

## Correspondence

### Progression of dystonia in complex regional pain syndrome

**To the Editor:** Oaklander's report<sup>1</sup> of a patient with complex regional pain syndrome (CRPS) in addition to a movement disorder is an excellent example of the value of videotape publications.

The patient is described as having progressive right lower extremity dystonia and tremor in the contralateral foot. That the movements began abruptly after vein stripping is stated as evidence that neither psychological factors nor disuse could have caused the movements, hence their organic nature as part of CRPS.

Psychogenic movement disorders can be difficult to diagnose and neurologists and other physicians are often reluctant to make the diagnosis despite well-established criteria.<sup>2,4</sup> In contrast to Oaklander's claim, the abrupt onset of a movement disorder is a clue about a psychogenic etiology, as is adult-onset dystonia beginning in the lower extremity. Another clue is the presence of more than one movement disorder. Furthermore, there is controversy about the organic etiology of posttraumatic movement disorders, such as following vein stripping. The videotape provides additional evidence: the patient exhibits a fixed dystonic posture of the right foot (another feature suggestive of psychogenic dystonia) with an atypical low amplitude, high frequency tremor of the involved foot (not typical of dystonic tremor) and an equally atypical "bouncy" whole-leg tremor of the contralateral lower extremity.

The historical and physical features of this patient support a psychogenic movement disorder. This report should not be used as evidence that movement disorders are an accepted part of the complex regional pain syndrome.

Stephen G. Reich, MD, William J. Weiner, MD, *Baltimore, MD*

**To the Editor:** We read with interest Oaklander's description of a "healthy" 35-year-old woman with a progressive and eventually fixed right foot plantarflexion-inversion dystonia.<sup>1</sup> The videotape also demonstrates an irregular, low amplitude tremor in the right foot and a very regular plantarflexion-dorsiflexion tremor of her left foot that was thought to represent spread of her condition to the contralateral leg. We believe the clinical features of the patient's tremor are most consistent with psychogenic tremor as is possibly her entire condition.

The syndrome of CRPS associated with development of fixed dystonia has been termed causalgia-dystonia syndrome.<sup>5</sup> Fixed dystonias were recently reviewed by Schrag et al.,<sup>6</sup> and up to 37% of the 41 prospectively followed patients in this series met diagnostic criteria for psychogenic dystonia, and 29% fulfilled DSM-IV diagnostic criteria for somatization disorder.<sup>6</sup> In contrast, only two patients were previously diagnosed with somatization disorder in this series,<sup>6</sup> indicating that physicians frequently do not label patients with these psychiatric diagnoses despite evidence that they meet the diagnostic criteria. The majority of psychiatric diagnoses in this series were only evident after review of the primary care records and a structured neuropsychiatric interview.<sup>6</sup> Many patients with psychogenic movement disorders lack overt psychiatric features on initial assessment and patients with "neurologically unexplained symptoms" may frequently misreport their prior diagnoses.<sup>7</sup>

The patient's fixed right foot dystonia is typical of other psychogenic dystonias in that her foot is held in a plantarflexed and inverted posture.<sup>8</sup> Unfortunately, in fixed dystonia, it is difficult to distract patients from maintaining a fixed posture, unlike psychogenic tremor, which has a continuous rhythmical movement that is difficult for the patient to maintain with various distracting maneuvers.<sup>8</sup>

The left foot plantarflexion-dorsiflexion tremor does not appear consistent with dystonic tremor, Parkinsonian tremor or other forms of organic foot tremor. We suspect a psychogenic origin. In 6 of 41 fixed dystonia patients followed prospectively by Schrag et al, tremor was noted in other body parts, and often had psychogenic features (distractibility, variable frequency and amplitude, and entrainment).<sup>6</sup> Unfortunately, these were not specifically sought in the present case.

While the organic versus psychogenic nature of causalgia-dystonia continues to be debated, clinicians should be suspicious of additional psychogenic features and previously unknown psychiatric disorders in patients with this disorder.

John C. Morgan, MD, PhD, Kapil Sethi, MD, FRCP,  
Anthony E. Lang, MD, FRCPC, *Augusta, GA*

**Reply from the Author:** CRPS is a "pain-plus" syndrome of pathologic limb pain and autonomic dysfunction persisting after trauma. Many patients lack signs of nerve injury (atrophy, dropped reflexes, abnormal EMG/NCS). Some have motor symptoms, commonly fixed limb-dystonia. This paucity of objective signs understandably leads many physicians (including Drs. Morgan et al.) to suspect that CRPS is a psychiatric or psychological rather than a neurologic disorder. Fortunately, data are beginning to replace dogma.

