LIMB DYSTONIA HISTORY, PHENOMENOLOGY, EVALUATION, TREATMENT

Mark F. Lew, MD
Professor of Neurology
Vice-chair Department of Neurology
Vandermeulen Chair in PD Research
Director Division of Movement Disorders
KECK/USC School of Medicine
Los Angeles, CA
Disclosures


- Speaker’s Bureau participant: Acadia Pharmaceuticals, Inc., Impax Laboratories, Inc., Lundbeck, Teva Pharmaceuticals, UCB, and US WorldMeds LLC.

- Research funding; the Parkinson’s Study Group, Michael J. Fox Foundation, Civitas Therapeutics, Inc., Biotie Therapies, Cynapsus Therapeutics, Inc., IntecPharma, Neuroderm, and the National Institutes of Health.
LIMB DYSTONIA
GENERAL DEFINITION

- DYSTONIA IS CHARACTERIZED BY SUSTAINED MUSCLE CONTRACTIONS FREQUENTLY CAUSING REPETITIVE TWISTING MOVEMENTS OR ABNORMAL POSTURES
- PREVALENCE ESTIMATES OF DYSTONIA VARY:
  - 2.7/1,000,000 ROCHESTER MINNESOTA
  - 11.1/100,000 ASHKENAZI JEWISH NYC
  - 60/100,000 LATE ONSET NEW ENGLAND
  - 300/100,000 LATE ONSET ITALY >50yo

## Dystonia by Topography

<table>
<thead>
<tr>
<th>Type of Dystonia</th>
<th>Region or Part Affected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Focal</td>
<td>Single region</td>
</tr>
<tr>
<td>Segmental</td>
<td>Two or more adjacent regions</td>
</tr>
<tr>
<td>Multifocal</td>
<td>Two or more nonadjacent regions</td>
</tr>
<tr>
<td>Generalized</td>
<td>Leg or legs, trunk, and one other region</td>
</tr>
<tr>
<td>Hemidystonia</td>
<td>Ipsilateral arm and leg</td>
</tr>
</tbody>
</table>

FOCAL DYSTONIA: AGE OF ONSET

### Table 3. Primary Adult-Onset Focal Dystonias.

<table>
<thead>
<tr>
<th>Type of Dystonia</th>
<th>Main Clinical Features</th>
<th>Common Misdiagnoses</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervical dystonia (spasmodic torticollis)</td>
<td>Abnormal head posture, Head tremor, Neck pain</td>
<td>Muscle strain, Cervical disk disease, Osteoarthritis</td>
</tr>
<tr>
<td>Blepharospasm</td>
<td>Increased blink rate, Forced eye closure, Difficulty opening eyes</td>
<td>Myasthenia gravis, Dry eyes</td>
</tr>
<tr>
<td>Oromandibular dystonia</td>
<td>Jaw clenching (bruxism), Jaw in open position, Lateral jaw shift</td>
<td>Temporomandibular joint syndrome, Myasthenia gravis, Dental malocclusion, Edentulous movements</td>
</tr>
<tr>
<td>Orofacial dystonia</td>
<td>Action dystonias involving lips, tongue, or pharynx</td>
<td>Tic disorders</td>
</tr>
<tr>
<td>Spasmodic dysphonia</td>
<td></td>
<td>Chronic laryngitis, vocal-cord polyps, voice tremor, psychogenic causes</td>
</tr>
<tr>
<td>Adductor type</td>
<td>Voice breaks and strain</td>
<td>Nerve entrapment</td>
</tr>
<tr>
<td>Abductor type</td>
<td>Breathy voice</td>
<td>Overuse syndromes</td>
</tr>
<tr>
<td>Mixed type</td>
<td>Features of both</td>
<td>Muscle cramps</td>
</tr>
<tr>
<td>Limb dystonia</td>
<td>Action dystonias affecting writing, playing musical instruments, handling tools, walking</td>
<td></td>
</tr>
<tr>
<td>Axial dystonia</td>
<td>Movements of shoulders, back, or abdomen</td>
<td>Myoclonus, Motor tics, Psychogenic causes</td>
</tr>
</tbody>
</table>
LIMB DYSTONIA: PHENOMENOLOGY

