonitory sensations	ADHD, ODD	Risperidone	Failure to respond to sulpiride; risperidone controlled tics
3	44	F	90	80	21 motor tics 20 phonic tics	Complex motor tics—gyrating and shivering of torso Simple phonic tics—yawning	Coprolalia, mental coprolalia, copropraxia, palilalia, echolalia, SIB, NOSIB, OCB	Involuntary noise—suppressible	ADHD, ODD	Nil	NA
4	29	F	71	26	17 motor tics 10 phonic tics	Simple motor tics—facial grimacing (frowning; mouth opening; blowing); shoulder shrugging Complex motor tics—dystonic movements of upper body including arms; adjusting clothing Simple phonic tics—grunting Complex phonic tics—various vocalizations	Coprolalia, echolalia, SIB	Socially inappropriate—with premonitory urge and tic camouflage (e.g., with a cough or similar action)	OCD	Nil	NA
5	57	M	89	41	9 motor tics 6 phonic tics	Simple motor tics—facial grimacing (frowning; eyebrow raising; excessive blinking; winking; eyes staring); shoulder shrugging; arm swinging; placing hands in mouth Simple phonic tics—grunting; barking; squeaking; noisy breathing; moaning Complex phonic tics—odd pattern of speech (fluctuations in pitch); vocalizing to self	Coprolalia, palilalia, palipraxia, echopraxia, forced touching, SIB, OCB	Involuntary noise—suppressible and associated with premonitory urge	Panic disorder	Sulpiride, Clomipramine	Behavioral symptoms and tics controlled

(*Continued*)

TABLE 1. *(Continued)*

Case (n)	Age (yr)	Sex	DCI (%)	YGTSS (%)	Tic phenomenology (frequency)	Tic phenomenology (character)	Tic phenomenology (complex phenomena and tic-related symptoms)	Laughing-tic characteristics	Comorbid diagnoses	Medications	Treatment response
6	22	M	69	75	47 motor tics 17 phonic tics	Simple motor tics—facial grimacing (frowning; blinking) Complex motor tics—hopping; skipping; air swallowing (insuppressible) causing abdominal distension Simple phonic tics—yawning; barking; snorting Complex phonic tics—barely audible muttering; loudly saying the word "yes"	Mental coprolalia, palilalia, echolalia, forced touching, OCB	Socially inappropriate—insuppressible	Nil	Sulpiride, Paroxetine	Good response to Sulpiride and Paroxetine. Withdrawal of Clomipramine improved air swallowing tic and gastrointestinal symptoms but led to worsening of other motor and phonic tics
7	26	M	74	85	NA	Simple motor tics—intense eye blinking; violent head shaking; finger clicking and tapping; left leg twitching Complex motor tics—orchestrated jaw closing and lip puckering Simple phonic tics—episodic sniffing	Palilalia, echolalia, forced touching, SIB	Reflexive—in response to the word "tree." Distinct in character and louder than patient's usual laughter	OCD, depression, bipolar affective disorder	Lamotrigine	Initially treated with Guanfacine. Laughing tic progressively worsened over time
8	13	M	85	61	68 motor tics	Simple motor tics—facial grimacing; shoulder shrugging Complex motor tics—pirouetting, abnormal gait Simple phonic tics—throat clearing; gasping; wailing; blowing raspberries	Copropraxia, palilalia, echolalia, echopraxia, SIB OCB	Involuntary noise—first phonic tic to present	ADHD	Risperidone, Methylphenidate, Melatonin	Triple treatment provided adequate symptomatic control

YGTSS, Yale Global Tic Severity Scale; DCI, Diagnostic Confidence Index; SIB, self-injurious behaviors; OCB, obsessive-compulsive behaviors; NOSIB, nonobscene socially inappropriate behaviors; ADHD, attention-deficit hyperactivity disorder; ODD, oppositional defiant disorder; OCD, obsessive-compulsive disorder; NA, not available.

implicated. Within the second category, individuals experience involuntary outbursts of explosive laughter often accompanied by autonomic disturbances in heart rate, vasomotor, and sphincter control. This encompasses neurodegenerative conditions such as amyotrophic lateral sclerosis, multiple sclerosis, cerebrovascular accidents, and brain injury. Pathological crying can coexist. Diffuse regions of the brain are implicated, from frontal and temporal regions as well as pyramidal tracts to the ventral mesencephalon, cerebellum, and pons. Anatomical lesions generate disinhibition of laughter generating-circuits resulting in an inability to modulate or inhibit laughter.[11,34,35] Parkinson's disease features within this category. The subthalamic nucleus (STN) has been noted to be the most beneficial site in deep brain stimulation (DBS) for generating an antiparkinsonism effect.[36] The three principal constituents of the cortical-basal ganglia-cortical circuits (motor, associative, and limbic) pass through the STN. The medial part of the STN and the adjacent lateral hypothalamus are connected with limbic parts of the basal ganglia; similarly, the lateral STN is connected with motor-related parts of the basal ganglia.[37] Stimulation from an electrode within the sensorimotor STN may propagate to affect motor and nonmotor areas simultaneously. In two patients with medication-refractory Parkinson's disease, acute high amplitude stimulation of the STN produced laughter and merriment.[38] Laughter was accompanied by an elated mood and feeling of amusement but eventually evolved into an uncomfortable irritation due to its inappropriate, almost uncontrollable, and fatiguing nature. As in our cases discussed below, these patients did not laugh constantly but required some form of external stimuli to trigger the bout. It has been shown that the STN, with its sensorimotor, cognitive, and limbic parts, is predominantly involved in motor regulation, but additionally may play a role in psychomotor regulation.[38]

Laughter occurring within the framework of an epileptic seizure constitutes the final category. Gelastic epilepsy defines those seizures in which sudden, paroxysmal bouts of laughter feature as a cardinal symptom. Typically ictal laughter is mechanical and unnatural. Some patients experience the laughter to be accompanied by feelings of mirth and exhilaration,[39,40] conversely, others feel no positive emotions and regard the experience as unpleasant.[41,42] Imaging studies have identified the hypothalamus, temporal lobes, and medial frontal lobe to be implicated.[43]

This communication presents the first report of subjects with GTS experiencing PL as a tic, i.e., a manifestation of the motor (diaphragmatic) concomitant of affective expression, unrelated to emotional disturbances or the effects of psychoactive substances All our patients spontaneously reported the presence of specific premonitory urges preceding the expression of laughter in inappropriate contexts. This tic was invariably described as distressing and socially disabling. Amongst the eight cases, laughter was displayed in three distinct ways.