Pathologic examination of tissues from CRPS-affected limbs has demonstrated subtle focal axonal degeneration primarily of nociceptive/autonomic axons.<sup>9,10</sup> Although CRPS patients, like all chronic-pain sufferers, often develop secondary psychological difficulties, prospective study has found no increased psychopathology among patients who developed CRPS/dystonia after fracture than in control subjects who did not.<sup>11</sup>

Some people develop chronic pain, acquired distal limb dystonia (ADLD), or both as unconscious symptoms of psychiatric illness, and others consciously feign them for gain, but this can occur with any symptom. Even though some patients have proven pseudo-seizures, it does not imply that all epilepsy is psychogenic. The situation is analogous here, and the real task is to develop tools to differentiate patients with neurological CRPS and "pseudo-CRPS" to improve treatment of both. A recent report by Schrag et al.<sup>6</sup> provides much-needed data. In a sample of 41 fixed dystonia patients, 90% with ADLD (20% of whom also met CRPS criteria), 42% had "psychogenic dystonia" according to either DSM-IV criteria or those of Fahn and Williams,<sup>3</sup> but 58% did not. My patient belongs to this latter group.

I agree with Dr. Reich and others that abrupt onset is more typical of "pseudo-CRPS" than neurologic CRPS, which is why I interpret these serial photos demonstrating gradual progression from early and subtle symptoms to severe CRPS/dystonia as evidence against pseudo-CRPS in this patient. Schrag's data fails to support Reich's dogma that all dystonias other than classical childhood-onset axial dystonia (COAD) are likely to be psychogenic. It appears increasingly likely that ADLD is a different condition than COAD. Similarly, the data confirm that ADLD affecting lower limbs is less common than upper limb ADLD,<sup>6</sup> but this does not imply that lower-limb cases are more likely pseudo-CRPS. Patterns of use, injury, and patient referral may also contribute.

I also disagree with Reich that mixed movement disorders imply psychological causation, since mixed symptoms also appear in non-controversial dystonias such as Meige syndrome. Otherwise-unexplained symptoms alone cannot be sufficient to diagnose psychological disturbance. To do so risks circular reasoning. The term used above, "psychogenic movement disorder," is not a diagnostic classification (DSM-IV). All movement, both normal and disordered, is psychologically influenced. This patient's dystonia was fixed, but her tremor was intermittent, precipitated by anxiety, cold, or pain exacerbations. It was unusually severe during videotaping, which followed lumbar puncture.

Detailed psychological data had already been obtained, but space constraints had precluding mentioning them in my original report.<sup>1</sup> A psychologist had already established that neither this patient's dystonia nor her CRPS met either DSM IV or Fahn & Marsden criteria.<sup>3</sup> Somatization had been excluded by absence of previous unexplained complaints or false or inconsistent signs or symptoms. Conversion disorder, where a symptom develops to unconsciously protect from psychological conflict, had been excluded by absence of psychological motivators, and by long illness duration without remission. Electrophysiological testing had confirmed the presence of right-leg nerve injuries consistent with her symptoms, which would be unusual for conversion. There was no

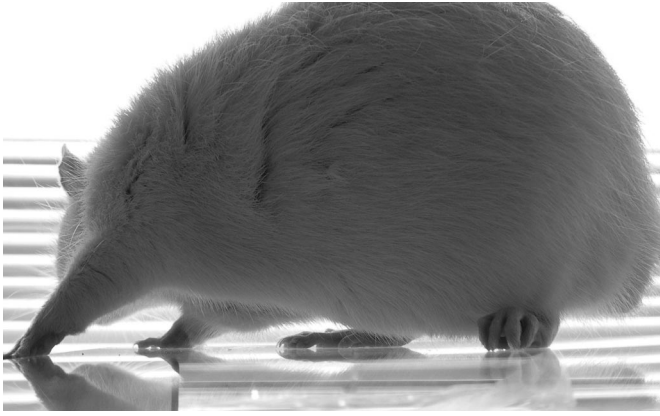


Figure. Rat with fixed hindpaw planter-flexion and hyperalgesia persisting 7 months after tibial nerve injury.

evidence that she maximized disability or sought secondary gain (malingering). She initiated and complied with treatment, and is a busy homemaker who cares for a toddler. She walks with crutches, drives, and attends yoga classes.

