Trihexyphenidyl for Acute Life-Threatening Episodes Due to a Dystonic Movement Disorder in Rett Syndrome

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Abstract: In Rett syndrome (RS), acute life-threatening episodes (ALTEs) are usually attributed to epilepsy or autonomic dysfunction but they can represent a movement disorder (MD). We describe three girls with RS who experienced ALTEs from an early age. These were initially considered epileptic until video-EEG in Patients 1 and 3 revealed their non-epileptic nature. A primary dystonic mechanism was suspected and Patients 1 and 2 were treated with Trihexyphenidyl with significantly reduced frequency of the ALTEs. Patient 3 died before Trihexyphenidyl was tried. Trihexyphenidyl in RS patients with similar presentations can modify the dystonia and prevent ALTEs. © 2010 Movement Disorder Society

Key words: Rett syndrome; dystonia; epilepsy; acute life threatening episodes; trihexyphenidyl

INTRODUCTION

Rett syndrome (RS) is a neurodevelopmental disorder which, in the majority of cases, is caused by mutations in the MECP2 gene and mainly affects females. The hallmark of the disease is the intense stereotypic hand movements, which coincide with or even precede the loss of purposeful hand movements. Other abnormal movements, including dystonia, are also described but the whole spectrum of movement disorders in RS is less well documented. Epilepsy, on the other hand, is recognized as an important problem in patients with RS, however, many events classified as seizures in RS may be nonepileptic in origin. As autonomic dysfunction along with patterns of abnormal breathing in the awake state are also observed in RS, many of the clinical “seizures” are considered to be a manifestation of this dysfunction. However, episodes accompanied by respiratory compromise or acute life-threatening episodes (ALTEs) can also represent a dystonic movement disorder.

We report three girls with RS and confirmed MECP2 mutations who presented with longstanding histories of “seizures” and ALTEs. We focus on the description of their episodes and their treatment with the aim to differentiate between the movement disorder and other processes in patients with RS.

Case Histories

Patient 1, aged 13 years, started experiencing paroxysmal ALTEs, which were thought to be epileptic seizures at age 4 years. These were initially well controlled on two antiepileptic drugs (AEDs) but recurred at age 7 years with increased severity despite addition of a third AED. The episodes were characterized by grimming, staring, tonic stiffening of arms, facial redness, and jaw stiffening. As the episode progressed, cyanosis occurred, but if posturing was recognized early, soothing with voice and touch could prevent progression. A typical episode was captured during video-EEG telemetry (Video and Fig. 1) at 12 years. The episode was not associated with any epileptiform activity on EEG.
thus demonstrating its nonepileptic nature. EEG attenuation was noted during the event secondary to hypoxia (Fig. 1) while the interictal EEG was abnormal (Fig. 2). Further assessment of the patient revealed a background dystonic movement disorder with bilateral spontaneous extensor plantars (striatal toe), which flexed on eliciting the Babinski manoeuvre. Trihexyphenidyl (THP) was commenced, which led to improvement of the movement disorder and increased alertness while the patient stopped experiencing ALTEs.

Patient 2, aged 9 years, started having generalized tonic-clonic seizures at age 2 years. At age 3 years, different episodes were noted, described as staring, tonic extension of arms followed by apnoea and cyanosis. Routine EEG at the time showed some interictal parietal spikes but no episodes were captured. Over the course of the next few years she received three AEDs without effect. Her ALTEs were suspected to be dystonic in nature and she was thus given THP which resulted in cessation of the dystonic episodes and increased alertness.

Patient 3, who died at the age of 20, started having ALTEs at age 4 years. These were characterized by staring associated with tonic extension and shaking of head and limbs and were followed by apnoea and cyanosis. The episodes could be occasionally modified by head positioning. Intercital EEG was abnormal and she was treated with three different AEDs over the next years without any effect. Although after some time, her ALTEs were thought to be nonepileptic, they continued being managed with AEDs especially in emer-

![FIG. 1. EEG/ECG/EMG recording on Patient 1 corresponding to Video. A: Arrow, onset of muscle artefact corresponding with onset of ALTE; double arrow, onset of secondary ECG changes (QRS amplitude reduction, relative bradycardia); (a) grimaces, tongue out; (b) leans forward, gasping noise; (c) head shaking, still gasping. B: arrow, onset of EEG attenuation secondary to hypoxia; (d) falls back onto bed; (e) arms raised; (f) still gasping. C: (g) doctor points to colour change (cyanosis).]
gency situations. Video-EEG telemetry at the age of 16 years confirmed the nonepileptic nature of these events. Additionally, she was noted to have a background dystonic movement disorder with scoliosis. Different antidystonic drugs were used including baclofen, tizanidine, gabapentin, and benzodiazepines with only partial response of her dystonia but she unfortunately died of respiratory complications before THP was tried.

DISCUSSION

We have described three girls with RS who all had ALTEs from an early age. The episodes were very similar in all girls, consisting of dystonic posturing with subsequent respiratory compromise. These had been thought to represent epileptic seizures until prolonged Video-EEG confirmed their nonepileptic nature in two of the three patients (Patients 1 and 3). Two of the girls (Patients 1 and 2) responded well to treatment with THP while Patient 3 unfortunately died before treatment could be commenced.

Dystonia, although a common feature, is not always well recognized in girls with RS. In the first analysis of movement disorders in patients with RS, approximately 60% manifested some sort of dystonic movements. Similar results were recently reported among MECP2 positive patients and genotype-phenotype correlation was attempted with dystonia being more frequent in patients with truncating mutations. Furthermore, other movement disorders, like bruxism and oculogyric crises and importantly scoliosis, a common feature of RS, are thought to represent forms of focal dystonia. All our patients presented with episodes of dystonic posturing from an early age. Their episodes consisted of grimacing, tongue protrusion, staring, and tonic stiffening of both arms followed by jaw stiffening, apnoea and cyanosis, most likely as a result of laryngeal dystonia. Patients 1 and 3 also demonstrated a background dystonic movement disorder. Although dystonia in RS is believed to become more common with age, dystonic movements have been reported early in the course of the disease and even before developmental regression occurs. A role for neurotransmitter disturbances in the pathogenesis of neurological symptoms such as the movement and sleep disorders in RS has been postulated but results from CSF studies have been contradictory. A reduction of dopamine and norepinephrine metabolites in the substantia nigra has, however, been shown in neuropathological
Involvement of the autonomic nervous system in RS is suggested by clinical observations including the frequent occurrence of cold and blue lower extremities, chronic constipation, and dilated pupils and supported by autonomic monitoring studies describing low cardiovascular parasympathetic tone in patients with RS. Breathing dysrhythmia is indeed considered by most authors as a sign of brainstem dysfunction and neurotransmitter dysregulation; however, patients only exhibit these breathing disorders when awake suggesting involvement of higher centres and favoring the alternative concept that they may be a type of stereotypy or a dystonia. Furthermore, it is well known that all dystonias, tics and choreas are abolished by sleep. Our Video and simultaneous EEG/ECG/EMG monitoring (Figure 1) on Patient 1 suggests that chronologically the episode begins with the occurrence of muscle artefact on the EEG and with EMG changes, which correspond with the onset of the ALTE on the Video (grimace, tongue protrusion); secondary ECG changes including reduction in QRS amplitude and relative bradycardia follow thus pointing toward a primary dystonic rather than autonomic onset. This is further supported by an excellent response of the ALTEs to treatment with THP in Patients 1 and 2 as well as the background dystonic movement disorder observed in Patients 1 and 3.