In three cases, PL was triggered by stimuli that had an emotional valence contrary to the expressed tic, i.e., laughing in response to distress or injury. The patients were aware of the inappropriate context but remained powerless to control the laughter. Laughter in cue with inappropriate situations, with its potentially provocative, insulting nature and high potential for stigmatising patient and family members, is in keeping with NOSIB.[2]

In two cases laughter took form of "reflexive" tics, whereby certain words would trigger the laughing tic. This is consistent with the notion that patients with GTS can be impaired at inhibiting reflexively triggered actions, in turn consistent with views that posit a dysfunction of the neural circuits linking the frontal lobes and the striatum to be the basis of GTS.[1] Most commonly, laughter was experienced as an involuntary noise, typical of a phonic tic—a sudden, rapid vocalization. Accordingly, a premonitory sensation preceded the tic, which in the majority of cases (7 of 8) was actively suppressible. More than 90% of adults[44,45] and 37% of children with GTS[46] report "premonitory sensations," commonly described as an urge, pressure, or itch feeling preceding tic expression.[47,48]

In our case series of patients with mild-to-moderate GTS, the socially inappropriate expression of laughter as a tic parallels the presence of complex tic-related symptoms, comorbid attention-deficit hyperactivity disorder, and repetitive impulsive behaviors, as previously reported with other NOSIB.[2]

Relatively little is known about the neural mechanisms of PL. Physiological laughter is a complex phenomenon that cannot be attributed to a unitary neuroanatomical location, on the contrary, it is dependent on the coordinated activity of various functional networks.[11] Both lesional and stimulation case studies suggest that two main pathways are involved in regulating automatic emotion-related behaviors as in PL: (1) descending pathways from the dorsomedial and dorsolateral prefrontal cortex to the basal ganglia, and (2) limbic and paralimbic networks, modulated by the cerebellum *via* connections through the basis points.[14,49–52] We suggest that the pathophysiological mechanisms underlying the expression of PL as a tic could involve a dissociation between the frontostriatal and limbic networks. This hypothesis is in accordance with converging evidence

showing dysfunctional processing within the ventral striatum and other key structures interconnecting subcortical motor and limbic loops in GTS.[53–55]

Finally, with regard to neurochemical transmission, evidence suggests the involvement of serotonergic and dopaminergic pathways in PL and favorable treatment results have been noted in patients given selective serotonin reuptake inhibitors and tricyclic antidepressants.[14,49] Consistent with previous findings, the combination of dopamine antagonists and serotonergic agents has demonstrated potential in controlling PL in 4 of 5 patients with GTS in our case series.[56]

The cases described in this article detail the possible presence of involuntary laughter as part of the extended GTS phenotype, and previous research on the pathophysiology of PL highlights the presence of shared brain mechanisms with tic generation. Scientific literature remains devoid of any appropriately detailed and consistent nosology considering PL in neuropsychiatric disorders; we offer the inclusion of GTS within larger classification systems.

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Long-Term Effects of Coordinative Training in Degenerative Cerebellar Disease

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Abstract: **Few clinical studies have evaluated physiotherapeutic interventions for patients with degenerative cerebellar disease. In particular, evidence for long-term effects and transfer to activities of daily life is rare. We have recently shown that coordinative training leads to short-term improvements in motor performance. To evaluate long-term benefits and translation to real world function, we here assessed motor performance and achievements in activities of daily life 1 year after a 4 week intensive coordinative training, which was followed by a home training program. Effects were assessed by clinical rating scales, a goal attainment score and quantitative movement analysis. Despite gradual decline of motor performance and gradual increase of ataxia symptoms due to progression of disease after 1 year, improvements in motor performance and achievements in activities of daily life persisted. Thus, also in patients with degenerative cerebellar disease, continuous coordinative training leads to long-term improvements, which translate to real world function.** © 2010 Movement Disorder Society

Key words: cerebellum; cerebellar ataxia; neurorehabilitation; motor control; dynamic balance

Degenerative ataxias lead to progressive unsteadiness of gait with a high risk of falling and severe impairments in daily life.[1–3] As no pharmacologic treatments

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are available, physiotherapeutic training currently presents the only therapy to improve ataxia dysfunctions. Its benefit, however, remains controversial as the cerebellum functions as a primary site for adaptation of limb movements and dynamic regulation of balance, and as cerebellar patients are known to have deficits in motor learning.[4–9] So far, effects of physiotherapeutic interventions in ataxia patients have been assessed only rarely[10–17] and most studies failed to report any data about long-term effects and transfer to daily life activities.[18] Such data, however, are needed to show that improvements in clinical and laboratory tests are not just transient short-term effects but indeed translate to sustained improvements in real world function.[19]

We have recently shown that a 4-week intensive coordinative training leads to short-term improvements in motor performance.[20] Here, we present analyses concerning long-term effects 1 year after intervention with accompanying training according to a homework protocol.

PATIENTS AND METHODS

Patients

We examined 14 patients suffering from degenerative cerebellar disease including 8 patients (C1–C8) with predominant affection of the cerebellum and 6 patients (A1–A6) with predominant afferent ataxia (Table 1). From the short-term study,[20] two patients of the cerebellar group had to be excluded as they developed additional signs of orthostatic and urinary dysfunction, parkinsonism, and pyramidal dysfunction, thus fulfilling the criteria of probable multiple system atrophy of cerebellar type (MSA-C).[21]

All patients were able to walk a distance of 10 m with or without walking aid. All experimental procedures were approved by the local ethics committee. Patients gave written informed consent.

Study Design

We assessed the long-term effectiveness of a 4-week course of intensive coordinative training, followed by 1 year during which the patients were asked to continue exercises at home. To evaluate the long-term effects, we compare the results of three examinations: before training (BT), after 4-week training (AT), and at long-term assessment (LT) after 1 year.

Coordinative Physiotherapy

The physiotherapy program consisted of a 4-week intensive training with three sessions of 1 hour per week. Exercises included the following categories: (1) static balance e.g. standing on one leg; (2) dynamic balance e.g. sidesteps, climbing stairs; (3) whole-body movements to train trunk-limb coordination; (4) steps to prevent falling and falling strategies; (5) movements to treat or prevent contracture (Appendix A).

After the 4-week intervention period, all patients received an individual training schedule and were asked to perform exercises at home for 1 hour each day. All exercises were part of the preceding coordinative training program, but patients were instructed to perform only exercises at home that were safe depending on their respective individual motor skills. Home training was categorized on the basis of interview data, assessing the intensity and the composition of exercises (Table1, Appendix B).