- MOST COMMON FORM IS WRITER’S CRAMP
- INVOLUNTARY HAND POSTURES IMPAIR WRITING
- UNDERESTIMATED AS PATIENTS DON’T SEEK MEDICAL ADVICE
- MALE PREDOMINANCE
CASE PRESENTATION

- 53 Y/O RH FEMALE WITH 3 YRS OF PROG DIFF WRITING
- NO DIFFICULTY USING HER HANDS FOR OTHER TASKS
- NO CRAMPING, SPASM, OR INVOLUNTARY MVMT ELSEWHERE
TREATMENT

- ONABOTULINUM TOXIN INJECTED AS FOLLOWS WITH EMG GUIDANCE:
  - 5 U R EXT INDICES PROPRIUS
  - 5 U R EXT DIGITORUM COMMUNIS (FASCICLE FOR MIDDLE FINGER)
EXTENSOR DIGITORUM COMMUNIS (7)

EXTENSOR INDICES PROPRIUS (9)

LIMB DYSTONIA
HISTORY

- DESCRIPTIONS BACK TO 18TH CENTURY WITH SCRIBES REPORTING CRAMPING OF HANDS ONLY WHEN PERFORMING THEIR JOBS
- ABLE TO PERFORM VIRTUALLY ALL OTHER TASKS NORMALLY
- “OCCUPATIONAL PALSY”

LIMB DYSTONIA
WHAT IS IT???

- REPRESENTS A FOCAL/TASK SPECIFIC DYSTONIA
- UNCLEAR RELATIONSHIP TO PERIPHERAL/CENTRAL TRAUMA
- ABERRANT PLASTICITY FROM EXCESSIVE, REPETITIVE USE
- LIKELY THAT DISORDER IS A CONSEQUENCE OF REPETITIVE ACTIVITY ON BACKGROUND OF A GENETIC PREDISPOSITION

Limb Dystonia

Task Specific Dystonia

- May occur during skilled manual activities “occupational cramps”
- Other descriptions include string musicians, pianists, typists, typesetters, surgeons
- Dissimilar from orthopedic over-use syndromes as does not improve with rest
LIMB DYSTONIA
PATHOPHYSIOLOGY

- Impaired inhibition at multiple levels of the CNS
- Hallett et al disturbed surround inhibition with failure to suppress neuronal excitability in regions surrounding activated neural circuits may cause overflow movements in adjacent muscles
- Sensorimotor representation of affected body parts is enlarged in the cerebral cortex of patients with focal dystonia
- Unclear if sensorimotor abnormalities are primary or secondary??

IN CONCLUSION THESE FINDINGS FROM REACTION TIME TASKS IN PATIENTS WITH PRIMARY DYSTONIA PROVIDE EVIDENCE OF ABNORMAL PRE-MOVEMENT MOTOR CORTEX EXCITABILITY. THE ABNORMALITY IS DUE TO AN ALTERED RELEASE OR RUNNING OF MOTOR PROGRAMS.

Time–frequency analysis reveals decreased high-frequency oscillations in writer’s cramp

Zoé Cimatti,1,2 Denis P Schwartz,3 Frédéric Bourdais,4 Sabine Meunier,5 Jean-Pierre Bleton,6 Marie Vidailhet,1,4,7 Bernard Renault2 and Line Garnero2

1Pierre & Marie Curie University, 2Cognitive Neuroscience & Brain Imaging Laboratory, 3MEGC Center, Pitié-Salpêtrière Hospital, 4Neurology Department, Saint Antoine Hospital, 5Laboratory of Neurology, Raymond Poincaré Hospital, 6Neurology Department, Raymond Poincaré Hospital, 7Therapeutics Laboratory, Paris, France.

Correspondence to: Zoé Cimatti, Cognitive Neuroscience & Brain Imaging Laboratory, 3MEGC Center, Pitié-Salpêtrière Hospital, 43, Boulevard de l’hôpital, 75651 Paris Cedex 13, France. E-mail: cimatti@chups.jussieu.fr

High-frequency oscillations (HFO) have been described in intracortical neurons bursting at high frequencies as potential mechanisms of focal dystonia. In healthy subjects, HFO patterns evoked by dominant-hand median-nerve stimulation, using magnetoencephalography coupled with time–frequency analysis. Then, we investigated HFO in patients with writer’s cramp and found that HFO patterns are strongly decreased in power and disorganized in time. This supports the assumption that abnormal HFOs reflect pathophysiological mechanisms occurring in focal dystonia, possibly resulting from a dysfunction of somatosensory processing.