The events experienced by our patients were long thought to be epileptic seizures. This was supported by certain clinical characteristics of the events, including the staring and stiffening with associated respiratory compromise; it was also apparently supported by the fact that they all had abnormal interictal EEGs. Patients 1 (Video) and 3 eventually had video-EEG telemetry which clearly demonstrated the nonepileptic nature of their events; hypoxia-induced EEG attenuation was noted during the event in Patient 1. Epileptic seizures occur in RS patients and AEDs are often prescribed. Additionally, interictal EEG is almost invariably abnormal in patients with RS after 2 years of age although there is no electroencephalographic pattern considered pathognomonic for RS. Many events classified as seizures in patients with RS are nonepileptic in origin and this has been confirmed by studies using video-EEG monitoring. Moreover, a number of RS patients are considered to have intractable seizures despite AED polytherapy and this was indeed the case with our patients for many years before the nonepileptic nature of their events was confirmed. Video-EEG recording for characterisation of clinical events in RS is essential for accurate diagnosis of ALTEs and in order to avoid unnecessary polytherapy.

THP is one of the few validated treatments and perhaps the most commonly used medication for dystonia. Children have long been known to respond more favorably and with fewer adverse effects than adults to treatment with THP. The mechanism of THP action for treatment of dystonia is not known although it is presumed to be associated with central anticholinergic effects. The use of THP for treatment of dystonia and specifically for ALTEs in patients with RS has not, to our knowledge, been previously reported. Other drugs, such as the serotonin agonist buspirone, have been suggested for treatment of “apneusis” in RS but their use is not widespread.

In conclusion, episodes of posturing followed by respiratory compromise can be mistaken as seizures or autonomic dysfunction in RS leading to increased morbidity and mortality if untreated. The clinical presentation, video-EEG findings and response to THP support a primary dystonic mechanism. A trial of THP in RS patients with similar presentations can modify the dystonia leading to reduction in unnecessary use of AEDs, improve quality of life, and prevent respiratory crises presenting as ALTEs.

LEGEND TO THE VIDEO

The video demonstrates Patient 1 having an acute life-threatening episode (ALTE). The recording corresponds with the EEG/ECG/EMG recording on Figure 1 and was taken during video-EEG telemetry.


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REFERENCES


Abstract: Musician’s dystonia (MD) is a task-specific movement disorder with a loss of voluntary motor control in highly trained movements. Defective inhibition on different levels of the central nervous system is involved in its pathophysiology. Cathodal transcranial direct current stimulation (ctDCS) diminishes excitability of the motor cortex and improves performance in overlearned tasks in healthy subjects. The aim of this study was to investigate whether ctDCS improves fine motor control in MD. Professional guitarists (n = 10) with MD played exercises before, directly after ctDCS, and 60 min after ctDCS. ctDCS (2 mA, 20 min) was applied on the primary motor cortex contralateral to the affected hand. Guitar exercises were video-documented and symptoms were evaluated by three independent experts. No beneficial effect of ctDCS on fine motor control was found for the entire group. However, motor control of one guitarist improved after stimulation. This patient suffered from arm dystonia, whereas the other guitarists suffered from hand dystonia. © 2010 Movement Disorder Society

Key words: focal dystonia; musician’s cramp; transcranial direct current stimulation; neuroplasticity

Focal dystonia in musicians (MD) is a task-specific movement disorder, which presents itself as a loss of voluntary motor control of extensively trained movements while playing a musical instrument. Deficient inhibition at different levels of the CNS is involved in its pathophysiology. Transcranial direct current stimu-
lation (tDCS) modulates cortical excitability of the motor cortex. Cathodal (ct)DCS decreases cortical excitability and hereby may facilitate fine motor control considering the specific pathophysiology of reduced cortical inhibition in MD. Moreover, ctDCS applied over V5 was reported to improve performance in overlearned visuomotor tracking tasks in healthy subjects, probably due to an enhanced signal-to-noise ratio.

The aim of this placebo-controlled and double-blinded study was to investigate whether single-session ctDCS of the primary motor cortex facilitates fine motor control in a group of professional guitarists with MD via reducing motor cortex excitability.

**METHODS**

**Participants**

A group of 10 professional guitarists (all men) suffering from MD participated in the study (mean age: 48.8 ± 6.4 years). Task-related dystonia was diagnosed in our out-patient clinic and presented itself in the typical manner as painless cramping of one or more fingers of the right hand while playing the guitar. One guitarist suffered also from cramping of the right forearm with stiffening of the wrist. Mean duration of MD was 8.7 years (range: 6 months–26 years), severity varied between patients. Patients were not pharmacologically treated for MD during the time of the study. Six guitarists had received botulinum toxin in their past history of MD. One patient received a botulinum toxin injection 5 weeks before participating; however, the effect concerning weakness and motor improvement had completely worn off at the time of the experiments. In all other cases, there was at least a time interval of 8 weeks between injection and experiments of the study.

Patients were informed about all aspects of the experiment and signed an informed consent form. The study was approved by local ethics committee, and we conform to the Declaration of Helsinki.

**Stimulation**

Cathodal direct current stimulation was induced through water-soaked sponge electrodes (surface 35 cm²) and delivered by a battery-driven, constant current stimulator (eldith GmbH, Ilmenau, Germany). The stimulating electrode was placed over the left primary motor cortex (C3 according to the international 10–20 system), and the reference electrode was placed over the right supraorbital area. As the study was placebo-controlled and double-blinded, tDCS was operated by an independent assistant. Current strength was 2 mA (20 min) for the active condition and 0.2 mA for the placebo condition (20 seconds). Both sessions were separated by at least 1 week. Active condition and placebo condition were conducted in balanced order.