Clinical Scales and Individual Goal Attainment

Primary outcome measure was the scale for the assessment and rating of ataxia (SARA),[22] which has been approved as a valid measure of disease severity in spinocerebellar and idiopathic ataxias[23] as well as in Friedreich's Ataxia.[24] SARA was assessed by a neurologist experienced in ataxia (M.S.). A physiotherapist (S.B.) rated balance-control capacities using the Berg balance score (BBS).[25] In addition, each patient selected a personal goal reflecting an individually important activity of daily life. These goals were determined before training and achievements were rated within a goal attainment score (GAS).[26] A score of "0" reflects function at baseline, "−1" means worse than baseline and "+1" to "+4" indicates different degrees of improvement (Table1, Appendix C).

Quantitative Movement Analysis

Motor performance was evaluated by quantitative movement analysis using a motion capture system (see Ref. 20 for details). We examined gait and a dynamic balance task. For gait, patients were instructed to walk at a self-determined pace. We examined standard gait parameters[27] and a specific measure for temporal variability of intra-limb coordination. This measure vb_τ has been shown to detect temporal abnormalities in intra-limb coordination that are specific for patients with cerebellar dysfunctions.[28,29]

In the dynamic balance task, subjects stood in an upright position with both legs on a treadmill and were warned that the treadmill would be activated in the next few seconds. The treadmill was programmed to run for one second with an acceleration of 6 m/s^2 and a

TABLE 1. *Clinical data of the study participants*

Patient	Age	Age of onset	Gender	Diagnosis	Home training		SARA			GAS-Individually selected goals	GAS	
					Intensity	Demand	BT	AT	LT		AT	LT
C1	55	52	F	IDCA	5/5	4/5	17	13	13	Walking on a narrow path (<50 cm)	4	2
C2	79	76	F	SCA 6	3/5	3/5	13.5	6	8	Walking up a staircase without using a stair-rail	4	4
C3	66	56	M	ADCA	5/5	3/5	15	9	10.5	Reaching the mailbox in a distance of 600 m without using a walking aid	2	0
C4	71	67	M	IDCA	5/5	5/5	13.5	9.5	10	Walking around a table with small distance without swaying	3	3
C5	71	51	F	SCA 6	4/5	2/5	17	13	19	Walking with a trolley over a distance of 50 m	2	0
C6	47	31	M	IDCA	5/5	3/5	14	8.5	13	Walking over a distance of about 300 m without a walking aid or a helping person	4	4
C7	67	43	M	IDCA	3/5	5/5	24.5	19	17.5	Walking over a distance of 50 m with a trolley, without bumping with the feet into it	3	3
C8	69	57	M	SCA 2	5/5	4/5	11.5	8.5	10.5	Walking free on a small staircase (3 steps) in an alternating way with a distance of 1 m to the stair-rail	1	1
ØC	65.6						15.7	10.8	12.6		2.87	2.12
A1	44	34	F	SANDO	3/5	3/5	14	12	13	Walking independently over longer distances (>500 m)	3	4
A2	69	56	M	IDCA with SA	4/5	1/5	23	16.5	22.5	Reducing danger of falling	2	4
A3	40	22	F	SANDO	2/5	4/5	12.5	8	14.5	Walking a distance of 30 m with a full cup without to spill something	1	2
A4	51	31	M	FA	2/5	5/5	19	16	21.5	Walking with a trolley over a distance of 2000m without dropping feet and strong support from the arms	1	-1
A5	69	44	M	FA	5/5	3/5	20	17	21	Walking over a distance of 100 m with a trolley, without bumping with the feet into it	4	3
A6	64	44	F	FA	1/5	1/5	17	14	20.5	Walking with a trolley over a distance of 500m	2	0
ØA	56.1						17.5	13.9	18.8		2.16	2.0
ØAll	61.5						16.5	12.1	15.1		2.57	2.07

Ataxia was clinically assessed using the scale for the assessment and rating of ataxia (SARA) as primary outcome measure at the three time points: BT: Before training, AT: after training and LT: at long-term examination after one year.

In the patient column, "C" indicates individuals with predominantly cerebellar ataxia while "A" indicates patients with afferent ataxia, Ø, denotes average, IDCA, idiopathic cerebellar ataxia; SA, sensory neuropathy; ADCA: autosomal dominant cerebellar ataxia; SCA 6, spinocerebellar ataxia type 6; SCA 2, spinocerebellar ataxia type 2; SANDO, Sensory ataxic neuropathy with dysarthria and ophthalmoparesis caused by mutations in the polymerase gamma gene (POLG);[30] FA, Friedreich's ataxia.

Home training: categorization based on interview data, assessing the intensity and the composition of exercises; maximal score is 5, higher scores mean more demanding exercises or higher intensity respectively (see AppendixB). Goal attainment score (GAS): Personally selected goals of the goal attainment score and the scores obtained after the intervention period (AT) and after one year (LT). Described goals correspond to score 2. Scores range from −1 to 4 (−1 is worse than baseline, 0 is baseline, 1 is less than expected outcome, 2 is expected outcome, 3 is greater than expected outcome, 4 is much greater than expected outcome).

maximal velocity of 0.4 m/s in posterior direction. Subjects were protected from falling by a safety harness and were instructed to compensate the perturbation by anteriorly directed steps (see Ref. 20 for details).

Statistical Analysis

Correlations between training intensity and course of ataxia symptoms (SARA scores) were computed using Spearman rank correlation. Group differences between assessments BT, AT, and LT were confirmed by using a Wilcoxon signed-rank test for pair-wise comparisons. For the latter we report two significance levels: uncorrected ($P < 0.05$*) and Bonferroni-corrected for multiple comparisons ($P < 0.05/3 = 0.016$**).

RESULTS

The SARA score decreased significantly (−4.4 points on average) when comparing pre/post intervention (BT/AT, Wilcoxon signed-rank test: Z: −3.3, P = 0.001**). After 1 year, ataxia deteriorated again (AT/LT; $Z = -2.9$, $P = 0.003$**). However, SARA scores were still significantly better than at baseline for the cerebellar group (BT/LT; $Z = -2.1$, $P = 0.03$*) whereas the afferent group was stable compared to baseline (Fig. 1A,B). Importantly, long-term benefit seems to depend on training: training intensity in coordination exercises (Table1) correlated significantly with differences in SARA scores after 1 year (BT/LT; $r = -0.64$, $P = 0.01$).

Assessments of balance capacities using the BBS showed significantly improved performance for all patients after intervention (BT/AT; $Z = -3.1$, P = 0.003**). Although long-term assessment revealed a significant decrease of capacities (AT/LT; $Z = -2.9$, $P = 0.003$**), average BBS scores were slightly - not significantly - higher after 1 year compared to baseline ($Z = -1.1$, $P = 0.24$, BT: 44.4 ± 8.5; LT: 45.9 ± 8.6).