“ In writers camp we found that HFO patterns are strongly decreased in power and disorganized in time. This supports the assumption that abnormal HFOs reflect pathophysiological mechanisms occurring in focal dystonia, possibly resulting from a dysfunction of somatosensory processing.”

DISRUPTED SOMATOTOPY OF THE FINGERS IN THE SOMATOSENSORY CORTEX IN FOCAL HAND DYSTONIA

LIMB DYSTONIA DIFFERENTIAL DIAGNOSIS

- EPISODIC
  - TETANY, OTHER METABOLIC CHANGES
    - LOW CALCIUM, MAGNESIUM, GLUCOSE, HYPERVENTILATION
  - MYOTONIA
  - FOCAL EPILEPSY, INCLUDING FRONTAL LOBE SEIZURES
  - TONIC SPASMS

- PERSISTENT
  - GROWTH DEFORMITY, DUPUYTREN’S CONTRACTURE
  - ARTHRITIS, REPETITIVE STRAIN INJURY, CRPS
  - UMN OR LMN LESION
    - CARPAL TUNNEL SYNDROME
LIMB DYSTONIA DIFFERENTIAL DIAGNOSIS

- Differential diagnosis of Parkinson’s disease, atypical Parkinsonian syndromes/multiple system atrophy must be considered in patients of appropriate age with foot/leg dystonia.
- Younger patients DYT1/PTD.
- Need to consider peripheral nerve injury/entrapment based on exam.
- Overuse syndromes, task specific tremors.
- Must rule out structural lesion thalamus/putamen with neuroimaging/careful neurologic exam.
The behavioural and motor consequences of focal lesions of the basal ganglia in man

Kailash P. Bhatia and C. David Marsden

University Department of Clinical Neurology, Institute of Neurology and the National Hospital for Neurology and Correspondence to: Professor C. D. Marsden, Institute of Neurology, Queen Square, London WC1N 3BG, UK

Table 2 Metanalysis of isolated basal ganglia lesions

<table>
<thead>
<tr>
<th></th>
<th>Motor disorders</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Caudate (43)</td>
</tr>
<tr>
<td>Chorea</td>
<td>3 (u)</td>
</tr>
<tr>
<td>Dystonia</td>
<td>6 (u)</td>
</tr>
<tr>
<td>Parkinsonism</td>
<td>—</td>
</tr>
<tr>
<td>Dystonia plus</td>
<td>1 (b)</td>
</tr>
<tr>
<td>parkinsonism</td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td>—</td>
</tr>
<tr>
<td>Total</td>
<td>10 (23%)</td>
</tr>
</tbody>
</table>

*Others: one with stereotypies and a gait disorder, and one with contralateral asterixis; †one with arm tremor. u = unilateral lesion, b = bilateral lesions.

Unilateral lesions of the globus pallidus: report of four patients presenting with focal or segmental dystonia

A Münchau, D Mathen, T Cox, N P Quinn, C D Marsden,* K P Bhatia

Motor and other effects produced by selective lesions affecting the basal ganglia may give clues to their function. Focal lesions restricted to the globus pallidus (GP), particularly unilateral, are rare. In a recent review of behavioural and motor consequences of focal lesions of the basal ganglia in humans only 17 patients with lesions restricted to the GP were identified but in only two was the lesion unilateral. Since then only nine additional patients with bilateral palilidal lesion have been reported. Here we describe four patients with discrete unilateral lesions of the GP (table).


**Limb Dystonia**

**Structural Lesion**

10/16 cases with hemi-dystonia
THALAMIC INFARCT
Dystonia in multiple system atrophy

S M Boesch, G K Wenning, G Ransmayr, W Poewe


5/24 MSA PTS PRESENTED WITH LIMB DYSTONIA

See end of article for authors' affiliations.