**Assessment of Fine Motor Control**

Patients played 14 guitar-specific exercises before, directly after ctDCS, and 60 min after tDCS. The exercises contained scales, arpeggios, and chords. Movements of the affected hand were recorded with a video camera. Video segments were arranged randomly with respect to condition and time. Three independent experts evaluated symptoms of MD in a standardized video rating procedure. One of the experts was neurologist and expert in musician’s movement disorders, and the others were guitar teachers.

Evaluation of symptoms was based on the following criteria: Overall impression, temporal evenness, constancy in loudness, sound quality, abnormal gross movements, and one scale of the Arm Dystonia Dis-

<table>
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<th>Evaluation criterion</th>
<th>ctDCS</th>
<th>Placebo</th>
<th>ctDCS</th>
<th>Placebo</th>
<th>ctDCS</th>
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<td>Overall impression</td>
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<td>0.56</td>
<td>0.92</td>
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<td>0.79</td>
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<tr>
<td>Quality of sound</td>
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<td>0.74</td>
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<td>ADDS</td>
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<tr>
<td>Abnormal gross motor movements</td>
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<td>0.96</td>
<td>0.93</td>
<td>0.96</td>
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<td>FAM: dystonic flexions</td>
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<td>FAM: compensatory extensions</td>
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<td>0.81</td>
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**TABLE 1. Intraclass correlations (ICC) for each evaluation criterion, time, and condition**

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ability Scale\textsuperscript{5} (ADDS). The experts also filled in the Frequency of Abnormal Movements Scale\textsuperscript{6} (FAM) counting flexions and compensatory finger movements. This scale was originally developed for pianists and was slightly modified. Except for the FAM scale, all criteria were evaluated with Likert scales (with a range of 0–3 similar to the ADDS: 0 = no difficulty, 1 = mild difficulties, 2 = moderate difficulties, and 3 = marked difficulties). The experts received a careful coaching of the rating process by the authors. Additionally, guitarists gave a self-report of their perceived motor abilities in percent for each exercise before and after ctDCS.

### Statistical Analysis

Mean values of expert ratings were calculated for the 14 exercises played at each time point for every guitarist and each criterion. All criteria were assessed for inter-rater reliability using intraclass correlation coefficients. As inter-rater reliabilities for all categories were good (Table 1), mean values of the expert ratings were used for further analysis of each criterion.\textsuperscript{7}

Two-factor analyses of variance (general linear model) with repeated measurements for experimental condition and for time were performed on each evaluation criterion. The experimental condition factor consisted of two levels: ctDCS and placebo-tDCS. The factor of time consisted of three levels: guitar playing before, directly after tDCS, and 60 min after tDCS.

The alpha level was set at 0.05. Data analysis was performed with SPSS 16 (SPSS, Chicago, IL). Additionally, to group statistics, data were analyzed on a single-patient level.

### RESULTS

Inter-rater reliability of the video rating process was tested with intraclass correlations for each criterion at each time point of measurement (Table 1). The highest inter-rater reliability was calculated for the criterion “overall impression” (ICC = 0.97), and the lowest was calculated for “constancy in loudness” (ICC = 0.56).

Results of two-factor analyses of variance with regard to the factors time, condition, and interaction factors are given in Table 2. Expert rating before active condition and before placebo condition did not differ between conditions. There was no statistically significant main effect of both factors for any criterion. No statistically significant interaction between condition and time was found. These results indicate a stable standard of playing during the experiment for the group of guitarists. Expert rating of the “overall impression” is exemplified in Figure 1A. In none of the seven criteria, expert rating showed a tendency for improvement or deterioration after ctDCS.

Analysis of self-reports by the guitarists did not reveal improved perceived motor control after ctDCS for the entire group. However, the same guitarist benefiting from ctDCS according to the expert rating also reported a better perceived motor control after both ctDCS and placebo-tDCS.

### DISCUSSION

No beneficial effect of single-session ctDCS on fine motor control in guitarists with MD was found in this study. There was no tendency toward improvement of symptoms in any of seven criteria evaluated by three experts or in self-reports of the guitarists, although...
we used a high stimulation intensity of 2 mA. This might be due to several reasons. First, the most plausible conclusion is that neurophysiological improvement of dystonia as it is now established with deep brain stimulation needs time. As was recently shown, SICI and LTP like plasticity changes improve only over months after implantation in patients with dystonia. This may eventually lead to the consequence that also transcranial stimulation methods have to be applied possibly daily over months to obtain a beneficial effect. The positive aspect of this addresses safety. If single session of ctDCS would have a dramatic beneficial effect, maladaptive plasticity mechanisms might also lead to a dramatic worsening. Second, stimulation of M1 only might not be sufficient to change the neuronal pathways underlying dystonic symptoms. Guitar playing is a complex motor task, which requires a high level of movement preparation and precise movement execution. Thus, additional stimulation of premotor areas, the supplemental motor cortex, or even V5 might have beneficial effects on motor control in guitarists with MD. There is also the possibility that ctDCS was not capable to decrease cortical excitability because of the special pathology of MD. When ctDCS was applied on patients with another type of focal dystonia, writer’s cramp, the normal inhibitory effect of ctDCS on corticospinal excitability was absent.

FIG. 1. Results of single-session ctDCS on fine motor control in guitarists with musician’s dystonia. A: Bars show expert rating of motor performance on a four-point Likert scale. High values indicate poor motor control and vice versa. Active tDCS condition is displayed as gray bars, and placebo tDCS is displayed as open bars. Error bars depict standard deviations of expert ratings. B: Bars show expert rating of motor performance on a single-patient level. High values indicate poor motor control and vice versa.
Although group results revealed no beneficial effect of ctDCS on motor control, voluntary motor control of one patient was improved by ctDCS. In contrast to the other patients, he suffered from an atypical arm dystonia. Typical symptoms of MD are cramping of one or more fingers while playing the musical instrument but without segmental dystonia-like symptoms, such as cramping of the arm. This result suggests that ctDCS of the primary motor cortex should be investigated in musicians with nontypical, less focal types of MD.