The goal attainment scores show a substantial retention of training effects for activities of daily life (Table 1): for all patients, the average rating was 2.57 (2 = expected outcome, 3 = greater than expected outcome) after training (AT) and 2.07 after 1 year (LT). For example, patient A3 who was unable to walk 10 m unattended before training (=baseline score, 0) had initially indicated the goal to walk a distance of 30 m with a full cup without spilling something (=expected outcome, +2), as this has been a major problem to her in daily life. At long-term assessment, she was able to walk 30 m and more without spilling something.

Movement analysis revealed partly different results for the two patient subgroups. Only for the cerebellar group, gait velocity was significantly increased after intervention (BT/AT: $Z = -2.7$, $P = 0.007$**), which was not preserved at long-term assessment.

Quantifying the joint coordination variability using the measure vb_τ (see Methods) revealed a reduced temporal variability in intra-limb coordination after training ($Z = -2.29$, $P = 0.022$*) and at long-term assessment ($Z = -1.98$, $P = 0.047$*) for the group of cerebellar patients (Fig. 1E). For the dynamic balance task on the treadmill, cerebellar patients showed decreased body sway after intervention (BT/AT; $Z = 2.29$, P = 0.02*). This implies an improvement in dynamic balance control and the capability to compensate for perturbations, which has strong everyday relevance. However, long-term assessment revealed an increase of body sway (AT/LT, $Z = -1.96$, $P = 0.05$), indicating that improvements did - although still better by trend than baseline - not fully persist after intensive intervention.

DISCUSSION

This study focused on long-term effects of coordinative training for patients with degenerative ataxias. The results revealed a significant reduction of ataxia symptoms measured by the clinical scale SARA for the cerebellar group, which persisted after 1 year.

Thus, despite of a gradual decline of motor performance and gradual increase of ataxia symptoms due to progression of underlying neurodegeneration (and the lower intensity of home training), patient benefits did persist over a long-term period.

The natural disease progression of degenerative cerebellar ataxias is 0.6–2.5 points per year on the SARA scale depending on genotypes (data of the EUROSCA natural history study; Thomas Klockgether, personal communication). This implies that the average improvement achieved by training (−4.9 SARA points after intervention and −3.1 SARA points after 1 year for the cerebellar group) is equivalent to gaining back functional performance of two or more years of disease progression.

The results of the goal attainment score demonstrate that these training effects translate into an improvement in personally important functions of daily life.

For the afferent group, the improvement in ataxia symptoms were less pronounced than in the cerebellar group and did not persist for long-term assessment.

Specific improvements in balance and coordination tasks as well as the differential results for patient subgroups make it unlikely that the observed effects have

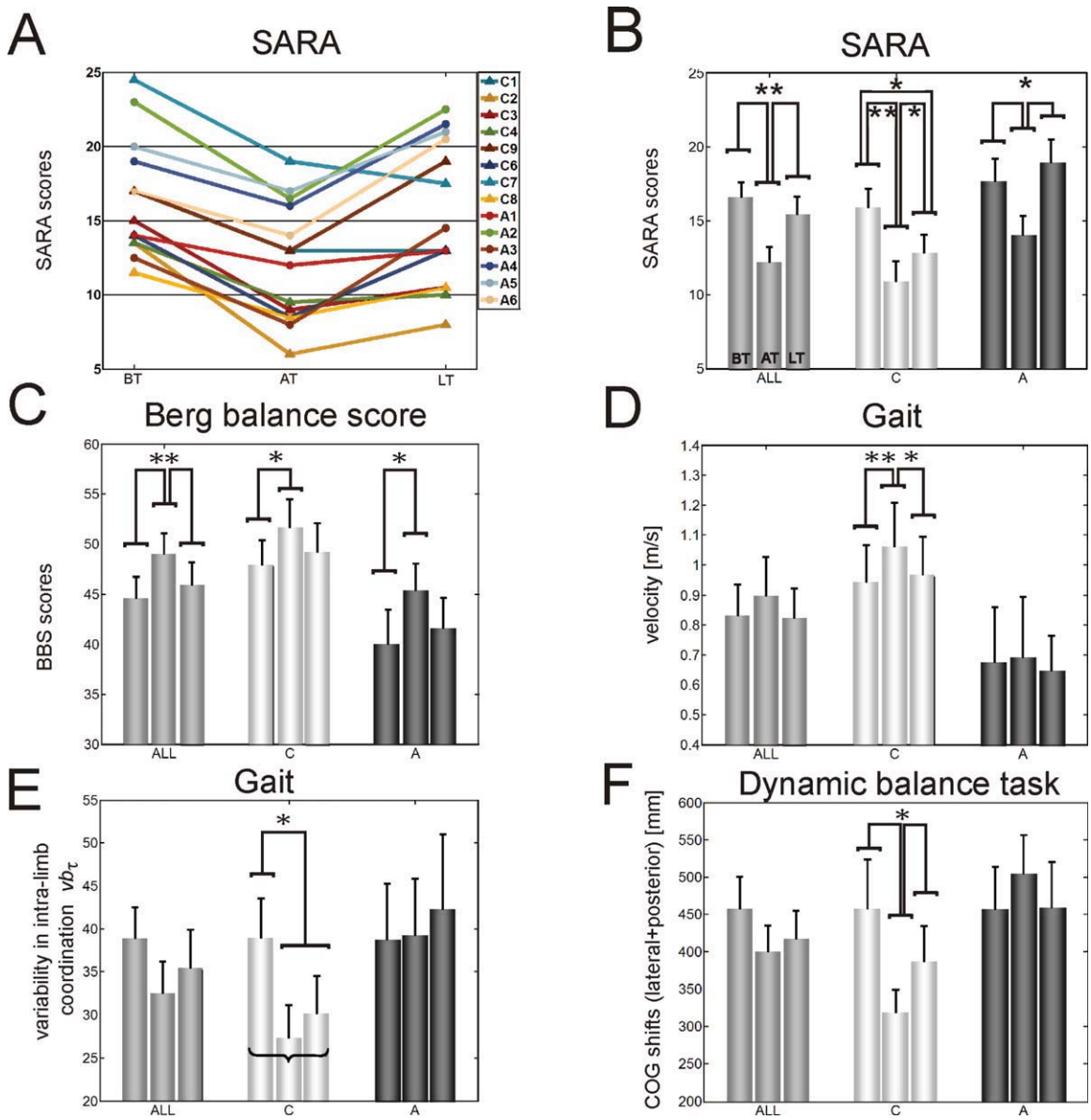

FIG. 1. (A) SARA scores of individual patients at baseline (BT), after 4 weeks of physiotherapy (AT) and at long-term examination (LT) after one-year. "C" indicates the group with predominantly cerebellar ataxia and "A" means patients with afferent ataxia. (B+C) Group comparisons of SARA and BBS scores. (D–F) Group comparisons of measures from quantitative movement analysis. Groups of three bars indicate the examinations BT, AT, and LT. Stars indicate significant differences between examinations (*:$P < 0.05$, **:$P < 0.016$). SARA: Scale for the assessment and rating of ataxia. BBS: Berg Balance score. Error bars denote standard errors. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

been mediated predominantly by nonspecific mechanisms such as improved cardiovascular endurance.