Our new minimal distal nerve injury (MDNI) rat model of CPRS<sup>12</sup> provides strong indirect evidence that limb injury, present in 63% of Schrag's subjects,<sup>6</sup> can produce lower-limb CRPS/ADLD. Partial or total distal tibial nerve damage can produce hindpaw hyperalgesia and fixed hindpaw planter flexion or inversion, remarkably like the symptoms of this tibial-nerve-injured patient. The figure shows an MDNI rat with hindpaw plantar-flexion and hyperalgesia persisting 7 months post-injury. The development of

animal models may finally change opinion about the cause of CRPS/ADLD.

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## Clinical characteristics of African Americans vs Caucasian Americans with multiple sclerosis

**To the Editor:** The genetic and clinical features of African Americans (AA) with multiple sclerosis (MS) reported in the article by Cree et al.<sup>1</sup> may also apply to Blacks with African genetics in the rest of the American continent. Africans, particularly West sub-Saharan Africans, were initially brought in large numbers during the late 17th century to this continent and readily intermixed with European Caucasians especially in some Latin American areas including: Caribbean islands, Central America, Venezuela, Colombia, Ecuador, Peru, and Brazil.

In Brazil, it has been reported that almost half of patients with MS (Rio de Janeiro) are “Afro-Brazilian” (mulattos) with a susceptibility locus in DQB1\*0602.<sup>2</sup> This may also suggest a European ancestry component.

Although an in-depth genetic analysis has not been completed, Colombian<sup>3</sup> and Brazilian<sup>4</sup> studies report high frequency of visual and spinal abnormalities at onset and during the course of MS and a higher frequency than expected in these groups (comparison to published data) for neuromyelitis optica.<sup>5</sup>

The Latin American Committee for Treatment and Research in MS (LACTRIMS) has identified similar clinical trends for the main racial core of Latin America: Mestizos. This group represents a complex admixture of Caucasian and American native inhabitants in whom ancestral Mongoloid genetics have been described, and that together with AA, constitute relatively recent genetic events developed over the last five centuries. According to

observations from LACTRIMS studies Mestizos appear to share genetics similar to Europeans at higher risk for MS. Studies on Genotypic responses to MS therapies among AA and Mestizos in Latin America should be encouraged considering the apparent increase in frequency of the disease in this region.

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**Note:** The author had the opportunity to respond to this correspondence but declined.

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## A fetal circle of Willis is associated with a decreased deep white matter lesion load

**To the Editor:** We read the article by van der Grond et al.<sup>1</sup> with great interest. We also examined healthy adults to determine whether fetal patterns are associated with risk factors of cerebrovascular disease and white matter lesions (WMLs).

Our study included 3,780 subjects (2,600 men and 1,180 women) who had examinations including brain MRI and 3-D time-

of-flight MR angiography (1.5 T; Hitachi Medical, Japan) between September 2003 and October 2004 at the PL Tokyo Health Care Center. Mean age (SD) of the subjects was 51.8 (11.3) years. Frequency of fetal posterior configuration of circle of Willis, deep and periventricular WMLs, and cerebrovascular risk factors were determined.<sup>2</sup> Those data were analyzed and the two groups were compared for absence or presence of fetal patterns. Fetal flows of the unilateral or the bilateral posterior cerebral arteries existed in 591 subjects (367 men and 224 women). A sex difference of fetal

patterns was seen in men (14.1 %) and women (19.0 %). Age and prevalence of hypertension, diabetes mellitus, hypercholesterolemia, obesity, and current smoking did not differ significantly between the fetal and the non-fetal group. Presence of deep and periventricular WMLs did not differ between the fetal (11.2 and 5.8%) and the non-fetal group (13.5 and 7.8%). The number of those WMLs also had no differences between both groups.

We would like to know the number of female subjects with a fetal circle of Willis in the study by van der Grond et al.<sup>1</sup> Atherosclerotic population of their study contains 210 men and 33 women in male-predominance. Logistic regression analysis adjusted with age, sex, and hypertension shows significant reduction of small- and medium-sized WMLs loads in the fetal posterior configuration group (n = 70). The selection bias of sex could contribute to WMLs load.