In summary, we can conclude that single-session ctDCS does not improve fine motor control in MD in this study. Nevertheless, this result helps to gain new insight into the pathophysiology of MD. Further research applying other stimulation parameters, such as changing electrode positions or using other stimulation patterns (repetitive stimulation, random noise stimulation), is needed to extend knowledge about effects of electrical stimulation. Physiological changes during and after electrical stimulation should be additionally measured with transcranial magnetic stimulation. It should also be noted that there is a marked interpatient phenotypic variability in dystonia, which may lead to the consequence of heterogenous stimulation techniques as possible treatment approaches. However, the outcome of this study also suggests that other therapeutical strategies for MD should be investigated with increased effort. Pedagogical retraining, botulinum toxin, and trihexyphenidyl are reported to show good results treating MD, but further research is needed to improve the currently available therapies.\(^\text{10}\)

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Table Tennis Dystonia

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Abstract: Focal task-specific dystonia (FTSD) occurs exclusively during a specific activity that usually involves a highly skilled movement. Classical FTSD dystonias include writer’s cramp and musician’s dystonia. Few cases of sport-related dystonia have been reported. We describe the first four cases of FTSD related to table tennis (TT), two involving professional international competitors. We also systematically analyzed the literature for reports of sport-related dystonia including detailed clinical descriptions. We collected a total of 13 cases of FTSD, including our four TT players. Before onset, all the patients had trained for many years, for a large number of hours per week. Practice time had frequently increased significantly in the year preceding onset. As TT is characterized by highly skilled hand/forearm movements acquired through repetitive exercises, it may carry a higher risk of FTSD than other sports. Intensive training may result in maladaptive responses and overwhelm homeostatic mechanisms that regulate cortical plasticity in vulnerable individuals. Our findings support the importance of environmental risk factors in sport-related FTSD, as also suggested in classical FTSD, and have important implications for clinical practice. © 2010 Movement Disorder Society

Key words: task-specific dystonia; risk factor; plasticity; pathophysiology; sport

INTRODUCTION

Focal task-specific dystonia (FTSD) occurs exclusively during a specific activity that usually requires highly skilled movements. Classical forms of FTSD include writer’s cramp, typist’s dystonia, and musician’s dystonia. Sport-related dystonia has occasionally been reported among persons engaging in golf1,2 trap shooting,3 pistol shooting,4 tennis,5 running,6 petanque,7 billiards, darts, snooker, and cricket.4

Intensive motor training in highly skilled movements may be crucial in FTSD onset.9 Table tennis (TT) is a sport that requires time-constrained goal-directed movements with high-level hand-eye coordination and perception-action coupling. At a competitive level, TT training is partly based on high-frequency repetition of stereotyped upper-limb movements, including robot training. Surprisingly, FTSD has never been reported in TT players. We report four cases of FTSD in TT players and analyze previous reports of sport-related dystonia.

PATIENTS AND METHODS

Four patients with TT-related dystonia were referred to our movement disorders clinics for clinical evaluation and management. In addition to a comprehensive neurological examination, the patients had a detailed history-taking and were questioned on their TT practice. The dystonia was analyzed after video recording of a normal TT training session. All the patients gave their written informed consent to participate in the study and to be filmed.

We also analyzed the literature on sport-related dystonia. The NIH Pubmed, SUDOC, and PASCAL BIOMED (Paris V University) databases were scanned up to 2009 for reports including the key words “sport” and “dystonia.” The reference lists of the reports thus retrieved were also scrutinized. We enrolled cases meeting all the following criteria: (1) typical clinical features of FTSD, (2) FTSD triggered electively by sporting practice, and (3) no other obvious cause of dystonia. Only reports including a detailed clinical description were considered for analysis. Cases of Golfer with “yips” were excluded as we considered that the cause of this disorder is controversial and the reported golf player patients with yips probably include both patients with a psychological cause and patients with dystonia.10,11

RESULTS

Illustrative Case Report

A 29-year-old right-handed professional TT player (Patient 1 in Table 1) complained of stiffness and
abnormal movements of his right upper arm, el ectively triggered when playing TT and affecting his performance. He began to play TT at age 5 years, playing for 5 to 15 hours per week between age 6 and 12 years, and for about 35 hours per week between age 12 and 28 years. At this latter age, following a period of more intensive training, he began to experience involuntary abnormal elbow flexion when serving. Owing to the resulting decline in his performance, he increased his training load and paid special attention to serving. The abnormal movements gradually became more severe over the following 6 months. After 3 months of highly intensive training (6–7 hours daily), he developed additional abnormal movements that interfered with “normal” forehand movements. Finally, he reported that the involuntary movement occasionally occurred during daily-life movements requiring elbow flexion, such as bringing a mobile phone to the ear. He stopped training after a further marked decline in performance.

When examined while playing TT, he was seen to have a dystonic movement characterized by elbow flexion associated with elevation and adduction of the shoulder that occurred almost each time he served or made a forehand stroke (see Video). The interfering movement only occurred when hitting a ball with a racket: the movement was fluid when performed without a racket and ball. He was able to attenuate the abnormal movement (1) by using a sensory trick, namely touching the right arm with a left finger and (2) by including a whirling movement before the normal forehand movement. When he played with the left hand, there was no abnormal movement of the left upper limb and no mirror dystonia of the right upper limb.

Abnormal posture and movements were absent at rest, and other voluntary movements did not trigger dystonia. Neurological findings were otherwise normal. There was no pain or joint limitation. Routine laboratory tests, brain and cervical MRI and neurophysiological investigations, including nerve conduction velocity studies, were normal.

We diagnosed TT-related primary task-specific focal dystonia. After 5 months without training, the dystonia improved somewhat, but it again worsened as soon as normal training sessions were resumed. Finally, we advised the patient to drastically reduce his total practice load and to exclude all repetitive movements. His condition had improved significantly 2 years after onset. He returned to the competitive circuit but did not regain his previous level. The dystonia persisted.

Table 1 shows the main characteristics of our four patients and on another nine cases of sport-related dystonia collected from the literature.

None of our four patients had family history of dystonia, Parkinson’s disease, tremor, tics, or scoliosis and there was no mention of such history in the nine patients of the literature except for Patient #12 who had a sister with dystonia. There was no psychiatric or cognitive comorbidity in our four patients and there was no mention of such comorbidity in the nine patients of the literature except for Patient #6 who had a diagnosis of social phobia. None of the 13 patients had a previous history of neuroleptics use.

**DISCUSSION**

We describe the first four cases of FTSD in TT players, including two international professionals, and
also analyze nine previously reported cases of sport-related dystonia. We found the following common features: (1) a large amount of time spent training each week (8–30 hours), (2) a long period of continuous training before onset (2–22 years), (3) a frequent increase in practice intensity in the year preceding onset, (4) no family history of dystonia (except for one patient), and (5) no cause of symptomatic dystonia.