Importantly, long-term outcome seems to be influenced by training intensity at home. Thus, continuous training of whole body coordination exercises seems crucial for stabilizing improvements in patients with ataxia. We therefore recommend professionally administered physiotherapy, which focuses on whole body coordination exercises and is complemented by home training as standard of care in patients with degenerative ataxia.

In conclusion, this study delivers evidence for long-term benefits of coordinative training for such patients. Future studies are required to examine in more detail e.g. necessary training intensities and durations, training strategies for different levels of severity of ataxia and a comparison with other types of interventions.

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APPENDIX A

Details of Physiotherapeutic Exercises

The physiotherapy program consisted of a 4-week course of intensive training with three sessions of 1 hour per week. Exercises included the following categories: (1) static balance e.g. standing on one leg; (2) dynamic balance e.g. sidesteps, climbing stairs; (3) whole-body movements to train trunk-limb coordination; (4) steps to prevent falling and falling strategies; (5) movements to treat or prevent contracture (Table A1).

After the 4-week intervention period, all patients received an individual training schedule and were asked to perform exercises by themselves at home for 1 hour each day. All exercises were part of the preceding coordinative training program, but patients were instructed to perform only exercises at home that were safe depending on their respective individual motor skills to prevent falling and injuries.

TABLE A1. *Details of physiotherapeutic exercises during the intervention period*

Static balance
Standing on one leg
Quadruped standing – stabilize the trunk – lift one arm
Quadruped standing – stabilize the trunk – lift one leg
Quadruped standing – lift one arm and the leg of the other side
Dynamic balance
Kneeling – put one foot in front and back alternately
Kneeling – put one foot to the side and back alternately
Kneeling – put one foot in front – stand up – put one leg back – kneeling alternately
Standing – swing arms, seesaw knees
Standing – step to the side
Standing – step in front
Standing – step back
Standing – cross over step*
Climbing stairs*
Walking over uneven ground*
Whole body movements to train the trunk-limb coordination
Quadruped standing - lift one arm and the leg of the other side – flex arm, leg and trunk – extend arm, leg and trunk alternately
"morning prayer" (Moshe Feldenkrais): kneeling – bend legs, arms and trunk ("package sitting)– extend legs, arms and trunk alternately
Kneeling – sit besides the heel on the right side – kneeling– sit besides the heel on the left side alternately
Steps to prevent falling and falling strategies in order to prevent trauma
Standing – step to the side, step in front, step back
Standing – crossover step in a dynamic alteration*
Standing – the therapist pushes the patient in altered directions – the patient has to react quickly with fall preventing steps+
Standing – bend the trunk and the knees to touch the floor – erect the body alternately*
Standing – bend the trunk and the knees, touch the floor and go down to quadruped standing*
Standing – the therapist pushes the patient – the patient has to react quickly – bend and go to the floor in a controlled manner+
Walking - the therapist pushes the patient – the patient has to react quickly – bend and go to the floor in a controlled manner+
Movements to treat or prevent contracture especially movements of shoulders and spine
Extension of the spine: prone lying, push up the shoulder girdle from prone lying; prone lying on a wedge
Rotation of the spine: supine lying – knees bended – rotate the knees to the right and left side
Flexion of the shoulder: supine lying – lift the arms in the direction of the head

For the homework protocol, some of the exercises were skipped for the more severe patients (label 1). The exercises, in which a therapist is needed (label 2) were skipped for all patients.

APPENDIX B

Assessing the Intensity and the Composition of Homework Exercises

Home training was categorized based on interview data, assessing the intensity and the composition of

TABLE B1. *Categorization of home training*

Intensity	Composition/Demand
1 = only with therapist 2×/week	1 = 0–20%
2 = only with therapist, 2×/week, >30 min p. session	2 = 21–40%
3 = 3×/week, > 30 min. p. session	3 = 41–60%
4 = 5–7×/week, < 20 min. p. session	4 = 61–80%
5 = 7×/week, > 20 min. p. session	5 = 81–100%

Higher scores mean more demanding exercises or higher intensity respectively. The demand of the exercises was categorized based on the degree of exercises requiring dynamic regulation of balance and whole body coordination.

exercises (Table B1). In this categorization we included exercises from ambulant physiotherapy, which was performed by several patients. The demand of the exercises was categorized based on the degree of exercises requiring dynamic regulation of balance and whole body coordination.

APPENDIX C

Goal Attainment Scaling

Goal Attainment Scaling (GAS)[25] is a method for setting personal goals and measuring the degree of goal achievement by creating an individualized point scale (−1,0, 1, 2, 3, 4) of potential outcomes for each activity undertaken. Each scale is created *de novo* starting from the individual skills of the patient at baseline (= score 0) and the expected level of achievement (=score +2) of a particular individual goal. Above and below this level, indicators of under-achievement and over-achievement (i.e., getting not as far as, or farther than expected) were created in order to evaluate the degree of success in achieving the goal. Tables C1 and C2 show individual examples.

TABLE C1. *Personally selected goal of the goal attainment score exemplarily shown for patient C4*

Individual goal patient C4: Walking around a table with small distance without swaying	Score
The patient walks around the table mainly by touching the table	0
The patient can walk around the table without touching the table most of the time	1
The patient can walk around the table without touching the table	2
The patient can walk around the table without touching the table and he is able to look around sometimes	3
The patient can walk around the table without touching the table and he is able to look around the whole time	4

Five levels of goal attainment were defined before the intervention started. After Intervention (AT) and at long-term assessment, the goal attainment is rated. Scores range from −1 to 4 (−1: worse than baseline, 0: baseline, 1: less than expected outcome, 2: expected outcome, 3: greater than expected outcome, 4; much greater than expected outcome).