The number of female subjects may impact the analyses of fetal patterns and WMLs. Accumulative rates for deep WMLs are twice as high in Dutch elderly women than in men who had a history or risk of vascular disease.<sup>3</sup> Our study<sup>2</sup> showed female predominant occurrence of fetal patterns and no association between fetal patterns and asymptomatic WMLs in middle-aged healthy adults.

Further longitudinal studies in healthy and atherosclerotic disease populations are needed to evaluate whether a fetal circle of Willis can protect against appearance of WMLs.

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**Reply from the Authors:** I thank Drs. Ikeda et al. for their comments and explanation of their study in which large popula-

tion configurations of the circle of Willis were associated with the presence of WMLs. In contrast to our study,<sup>1</sup> no association between a fetal posterior variation of the circle of Willis and the presence of WMLs was found.

Ikeda et al. correctly suggest that this might be caused by a high number of females in our fetal group. Of the 70 patients in the fetal group, eight were female (173/22 in the non-fetal group, difference  $p = 0.95$ ,  $\chi^2$ ). We do not believe that this could be the explanation of differences in the results. The main difference between our study and the study by Ikeda et al. is that we included only patients with proven atherosclerosis. These subjects had a relatively high white matter lesion load, whereas Ikeda et al. performed a population study, in which it is expected that the WML load is lower.

Furthermore, differences in the way of WML scoring could also be an underlying factor in the differences between these two studies. In this respect I believe that segmentation of WMLs and subsequent outcome of a WML load in "ml," could be helpful.

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## Strokes in the subsinsular territory: Clinical, topographical, and etiological patterns

**To the Editor:** We read the recent article concerning subsinsular stroke (subIS) by Kumral et al.<sup>1</sup> with great interest. They reported 11 patients with subIS and its clinical, topographical, and etiological patterns. We studied first-ever stroke patients, and found four cases in which responsible lesions were restricted to the subsinsular territory. All our patients exhibited faciobrachiorural motor deficit only. There was no sensory impairment, dizziness, dysarthria, or dysphagia. Aphasia and aphonia were absent in our patients. All had hypertension but no prominent internal carotid (IC) stenosis or cardioembolism (CE).

At stroke onset, two patients showed transient disturbance of consciousness. Motor deficits were very mild and hemiparesis was fully recovered within a few months. Kumral et al. evaluated stroke patients with first-ever attack. We see patients with multiple cerebral infarctions whose lesions occur in the subsinsular territory, and we think restricted stroke lesion in the subsinsular territory is not uncommon. Two of four of our patients exhibited transient disturbance of consciousness. We would like to inquire whether Kumral et al.'s patients showed alternation of consciousness. There were no cases with prominent IC stenosis and CE in our patients and it is conceivable there is an ethnic difference for the underlying condition for stroke.

Prognosis is good for subIS. Stroke in the subsinsular territory<sup>2,3</sup> is not familiar to the general physician and because many internists see stroke patients in the emergency department, the possibility of subIS should be considered.

Yasuo Iwasaki, MD, Osamu Igarashi, MD, PhD, Yasumitsu Ichikawa, MD, PhD, and Ken Ikeda, MD, PhD, *Tokyo, Japan*

**Reply from the Authors:** We thank Drs. Iwasaki et al. for their interest in our article.<sup>1</sup> SubIS without involvement of the insular cortex and striatum is very rare (0.4% of patients in our registry). In more than half of our cases, there was a source of embolism originating either from the large arteries or cardiac arrhythmia.

It is conceivable that ethnic differences or other factors may play a role in the pathogenesis of subIS. The subsinsular area is a long and relatively large area beginning from the peri-caudate nucleus to the temporal horn of lateral ventricle. Faciobrachial or faciobrachiorural somatosensory symptoms may develop depending on the corticobulbaire or thalamocortical pathways involved. The insula and routes crossing this area are also responsible for volitional swallowing, gustatory functions, and speech.

There are previous reports about dysphagia, gustatory dysfunctions, and speech arrest following insular and subsinsular lesions.<sup>4,5,6</sup> Transient disturbance of consciousness exhibited by Iwasaki et al.'s patients may be the result of multiple or large infarcts involving neighboring structures which could not be seen at the early stages of ischemia by conventional MRI techniques.

There are few reports on the consciousness disturbance due to deep cerebral infarcts extending to the subsinsular region.<sup>7</sup> We agree that subsinsular stroke may not be recognized by internists or even by neurologists who do not consider stroke subgroups.

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