TT training is characterized by highly skilled and highly repetitive hand movements, characteristics that may be associated with a higher risk of FTSD than in other sports. The two professional TT players described here improved significantly, albeit only partially, when they reduced their training intensity and abandoned exercises requiring repetitive movements.

As FTSD may be diagnosed very late in TT players and others sportspersons, leading to unnecessary concerns and investigations, neurologists, sports physicians, and competitive sportspersons should be aware of this disorder. Erroneous psychiatric diagnoses have been reported in sportspersons with dystonia,5,8; this was the case of our Patient #2, who suffered severe social, familial, and psychological consequences. The improvement noted in Patients #1 and #2 when their training strategy was adapted suggests that the disorder is at least partially reversible.

Our findings support the importance of environmental risk factors in the development of sport-related FTSD, as previously suggested in classical forms of FTSD. TT players’ training consists partly of high-frequency repetition of specific movements that are likely to favor the onset of dystonia, as in a primate model of focal dystonia induced by intensive motor training.12 In a case–control study of 104 consecutive patients with writer’s cramp and matched controls, we identified a dose-effect relationship with the amount of daily handwriting, an additional trigger being an unusual increase in the time spent writing in the year before onset.9 We found such a recent increase in practice time in the two professional TT players studied here (Patients 1 and 2), as previously reported in other sportspersons6,8 and in professional musicians.13,14 The total time spent practicing, and a recent unusual increase in the quantity or nature of training, may reflect the same disruptive phenomenon. Patients with focal dystonia have been found to have excessive sensorimotor cortex plasticity and an impaired homeostatic response.15,16 Pushing motor training to extremes can result in maladaptive responses to highly skilled movements. Homeostatic mechanisms that regulate cortical plasticity may thereby be overwhelmed in susceptible subjects, resulting in consolidation of abnormal motor programs with altered muscle activation patterns. Although probably underestimated, FTSD is likely to be less frequent in sportspersons than in musicians. The particular processing of the auditory feedback to monitor online the movements pattern may implies higher adaptive requirements in musicians.

Taking into account the low frequency of FTSD among regular practitioners of highly skilled activities, FTSD might involve a “double hint” model in which a preexisting disorder makes some individuals vulnerable to an FTSD triggering event. This particular susceptibility of some subjects to dystonia may reflect an endophenotype of the disease that could be either acquired or genetically influenced.15,16 We found only one case with dystonia in a relative.7 In contrast, a recent study based on systematic examination of family members found dystonic signs in a considerable number of relatives of index patients with FTSD.18 This points to a genetic component in FTSD vulnerability, in addition to environmental factors.

Our study population is too small to speculate on a possible link between sport-related dystonia and head or other focal body trauma. Only 1 of the 13 patients had a history of head trauma. Head trauma may facilitate the onset of dystonia by inducing subtle brain damage or transient cortical dysfunction. We and others have found that head trauma is a risk factor for adult-onset focal dystonia, but other studies focusing on cranial dystonia showed no such association.9,18 Two of the 13 patients in this study reported a history of local body injury, but sportspersons may be more exposed than the general population to peripheral trauma. Peripheral injury might facilitate the onset of dystonia by altering sensory inputs and leading to cortical reorganization. Various primary adult-onset focal dystonias have been linked to peripheral trauma.9,14

In conclusion, this study supports the crucial role of environmental factors as FTSD triggers and has important implications for clinical practice. Not only neurologists, but also sports physicians, trainers, and competitors should be aware of this disorder, in order (1) to adopt preventive strategies, (2) to detect FTSD rapidly, (3) to offer adequate emotional support and therapy, and (4) to adapt training accordingly.

**LEGEND TO THE VIDEO**

Patient 1 has an abnormal flexion of the elbow with adduction and elevation of the shoulder when he makes a forehand stroke. As a consequence, note that the racquet is very close to his forehead at the end of the movement. He attenuates the abnormal movement
by touching the right arm with a left finger, and then by including a whirling movement before the normal forehand movement. Patient 2 has an abnormal brisk cubital flexion of the wrist immediately before she makes a forehand topspin.

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**Author Roles:** Anne Le Floch: Research project: execution; manuscript: writing of the first draft. Marie Vidalihet: Research project: execution; manuscript: review and critique. Constance Flamand-Rouviere: Research project: conception and organization; manuscript: review and critique. David Grabl: Manuscript: writing of the first draft and review and critique. Jean-Michel Mayer: Research project: execution. Michel Gonce: Research project: organization and execution; manuscript: review and critique. Emmanuel Broussole: Research project: organization and execution; manuscript: review and critique. Emmanuel Roze: Research project: conception, organization, and execution; manuscript: writing of the first draft and review and critique.

**REFERENCES**


Prolonged Vastus Lateralis Denervation After Botulinum Toxin Type A Injection

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**Abstract:** Intramuscular injection of botulinum toxin (BoNT) produces reversible blockade of neuromuscular transmission. In animal experimental models, recovery begins within four weeks and is usually complete by twelve weeks. We present evidence of prolonged denervation following BoNT injection of the vastus lateralis (VL) muscle to correct quadriiceps muscle imbalance in patients with chronic anterior knee pain. Needle electromyography data were obtained from 10 subjects who had received a single BoNT treatment 5 to 19 months earlier as part of a clinical trial. Insertional and spontaneous activity, recruitment, and motor unit action potentials were examined. Clear differences between the injected and non-injected VL muscles, which correlated with the time since injec-
tion, were identified in all subjects. All 10 subjects studied with needle EMG showed evidence of persisting denervation in the BoNT-A injected VL muscle beyond the period of neuromotor recovery expected from animal experimental studies. © 2010 Movement Disorder Society

Key words: botulinum A toxin; muscle denervation; electromyography; neuromuscular blockade

Botulinum neurotoxin (BoNT) is produced by Clostridium botulinum. Seven serotypes have been identified, all of which inhibit acetylcholine release from nerve terminals. Botulinum toxin type A (BoNT-A) is the most commonly used serotype. In animal models, initial recovery of neuromuscular transmission commences within 4 weeks because of nerve terminal sprouting at the neuromuscular junction. The parent terminal remains nonfunctioning until approximately 8 weeks, at which time there is a return of vesicle turnover and the new sprouts begin to regress, with full recovery of the parent terminal apparent by three months post injection.

However, consistent clinical benefit has been demonstrated from BoNT-A injections in focal muscle overactivity, with some patients having improvements lasting greater than 3 months after a single treatment. Few data exist documenting the duration of neurophysiological effects following a single BoNT-A intervention; although a recent investigation in normal volunteers has described neurogenic muscle atrophy, which was still present at 12 months.