TABLE C2. *Personally selected goal of the goal attainment score for patient C2*

Individual goal patient C2: Walking up a staircase without using a stair-rail	Score
Patient can walk up 10 steps of a staircase with an alternating foot pattern; without support; with one hand on rail most of the time; patient feels safe	0
Patient can walk up 10 steps of a staircase with an alternating foot pattern; patient walks free without one hand on rail most of the time; 50 cm max. distance to the handrail; patient feels rather unsafe	1
Patient can walk up 10 steps of a staircase with an alternating foot pattern; patient walks free without one hand on rail most of the time; 50 cm max. distance to the handrail; patient feels safe	2
Patient can walk up 10 steps of a staircase with an alternating foot pattern; patient walks free in the middle of the staircase with distance > 1 m to the handrail; patient feels unsafe	3
Patient can walk up 10 steps of a staircase with an alternating foot pattern; patient walks free in the middle of the staircase with distance > 1 m to the handrail; patient feels safe	4

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No Increased Risk of Obstructive Sleep Apnea in Parkinson's Disease

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Abstract: **Pulmonary function abnormalities in Parkinson's disease (PD) might predispose patients to obstructive sleep apnea (OSA) and daytime sleepiness. Fifty-five idiopathic PD patients (mean age = 63.9) underwent three consecutive nights of in-laboratory polysomnography on their usual dopaminergic medications. Sleep apnea severity was compared to published, normative, population-based data from the Sleep Heart Health Study. Demographic and clinical data were compared in patients with and without OSA. The apnea-hyponea index (AHI) was stable across nights in PD patients, and was not different between PD patients and normative controls. Epworth Sleepiness Scale scores, Body Mass Index, and snoring did not correlate with AHI. Severity of OSA is stable across multiple nights in PD patients. Rates of OSA in PD are similar to those seen in the general population. Daytime sleepiness, snoring, and obesity may not be helpful in identifying OSA in PD.** © 2010 Movement Disorder Society

Key words: Parkinson's disease; obstructive sleep apnea; excessive daytime sleepiness

INTRODUCTION

Parkinson's disease (PD) predisposes patients to airway and lung function abnormalities that could increase risk for obstructive sleep apnea (OSA). Upper airway obstruction measured by spirometry occurs in 24–65% of PD patients,[1–3] and may be documented even in patients without respiratory symptoms.[4] This upper airway obstruction may occur as rhythmic oscillation with a 4–8 Hz rate or may occur irregularly as complete occlusion.[4] Complete occlusions are thought to be due to rigidity and hypokinesia affecting the upper airway.[4] Restrictive lung disease is also present

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in PD,[2] and is hypothesized to be due to chest wall rigidity resulting in decreased compliance,[4] autonomic dysfunction,[4] or a side effect of pleuropulmonary-toxic medications (i.e. ergot-derived dopamine agonists).[2] In those patients in whom kyphoscoliosis develops, lung volumes may be reduced.[4] We hypothesized that these pulmonary abnormalities would predispose PD patients to a higher frequency of OSA. Additionally, the early involvement of the autonomic nervous system in PD[5] could predispose patients to OSA. We evaluated whether patients with PD are more likely to have OSA than controls.

Apart from these pathophysiologic considerations, identification of OSA in PD may be important clinically as a cause of potentially treatable symptoms. For example, daytime sleepiness has been identified as a major problem in the day-to-day lives of PD patients.[6] Further, daytime sleepiness may be a prognostic indicator for incident PD,[7] and is thought to reflect both disease and medication effects.[6,8] An additional goal of the current work thus was to examine the association between reported sleepiness and OSA in a PD population.

SUBJECTS AND METHODS

Subjects

Subjects were 55 individuals (mean age = 63.9; SD = 9.1; 45.4% ≥ age 65) with idiopathic PD diagnosed by a neurologist specializing in movement disorders. A convenience sample of subjects was recruited from the movement disorders clinic of our academic medical center regardless of the presence or absence of daytime sleepiness or any sleep symptoms. There were 37 men and 18 women. The mean (SD) duration since PD diagnosis was 5.8 (4.4) years. Mean daily dose of dopamine agonists, measured as pergolide equivalents, was 2.1 (1.7) mg. Mean levodopa daily dosage was 331 (400) mg. Mean body mass index (BMI, kg/m^2) was 26.8 (8.8); 20% had BMI > 30.

Procedures

The study protocol was approved by our Institutional Review Board, and all subjects gave written informed consent before participating. Subjects were studied with in-laboratory polysomnography for three consecutive nights while taking their usual medications. Sleep staging followed conventional criteria. Apneas were scored regardless of the presence or absence of oxygen desaturation or arousal, but hypopneas were only scored if accompanied by at least a 4% oxygen desaturation from baseline.[9] Apnea-hypopnea index (AHI) was computed as apneas plus hypopneas per hour of sleep time. OSA of moderate or greater severity was defined by an AHI ≥ 15. Demographic information including gender, height, and weight was collected on all patients. Each completed a questionnaire, which included an Epworth Sleepiness Scale (ESS),[10] questions about their typical night of sleep (sleep duration, number of awakenings per night, sleep latency, presence of vivid dreams, presence of nightmares, trouble falling asleep, trouble staying asleep, early morning awakenings, snoring, and nocturia), and questions about daytime symptoms related to sleep (hours spent napping, presence of restless legs syndrome symptoms).

Internight reliabilities were calculated between nights 1, 2, and 3 using Spearman correlations and night-to-night differences were tested using Wilcoxon signed-rank tests. To compare rates of OSA in our patients to normative data, we employed previously published results from the very large (n = 6132), population-based Sleep Heart Health Study (SHHS), the overall cohort of which had a mean age 62.9 (SD 11.0).[9,11] This population consisted of middle-aged and older adults sampled from throughout the United States who were of comparable age and gender distribution to our PD population (47 vs. 45% above age 65, 47 vs. 67% male). Subjects were grouped by AHI severity ranges of < 1.5, 1.5–4.9, 5–14.9, 15–29.9, and ≥ 30 and PD patients were compared to normative controls using Chi-square. Relationships between AHI above or below 15/hour and demographic and clinical data were evaluated with *t* tests.

RESULTS

Mean (SD) AHIs for Nights 1, 2, and 3 were 6.3 (9.4), 8.0 (10.6), and 6.9 (9.2) respectively. Spearman correlation showed high correlation across the three nights, with correlation coefficients of 0.76 for nights 1 and 2, 0.61 for nights 1 and 3, and 0.76 for nights 2 and 3, all $P < 0.0001$. Pairwise comparisons of AHI between nights were all nonsignificant. Because of the relative stability of these measures across nights, 3-night data were averaged for all subsequent analyses. Table 1 summarizes comparisons between data from our patients and published normative data (SHHS) on breathing disturbance in sleep. These data clearly indicate that our PD patients had no more sleep apnea than the control population ($P = 0.53$ when using a single cut point of AHI = 15 to define the presence of apnea, $P = 0.87$ when stratifying AHI into five severity categories, as in Table 1).