Correspondence to:
Professor W Poewe,
Department of Neurology,
University Hospital,
Anichstrasse 35, A-6020
Innsbruck, Austria;
Weemer.Poewe@uibk.ac.at

Received
28 November 2000
In revised form 25 May
2001
Accepted 26 June 2001

We report here the case of dystonia in multiple system atrophy (MSA).

We report on 5/24 probable MSA over the past 10 years were prospectively followed up. Motor features were either dominated by parkinsonism (MSA-P subtype, n=18) or cerebellar ataxia (MSA-C, n=6). Classification of dystonic features and their changes with time was based on clinical observation during 6–12 monthly follow up visits. Parkinsonian features and complications of drug therapy were assessed. Most patients (22/24) died during the observation period. Neuropathological examination was confirmatory in all of the five necropsied patients.

Results: At first neurological visit dystonia was present in 11 (46%) patients all of whom had been levodopa naive at this time point. Six patients (25%) exhibited cervical dystonia (antecollis) (MSA-P n=4, MSA-C n=2), five patients (21%) showed unilateral limb dystonia (MSA-P n=4; MSA-C n=1). A definite initial response to levodopa treatment was seen in 15/18 patients with MSA-P, but in none of the six patients with MSA-C. A subgroup of 12 patients with MSA-P developed levodopa induced dyskinesias 2.3 years (range 0.5–4) after initiation of levodopa therapy. Most patients had peak dose cranio-cervical dystonia; however, some patients experienced limb or generalised dystonia. Isolated peak dose limb chorea occurred in only one patient.

Conclusion: The prospective clinical study suggests that dystonia is common in untreated MSA-P. This finding may reflect younger age at disease onset and putaminal pathology in MSA-P. Levodopa induced dyskinesias were almost exclusively dystonic affecting predominantly cranio-cervical musculature. Future studies are required to elucidate the underlying pathophysiology of dystonia in MSA.
LIMB DYSTONIA
GENETICS

THREE PTS WITH MUSICIAN’S DYSTONIA
7 RELATIVES WITH WRITER’S CRAMP

Dominantly transmitted focal dystonia in families of patients with musician’s cramp

Abstract—Musician’s dystonia is generally considered a sporadic disorder. We present three families with the index patient affected by musician’s dystonia, but other forms of upper limb focal task–specific dystonia (FTSD), mainly writer’s cramp, in seven relatives. Our results suggest a genetic contribution to FTSD with phenotypic variability, including musician’s dystonia.

NEUROLOGY 2006;67:691–693

A. Schmidt, MA; H.-C. Jabusch, MD; E. Altenmüller, MD, MA; J. Hagenah, MD; N. Brüggemann, MD; K. Hedrich, PhD; R. Saunders-Pullman, MD, MPH; S.B. Bressman, MD; P.L. Kramer, PhD; and C. Klein, MD

CASE PRESENTATION

- 49 Y/O VIOLONIST WITH 2 YEARS OF INVOLUNTARY FLEXION OF LEFT 4\textsuperscript{TH} AND 5\textsuperscript{TH} FINGER WHILE PLAYING VIOLIN
- NO MVMT ELSEWHERE
- ONLY OCCURS WHILE PLAYING VIOLIN
MUSICIANS DYSTONIA
KEYBOARD DYSTONIA
TREATMENT

- ONABOTULINUM TOXIN INJECTED AS FOLLOWS WITH EMG GUIDANCE:
  - 5 U FLEXOR DIGITORUM SUPERFICIALIS
  - 5 U FLEXOR DIGITORUM PROFUNDUS

INTO APPROPRIATE FINGER FASCICLES
Flexor Digitorum Superficialis
PIP Flexion

Flexor Digitorum Profundus
DIP Flexion

Perotto A. Anatomical Guide For The Electromyographer.
LIMB DYSTONIA
NEUROLOGIC EVALUATION

- Identify and carefully describe the dystonia:
  - Body region(s) involved, severity, spread at rest, during tasks that elicit dystonia and any modulating factors
  - Sort out compensatory movements and sensory tricks from primary pattern of dystonia

- Take into account:
  - Detailed subjective history of complaint
  - Palpate limb during abnormal movement
  - EMG assistance in identifying areas of excessive muscle activity
LIMB DYSTONIA
NEUROLOGIC EVALUATION 2