This report presents evidence of prolonged denervation following BoNT-A injection to the distal third of the vastus lateralis (VL) muscle for chronic anterior knee pain associated with quadriceps muscle imbalance. Clinical results have been published elsewhere. Improvements in functional mobility, knee extensor torques and activity induced knee pain were maintained at study follow up 12 months post-injection; however, many subjects had persistent focal atrophy of the injected area of VL muscle.

PATIENTS AND METHODS

Subjects

This study was approved by the institutional ethics review committee. Subjects who had participated in previous clinical investigations of a single BoNT injection for chronic anterior knee pain were approached to undergo needle EMG assessment to examine the extent of any residual BoNT-A effect. All subjects had received a standard dose of 500 units Dysport (Ipsen) diluted with 4 ml of normal saline into the distal third of the VL muscle, 5 to 19 months earlier.

Electromyography

Concentric bipolar needle electromyography (Viking IV EMG, Nicolet) was performed by an independent electromyographer who was blinded to the side and timing of BoNT-A injections. Subjects did not communicate information about which limb had been previously treated. Qualitative and quantitative EMG was performed on both limbs in random order. Recordings were made from two or three sites within the previously injected area (distal third of the VL muscle).

Qualitative EMG assessment employed a bandpass of 20 Hz–20 KHz, a sweep speed of 10 msec/division, and sensitivities of 50 μV/division for insertional and spontaneous activity and 200 μV/division for recruitment and motor unit action potential (MUP) assessment.

Quantitative multi-MUP analysis of at least 16 MUPs was recorded from each muscle using automatic template matching software, a bandpass of 2 Hz–10 kHz, a sweep speed of 5 msec/division and sensitivity of 100 μV–200 μV/division. MUPs were sampled from different depths using slight to moderate contraction, and mean amplitude and duration were derived. MUP parameters were considered abnormal if the mean MUP value or at least three individual MUPs were outside the reference range.

Needle electromyography interference pattern analysis in mild-moderate isometric muscle contraction was also performed, but without quantititation of the force of muscle contraction. A bandpass of 20 Hz –10 kHz and sensitivity of 1 mV/division were used, with the Nicolet system calculating from a 5 second EMG epoch. Peak-to-peak amplitude, mean rectified voltage, the root mean square (RMS) voltage, and turns per second (the number of peaks in the waveform exceeding a level of 100 μV) were calculated.

Subsequent to data analysis the data were coded according to treated side. MUP parameters from un.injected and injected limbs were compared utilising the paired t-test. A least squares linear regression was used to examine effects between limbs and time since injection. A probability of P < 0.05 was used as the criterion for determining meaningful differences between sides.

RESULTS

This study investigated a sample of convenience of subjects enrolled in clinical trials investigating the
TABLE 1. Qualitative and quantitative needle EMG examination findings of BT-A (Dysport®) injected and control distal VL muscles in 10 subjects

<table>
<thead>
<tr>
<th>Subject</th>
<th>Time since injection (month)</th>
<th>Spontaneous fibrillation</th>
<th>Recruitment pattern</th>
<th>MUP Amplit</th>
<th>MUP Dur.</th>
<th>Mean MUP amplitude (µV)</th>
<th>Mean MUP Dur (msec)</th>
<th>Mean phases</th>
<th>Peak to peak amplitude (µV)</th>
<th>MRV (µV)</th>
<th>RMS (µV)</th>
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<tr>
<td>1. (BT-A)</td>
<td>5</td>
<td>2+</td>
<td>1−</td>
<td>2−</td>
<td>1+</td>
<td>266*</td>
<td>3.7*</td>
<td>4*</td>
<td>833</td>
<td>13</td>
<td>32</td>
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<td>NL</td>
<td>NL</td>
<td>NL</td>
<td>1272</td>
<td>8.1</td>
<td>3.2</td>
<td>1083</td>
<td>20</td>
<td>49</td>
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<td>1−</td>
<td>1−</td>
<td>NL</td>
<td>507</td>
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<td>5.3*</td>
<td>1041</td>
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<td>49</td>
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<td>NL</td>
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<td>NL</td>
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<td>16.1</td>
<td>4</td>
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<td>83</td>
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<tr>
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<td>7.5</td>
<td>2+</td>
<td>NL</td>
<td>2−</td>
<td>1+</td>
<td>464*</td>
<td>7.9*</td>
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<td>NL</td>
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<td>38</td>
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<td>NL</td>
<td>2−</td>
<td>NL</td>
<td>299*</td>
<td>8.6*</td>
<td>11.3*</td>
<td>1375</td>
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<td>1+</td>
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<td>1−</td>
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<td>8.2*</td>
<td>4.8*</td>
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<td>7. (BT-A)</td>
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<td>2+</td>
<td>2−</td>
<td>1−</td>
<td>229*</td>
<td>6.8*</td>
<td>6.6*</td>
<td>916</td>
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<td>11.6</td>
<td>3.8</td>
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<td>358</td>
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<tr>
<td>8. (BT-A)</td>
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<td>1+</td>
<td>NL</td>
<td>1−</td>
<td>1−</td>
<td>852</td>
<td>8.1</td>
<td>3.7*</td>
<td>1708</td>
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<tr>
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<td>934</td>
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<td>984</td>
<td>8.7</td>
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<td>916</td>
<td>15.1</td>
<td>2.8</td>
<td>8000</td>
<td>105</td>
<td>258</td>
</tr>
</tbody>
</table>

Spontaneous fibrillation gradings: 1+ for persistent fibrillations and in at least two areas of the muscle, 2+ for moderate numbers of persistent fibrillations in ≥3 areas. MUP duration and amplitude abnormalities: 1 for mild and 2 for moderate, "—" decrease and "+" increase.

*mean values outside reference range and at least three individual MUPs outside reference range.

#at least three individual MUPs outside reference range.
effect of BoNT injection, to the distal portion of the VL muscle, for refractory anterior knee pain. Ten of 25 subjects contacted agreed to participate in the needle EMG investigation. Nine were women (mean age 27; range 16–56) and all were physically active. All 10 subjects reported ongoing relief of symptoms at the time of this investigation; however, two subsequently underwent surgery for exacerbation of knee related disability at 12 and 20 months, respectively, post BoNT injection.