TABLE 1. *Frequency of sleep apnea of varying severity in PD patients and controls*

	AHI < 1.5	AHI 1.5–4.9	AHI 5–14.9	AHI 15-29.9	AHI ≥ 30
PD patients	18 (32.7%)	13 (23.6%)	16 (29.1%)	6 (10.9%)	2 (3.6%)
SHHS controls	1691 (27.6%)	1598 (26.1%)	1751 (28.6%)	719 (11.7%)	373 (6.1%)

$P = 0.87$.

Data represent the total number of subjects in each category of AHI severity, followed by percentage of total number of subjects within the group (patients or controls). Data for controls from.[9]

Patients with an AHI ≥ 15 were more likely to be male ($P = 0.03$) and to have a shorter duration of PD diagnosis ($P = 0.048$). Those with AHI ≥ 15 had a nonsignificant trend toward being older ($P = 0.10$). BMI, ESS, levodopa daily dosage, dopamine agonist daily dosage, and other surveyed clinical features did not predict AHI.

DISCUSSION

Given the known upper airway and lung function abnormalities in PD, we expected an increased frequency of OSA relative to a control population, but our PD patients had similar rates of OSA to those seen in SHHS. A few previous polysomnographic studies of PD patients have reported on OSA, and these found rates of OSA of at least moderate severity (AHI > 15) of 20–27%;[12–16] using an AHI of greater than 10, another study found a higher prevalence of 56% in PD.[17] These rates are somewhat higher than what we saw here, but some of these studies may have used patients who were selected because of excessive daytime sleepiness or who were referred for polysomnography for clinical purposes, so some bias might exist to overestimate the prevalence of OSA in PD. In a study using hospitalized patients without PD as controls, Cochen de Cock and colleagues actually found a lower rate of OSA in PD than in controls, with 21% of PD patients showing moderate or severe OSA.[14] Taken together, these results suggest that OSA is unlikely to be more common in PD than in the general population. Our reporting of 165 total nights of sleep in 55 patients makes this one of the largest series to date to investigate OSA in PD. Further, the use of multiple nights within patients shows that sleep apnea severity is stable from night to night in this patient population.

Of the clinical and demographic features measured in our population, only male gender and shorter duration of PD were associated with sleep apnea. Factors commonly used to screen patients for potential sleep apnea before a diagnostic study, such as snoring, daytime sleepiness, and elevated BMI, were not predictive of sleep apnea in these PD patients. The absence of a relationship between ESS and OSA in our patients is particulary noteworthy. The frequent presence of daytime sleepiness in PD, whether a component of the disease itself or the medications used to treat it,[12] could weaken sleepiness as a relevant predictor of OSA in this population.

One limitation of our study is that we employed previously published data on normative levels of sleep apnea, rather than controls established within our laboratory. Although the latter are sometimes preferred, the population-based, age-comparable data on sleep apnea prevalence established by the SHHS, which encompasses a wide range of socioeconomic subpopulations from different geographic regions of the United States, may actually provide enhanced generalizability of the data on sleep apnea across a wide range of participants that could not be available at any single site. Our data do not argue against the fact that some patients with idiopathic PD or other parkinsonian conditions[18] may develop OSA and may benefit from treatment, but they do suggest that for idiopathic PD patients as a group, OSA does not represent a condition with higher than expected prevalence relative to a population of comparable demographics.

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Psychiatric Symptoms Associated with Focal Hand Dystonia

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Abstract: **Myoclonus dystonia and idiopathic dystonia are associated with a greater frequency of obsessive compulsive disorder (OCD) and major depression. We investigated the frequency of OCD in 39 patients with primary focal hand dystonia (FHD) using a semistructured interview. OCD and subsyndromal OCD was diagnosed in 5 of 39 (12.82%) patients with FHD, whereas OCD occurs in 2.3% of the general population. Recurrent depression occurred in (7 of 39) 17.95% of patients with FHD along with a family history of depression in (16 of 39) 41.02%. Overlapping mechanisms manifesting as FHD may also predispose to OC symptoms and likely implicates a common striatal dysfunction.** © 2010 Movement Disorder Society

Key words: obsessive compulsive disorder; depression; dystonia; striatum; obsession; compulsion

Focal hand dystonia (FHD) is characterized by task-specific sustained muscle contraction that leads to impaired use. Movement disorders such as Parkinson's disease, Tourette's syndrome, or Huntington's chorea are commonly associated with comorbid neuropsychiatric symptoms related to the underlying neurobiology of the movement disorder. More severe forms of dystonia have been associated with obsessive compulsive disorder (OCD). For instance, myoclonus dystonia and DYT 11[1,2] have been associated with a greater frequency of OCD. OCD had also been reported to be more frequent in idiopathic dystonia patients and their family mem-

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bers,[3] although no association with DYT1[4] has been observed. Blepharospasm has also been associated with a greater number of obsessive compulsive symptoms.[5] In a study of 86 patients with primary cervical dystonia or blepharospasm, the odds ratio of having OCD was 8.4 compared with their control group.[6]

OCD is a neuropsychiatric disorder characterized by obsessions or compulsions reflecting frontostriatal dysfunction. Obsessions are recurrent uncontrollable thoughts or impulses associated with anxiety or distress. Compulsions are repetitive behaviors or mental acts that are performed in response to an obsession or set of rules and aimed to reduce distress. For the diagnosis of the disorder of OCD, the symptoms must be associated with marked distress, occur more than 1 hour per day, or significantly interfere with social or occupational functioning.[7]

FHD has been associated with both striatal and cortical pathology with mechanisms of decreased inhibition, greater plasticity, and sensory impairments.[8] Pathology affecting the basal ganglia includes disorganized putaminal somatotopy,[9] larger putaminal volume,[10] and hyperechogenicity in the lenticular nucleus.[11] OCD is also characterized by frontostriatal dysfunction particularly implicating structural and functional abnormalities of the orbitofrontal-striatal circuitry along with abnormalities in tasks associated with striatal function such as implicit sequence learning, procedural learning, and response reversal.[12] In this study, we investigated the relationship between OCD and FHD by assessing the frequency of subsyndromal and syndromal OCD in patients with FHD.