▪ THOROUGH NEUROLOGIC EVALUATION/EXAM
  – PARTICULARLY PARKINSONIAN FEATURES, SPASTICITY, LOCALIZING PERIPHERAL NERVE OR ROOT ABNORMALITIES
  – EMG/NCS FREQUENTLY ORDERED
  – CNS NEUROIMAGING (BASAL GANGLIA/THALAMUS)
  – FURTHER STUDIES AS CLINICALLY WARRANTED
CASE PRESENTATION

- 68 Y/O CF W/ 8 YR HX OF FOOT CRAMPING AND INVOLUNTARY MOVEMENTS OF HER TOES ON WALKING
- EVAL BY PODIATRY- MANY SURGERIES W/OUT IMPROVEMENT
- INTERFERED WITH WALKING BUT O/W QUIESCENT
TREATMENT

- TRIALS OF ONABOTULINUM TOXIN VIA EMG GUIDANCE OFFERED NO BENEFIT ON MULTIPLE OCCASIONS
- FLEXOR DIGITORUM BREVIS, LONGUS-10U INTO DIGIT 3+4, FLEXOR HALLUCIS LONGUS 10U, FLEXOR HALLUCIS BREVIS 5U
- TREATED WITH PT, FOOT ORTHOTIC AND ORAL MEDICATIONS
- LORAZEPAM .5MG TID, LIORESAL 5 MG TID, TRIHEXYPHENIDYL 2 MG BID
46YO WITH R FOOT DYSTONIA AND RUE COGWHEEL RIGIDITY
LIMB DYSTONIA TREATMENT

- ROUTINE THERAPIES INCLUDE A MULTIDISCIPLINARY EVALUATION WITH OCCUPATIONAL HAND THERAPIST FOR POTENTIAL RETRAINING AND USE OF WRITING DEVICES

- UNFORTUNATELY ABOUT 50% WHO SWITCH TO USING THE UNAFFECTED/NON-DOMINANT SIDE DEVELOP SIMILAR DYSTONIA/WC
LIMB DYSTONIA TREATMENT

- Medications including anticholinergics, benzodiazepines, etc.
- EMG guided botulinum toxin injections. Literature predicts flexion and pronation respond best, tremor poor response.
- Sensorimotor re-training.
- Literature suggests limb immobilization for 5 weeks, sensory training (learning Braille), low frequency, repetitive TMS.

PENAGAIN

- WRITER’S CRAMP
Modified pen grip in the treatment of Writer’s Cramp

Barbara Baur *, Thomas Schenk, Waltraud Fürholzer, Johanna Scheuerecker, Christian Marquardt, Georg Kerckhoff, Joachim Hermsdörfer

Clinical Neuropsychology Research Group (EKN), Krankenhaus München-Bogenhausen, Dachauerstrasse 104, 81925 München, Germany

Abstract

Writer’s Cramp (WC) is a focal, action-related dystonia, which induces hypertonic co-contractions and severely impairs handwriting. One behavioral treatment approach is the handwriting training developed by Mai and Marquardt (1999). [Schreibtraining in der neurologischen Rehabilitation. In EKN-Materialien für die Rehabilitation Dortmund: Bergmann] which includes among various motor exercises the use of a modified pen grip (stabilized between index and middle finger). This pen grip has proven particularly successful in clinical practice. The current study aims at elucidating the immediate effects of the modified pen grip on writing in 23 WC patients and 11 healthy controls. All participants wrote a sentence with their usual and also with the modified pen grip. Movement and pressure were recorded with a digitizing table. Pressure, movement time for the whole sentence, script size and writing fluency were analyzed. When writing with their usual pen grip, pressure in the WC patients was elevated, and writing speed was decreased compared to healthy controls. Changing over to the modified pen grip reduced the pressure significantly in WC patients and controls, but left other aspects of their writing unaffected. This shows that the use of the modified pen grip is an effective way to normalize pen pressure in WC patients, thereby providing the best conditions for the training of speed and fluency.

© 2006 Elsevier B.V. All rights reserved.

Fig. 1. (A) Conventional (normal) and (B) modified pen grip demonstrated by a healthy control participant.

Motor Training as Treatment in Focal Hand Dystonia