The data are summarised in Table 1. Clear interlimb differences were evident for the VL muscle in all 10 subjects. No EMG qualitative or quantitative abnormality was found in the uninjected VL muscles. Qualitative EMG showed abnormalities in the injected VL muscle in all subjects. These findings included: increased insertional activity with spontaneous fibrillations in 8 subjects, reduced MUP amplitudes in all subjects and altered MUP duration in 8 subjects. Increased MUP turns/ phases were present in 9 of 10 subjects. MUP recruitment was reduced in 2 subjects at 5 months postinjection and increased in 5 subjects at longer durations postinjection (Table 1).

Quantitative MUP analysis revealed reduction in MUP amplitude, MUP duration or both in seven of the 10 subjects. Mean MUP phases were increased in 9 of 10 subjects. MUP recruitment was reduced in 2 subjects at 5 months postinjection and increased in 5 subjects at longer durations postinjection (Table 1).

Quantitative MUP analysis revealed reduction in MUP amplitude, MUP duration or both in seven of the 10 subjects. Mean MUP phases were increased in 9 of 10 subjects. All 10 subjects showed significant quantitative differences in the injected compared with the control limb including: a mean MUP amplitude reduction of 452 µV or 49% (range 0–79%) ($P = 0.0005$), a mean MUP duration reduction of 4.4 msec or 36% (range 0–58%) ($P = 0.0003$), and MUPs with a mean of two more phases ($P = 0.03$) (Table 1). Interference pattern analysis of the injected VL compared with the other side showed a mean peak to peak amplitude reduction of 2227 µV or 49% (range 17–84%) ($P = 0.007$), mean rectified voltage reduction of 53 µV or 47% (range 0–84%) ($P = 0.03$) and RMS reduction of 112 µV or 48% (range 8–83%) ($P = 0.02$). Turns per second did not reveal consistent side to side differences (see Table 1).

Linear regression showed an association between degree of MUP amplitude reduction and time since BoNT-A treatment ($P = 0.02$; Fig. 1), with a mean return to the untreated limb MUP amplitudes at 19 months (lower 95% confidence band of 14 months).

**DISCUSSION**

We have found both qualitative and quantitative needle EMG evidence of prolonged denervation in all 10 subjects injected with BoNT-A between 5 and 19 months previously. Blinded qualitative EMG was as sensitive and specific as quantitative EMG in identifying the injected limb in all subjects. The extent of the identified abnormalities correlated with time since injection.

Increased insertional activity with spontaneous fibrillations was found in 8 subjects. Fibrillations are the spontaneous action potentials of single muscle fibres, and arise in functionally denervated muscle fibres.13 The loss of functioning muscle fibres in a motor unit causes a reduction in MUP amplitude and duration, with an increase in turns and phases because of random fibre loss and desynchronisation amongst remaining muscle fibres. As we have found in this study, MUP recruitment may be influenced variably by neuromuscular blockade, with reduced recruitment seen in 2 subjects who were 5 months postinjection and increased recruitment in four subjects at longer durations post-injection. Functional blockade of random muscle fibres within a motor unit may reduce recruitment, since more motor units are required to compensate for a smaller force generated per motor unit. Conversely, functional blockade of whole motor units may reduce recruitment. It is important to note that there was no clinical evidence of a neurogenic disorder in any of the subjects studied. The EMG changes observed are characteristic of BoNT effect on neuromuscular transmission. In contrast, in a chronic neurogenic process, EMG examination reveals high amplitude and long duration motor unit potentials with reduced recruitment.
Electrophysiological changes in the VL muscle were evident after this single BoNT-A treatment beyond the period of recovery of the neuromuscular junction expected from previously reported animal studies.2-4 Despite this, at the time of investigation, most subjects reported significantly improved symptoms compared with preinjection status. We consider this to represent a lasting improvement in balance between the medial and lateral components of the quadriceps muscle.10 Very few studies have examined the persistence of neurophysiological effects from a single BoNT injection. A recent investigation in normal volunteers reported reduction in the cross sectional area of the injected lateral head of gastrocnemius muscle, as well as histopathological evidence of neurogenic atrophy at 12 months post injection of BoNT-A.8 These changes were not associated with functional impairment. It is possible that the persistent change observed in these individuals, and in our cohort, is the rule, not the exception. Findings of this study may also reflect a dose-dependent effect.14 The dose was selected empirically based on the size of the VL muscle and our prior clinical experience. The duration of BoNT-A effect may also be muscle and condition specific. Further investigation is required to establish the duration of muscle denervation in addition to clinical benefit.

CONCLUSIONS

All 10 subjects studied with needle EMG showed evidence of persisting denervation in the BoNT-A injected muscle beyond the period of neuromotor recovery expected from animal experimental studies.

Author Roles: John Dunne: Conception, design and execution of research project, statistical analysis, manuscript review and critique. Barbara Singer: Conception and design of research project, writing first draft of manuscript. Peter Silbert: Execution of research project, manuscript review and critique. Kevin P Singer: Conception and design of research project, manuscript review and critique.

Financial disclosure: Product (Dysport®) for the clinical trial from which these data are derived, was provided by Ipsen Australia to Royal Perth hospital at no cost. Data were collected and analyzed independently by authors. Ipsen Australia had no role in data management. One author (BJS) received partial salary support (2005–6) for the clinical trial from which these data are derived from the Raine Medical Research Foundation, at The University of Western Australia. This body places no restriction on data collection, analysis or reporting. All authors have full-time university or clinical practice employment contracts. There are no other sources of financial support or funding for the preceding twelve months for Dr John Dunne, Dr Peter Silbert, Dr Kevin Singer. Dr Barbara Singer has a full-time academic appointment and has also received funding support in 2008-9. The effect of repeated passive dorsiflexion on reducing calf muscle stiffness following acquired brain injury. Neurotrauma Research Program, Western Australia ($116,000). Move Again Project®—establishing an exercise network to improve functional, physical, mental and social health in the neurologically impaired’. Neurotrauma Research Program, Western Australia ($100,000). The impact of a NMES based bilateral training program on left neglect, anosognosia and arm function after stroke. Neurotrauma Research Program, Western Australia.

REFERENCES

The Montreal Cognitive Assessment as a Screening Tool for Cognitive Dysfunction in Huntington’s Disease

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Abstract: Cognitive dysfunction is one of the hallmarks of Huntington’s disease (HD) and may precede the onset of motor symptoms. The Montreal Cognitive Assessment (MoCA), a brief cognitive screening instrument with high specificity and sensitivity for detecting early cognitive impairments, has not been studied in the HD population. In this study, we compare the MoCA with the mini-mental state examination (MMSE) as a screening tool for cognitive dysfunction among 53 patients with HD. The mean MMSE score was 26 ± 2.4, and mean MoCA score was 21 ± 4.4. Twenty-one patients (81%) of those who scored <26 on the MMSE had the MoCA score <26. Thirty-two patients (78%) of those who scored <24 on the MMSE had the MoCA score <24. The MoCA may be a more sensitive screening tool for cognitive impairments in HD relative to the MMSE.