PATIENTS AND METHODS

Patients with FHD were recruited from a convenience sample of patients who had been seen at the Human Motor Control Section (HMCS) clinic or at the Botox clinic at the National Institute of Neurological Disorders and Stroke, National Institutes of Health (NIH). Over the 6-month period of the study, subjects who were being seen at the Botox clinic were contacted prior to their appointment for either a same day assessment or to make a new appointment. Newly diagnosed subjects on the HMCS database (diagnosed within the last 2 years) were also contacted. Inclusion criteria included patients >19 years of age with FHD and no other serious neurological or medical illnesses. The study was approved by the NIH Institutional Review Board and patients signed informed consent.

Subjects underwent a semistructured interview by a psychiatrist or psychologist for the assessment of psychiatric disorders (Structured Clinical Interview for the diagnosis of DSM-IV Axis I disorders). Subsyndromal OCD was identified if patients fulfilled all criteria for OCD except for the criterion of functional impairment. All identified cases were reviewed with an expert in OCD for diagnostic confirmation. Patients were assessed with the clinician-rated Yale-Brown Obsessive Compulsive Scale (Y-BOCS), a 10-item scale in which each item is rated from 0 to 40.[13] The scale assessed the amount of time spent and the impairment, distress and degree of resistance, and control over the obsessions and compulsions. A score of 0 to 7 is subclinical, 8 to 15 mild, 16 to 23 moderate, 24 to 31 severe, and 32 to 40 extreme. Family psychiatric history was questioned based on any known diagnoses of depression, alcohol abuse, bipolar disorder, or schizophrenia that interfered with function in siblings, parents, or grandparents but the diagnosis was not confirmed with diagnostic criteria or assessment of the family member. Subjects also completed the Beck Depression Inventory, the Beck Anxiety Inventory, and the Sheehan Disability Scale.

RESULTS

Forty patients with FHD were assessed [mean age 48.1 (SD 10.3), 14 women, FHD duration mean 12.14 (SD 9.12) years] from 68 patients contacted. Twenty-eight patients did not enter the study because of lack of interest, lack of time, or inability to schedule an appointment that suited their schedule as the majority of patients were working. Twenty-seven patients had dystonia secondary to writing, 12 patients had dystonia secondary to use of a musical instrument, and 1 patient had dystonia secondary to typing. Thirty-nine of forty patients had primary dystonia and 1 patient had dystonia secondary to head trauma with secondary FHD and focal epilepsy. This patient's family history was positive for epilepsy but negative for dystonia. Ten of forty patients had a family history (including cousins) positive for either tremor or dystonia. At the time the study was conducted, there was no indication for genetic testing. Six of forty patients were on an antidepressant for depression, anxiety, or pain and 6 of 40 were on an anticonvulsant for pain with one for a seizure disorder. Twenty of forty were receiving regular Botox treatment for their FHD symptoms.

In the following, we base the analysis on patients with primary FHD (N = 39). Lifetime OCD was identified in 4 of 39 (10.25%) with current OCD in 3 of 39 and subsyndromal OCD in 1 of 39 (2.56%) with symptoms preceding the dystonia onset. Six of thirty-nine (15.38%) patients had generalized anxiety disorder; 2 of 39 (5.13%) had simple phobia and 3 of 39 (7.69%) had social phobia with fear of public speaking that preceded

the onset of dystonia; and 1 of 39 (2.56%) had panic disorder. The diagnoses of anxiety disorders overlapped with a total diagnosis in 10 of 39 (25.64%). A lifetime history of major depression was identified in 10 of 39 (25.60%) with recurrent major depression in 7 of 39 (17.95%), current major depression in 3 of 39 (7.69%), and current dysthymia in 2 of 39 (5.13%). In total, 13 of 39 (33.33%) patients had a previous or current history of a depressive disorder. All patients with OCD and subsyndromal OCD had comorbid depression. One patient had a diagnosis of a substance use disorder. There were no diagnoses of psychotic disorders, bipolar affective disorder, or post-traumatic stress disorder. There was a family history of depression in 16 of 39 (41.02%), "nervous breakdowns" in an additional 3 of 39 (7.69%), and alcohol use disorders 8 of 39 (20.51%). In the following, we only assess differences between OCD and non-OCD in primary FHD and do not include subsyndromal OCD. As expected, the Y-BOCS total score was greater in patients with OCD [17.25 (SD 5.40)] than without [0.96 (SD 2.4)] ($t = 7.95$, $df = 36$, $P < 0.0001$). BAI scores were also higher in the patients with OCD [11.25 (SD 5.90)] compared with those without [4.75 (SD 5.01)] ($t = 2.41$, $df = 36$, $P = 0.02$). There was a trend toward higher BDI scores in patients with OCD [11.25 (SD 6.70)] compared with those without [5.75 (SD 5.43)] ($t = 1.87$, $df = 36$, $P = 0.07$). There were no differences in Sheehan Disability Scale scores in patients with OCD [8.21 (SD 4.29)] compared with those without [7.10 (SD 7.01)] ($t = 0.31$, $df = 36$, $P = 0.77$).

DISCUSSION

In this study, we demonstrate a frequency of OCD of 10.25% and subsyndromal OCD of 2.56% in patients with primary FHD. This frequency contrasts with the lifetime prevalence of 2.3% of OCD in the general population.[14] Our study results dovetail with previous reports of elevated frequency of OCD in patients with more severe forms of dystonia such as idiopathic dystonia and myoclonus dystonia.[1,3,6] The lifetime prevalence of major depression in primary FHD was 25.60%, recurrent major depression was 17.95%, and a family history of depression in immediate relatives was 41.02% in FHD. These rates contrast with the lifetime prevalence of major depression in the general population of 17%.[15] Recurrent major depression is associated with DYT1 with a similar rate of expression in manifesting carriers (13.5%) as nonmanifesting carriers (13.3%) when compared with noncarriers (4.6%) (odds ratio of development of OCD in carriers versus noncarriers = 3.04). Although we did not intend to focus on other psychiatric disorders, recurrent major depression along with a family history of depression may be similarly elevated consistent with other reported studies of an association between idiopathic dystonia and DYT1 with recurrent major depression.[16] We caution that this is a small sample size without a control group and more extensive studies with a larger population along with more systematic assessment of family members would be necessary. Our study suggests overlaps in the pathophysiology of OC symptoms and FHD likely implicating a common striatal dysfunction. The pathophysiology may be related to a similar underlying genetic diathesis or the neurobiology of FHD may affect similar striatal regions to that of OCD. These observations are convergent with the greater comorbidity of psychiatric disorders observed in patients with other movement disorders.

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