Key words: Huntington’s disease; MoCA; MMSE; cognition

Huntington’s disease (HD) is an autosomal dominant neurodegenerative disorder characterized by abnormal movements, cognitive impairment, and behavioral symptoms. Early cognitive deficits in HD are changes in visuospatial abilities, visual-motor skills, executive function, and facial expression recognition.1 These changes may emerge before the onset of frank motor signs in some individuals carrying the HD mutation. There is, therefore, a need for screening and detection of these early cognitive changes in the HD population.

As the disease progresses, it is important to have a sensitive tool to measure the rate of cognitive decline.

The mini-mental state examination (MMSE) is a widely used screening instrument for detecting cognitive deficits.2 Although it may be completed quickly and user friendly, the MMSE may not capture cognitive domains affected across a wide spectrum of dementia syndromes, and it lacks adequate sensitivity for detection of mild cognitive impairment.3,4 Neuropsychological testing, although the gold standard for measuring cognitive performance, is lengthy and requires expertise for its administration and interpretation.

The Montreal Cognitive Assessment (MoCA) is a brief cognitive screening tool with high specificity and sensitivity for detecting mild cognitive impairment.5 Executive function, language abilities, and visuospatial processing are assessed more rigorously with the MoCA relative to the MMSE. As the MoCA has not been studied as a measure of cognitive performance in the HD population, we conducted this study to compare MoCA with MMSE as a screening tool for cognitive dysfunction in HD.

PATIENTS AND METHODS

Consecutive patients with HD presenting for a routine follow-up assessment, were recruited from the HD clinic at Rush University Movement Disorders Center over a 5-month period. All study participants signed informed consent. The study protocol was approved by the Institutional Review Board of Rush University. Standardized evaluations used were the Unified Huntington’s Disease Rating Scale (UHDRS)6 and the Total Functional Capacity Scale (TFC).6 The demographics, education level, and disease duration of the patients were ascertained as well.

Study instruments included the MMSE and MoCA, and were administered on the same day in alternating order. Participants completed both scales in their original format. Cut off scores of <26 and <24 were used as values indicative of cognitive impairment. These cut off scores were chosen based on the cut off values in studies assessing cognitive performance.2,5,7

Associations of MoCA and MMSE scores with disease severity, UHDRS, and TFC were evaluated via Spearman rank correlations, with a significance level of P < 0.05. Frequencies and percents were calculated for categorical variables. Mean and standard deviations were calculated for continuous variables.

RESULTS

Fifty-three patients (27 M, 26 F) participated in this study. The mean age of the study cohort was 53 ±
11.4 years, and mean duration of symptoms was 8 ± 5.9 years. The diagnosis was confirmed genetically in 47 participants. For the remaining six participants, the diagnosis was based on the clinical features of HD and positive family history. Forty-nine participants (93%) completed high school. The mean motor UHDRS score was 33 ± 16.7 and mean TFC was 7 ± 3.4.

The mean MMSE score was 26 ± 2.4 and mean MoCA score was 21 ± 4.4 (Fig. 1). The MMSE score correlated with TFC ($r = 0.3$, $P = 0.03$). The MoCA score correlated with TFC ($r = 0.5$, $P = 0.0001$) and motor UHDRS ($r = -0.5$, $P = 0.0001$).

The range of scores on the MMSE was 17–30 and on the MoCA 11–30 (Fig. 2). The ceiling effect was mild, and maximal scores on the MMSE and MoCA were obtained in one participant. Twenty-seven patients (51%) scored <26 on the MMSE, and 48 patients (91%) scored <26 on the MoCA. The MMSE scores were <24 in 12 patients (23%), and MoCA scores were <24 in 43 patients (81%). Twenty-one patients (81%) of those who scored ≥26 on the MMSE had the MoCA score <26. Thirty-two patients (78%) of those who scored ≥24 on the MMSE had the MoCA score <24. None of the subjects who scored >24 or >26 on the MoCA had MMSE scores <24 or <26, respectively.

**DISCUSSION**

Standardized cognitive batteries, such as the MMSE and the Cambridge Mental Disorders of Elderly Examination, have been developed to streamline screening for cognitive impairment and decline. Ceiling effects and lack of adequate sampling of various cognitive domains in testing paradigms limit the sensitivity of these instruments for detecting cognitive impairment. High MMSE scores have been reported in individuals with well-ascertained dementia.

This is, to our knowledge, the first report of the MoCA as a screening instrument for cognitive impairment in the HD population. The MoCA scores were less than the MMSE scores in our cohort. Using the cut off scores of 24 and 26, more patients with HD were identified as having cognitive impairment on the MoCA relative to the MMSE. No significant ceiling effect was observed on the MoCA. We therefore believe that the MoCA may be a more sensitive screening instrument for cognitive impairment in HD relative to the MMSE.

The MoCA was designed to be more sensitive to abnormal performance in memory, language, and executive function domains in mildly impaired individuals. We therefore speculate that differences in performance on the MMSE and MoCA in our cohort may be explained by the better ability of the MoCA to capture memory, high-level language abilities, executive cognitive function, and visuospatial processing in HD patients.

Although the MoCA has not been systematically studied in the HD population, several reports assessed the utility of the instrument as a screening tool for cognitive impairment in Parkinson’s disease (PD). These reports suggest that the MoCA may provide more insight into the cognitive status of patients with PD, relative to the widely used MMSE. In PD, the MoCA demonstrated good test–retest and inter-rater reliability, as well as good convergent validity with a neuropsychological battery.

We recognize several important limitations of our study. The study cohort is relatively small. We did not conduct a neuropsychological testing that is a gold standard for the assessment of cognitive performance. We used cutoff scores of 24 and 26 as indicators of...
cognitive impairment. It is, however, not known if these values are a good representative of cognitive impairments in the HD population. Further studies that will use neuropsychological evaluations will better define cutoff scores in the HD population.

Despite these limitations, our findings suggest that the MoCA may be a more sensitive screening instrument relative to the MMSE for detecting cognitive impairment in the HD population. Longitudinal validation studies of the MoCA against neuropsychological batteries in larger cohorts of patients with HD are needed to establish the role of the MoCA as a cognitive screening tool in the HD population.


REFERENCES