

The Preservation of Consciousness, Automatism, and Movement Control

SIR: The paper by Devinsky et al.¹ contains important laterality indexed information concerning the preservation of consciousness, automatism, and movement control, which deserve to be put in a more cohesive perspective. This in turn could have helped to present the data in a more scientific manner. Specifically, I am referring to the works of Serafetinides² on the role of the major hemisphere in preservation of consciousness and Serafetinides and Falconer³ on the role of the right (minor) hemisphere in speech automatism. The results of these large numbered and meticulously conducted studies have been confirmed in more recent times,^{4,5} all indicating that when a seizure occurs with speech arrest, loss of consciousness, and presence of memory of preictal events, the lesion is in the major hemisphere. As these authors recorded epileptiform EEG activity in such patients the process is epileptic by definition, and calling the process convulsive is appropriate in those in which actual convulsion is seen (majority occurring in major hemispheric lesions). To a neurologist, "nonepileptic seizure" is an oxymoron. Of course, "hysterical seizures" do occur, but if the behavior is associated with the rest of the items enumerated above and is seen with a brain lesion in either hemisphere, one must avoid using that confused and confusing terminology.

The role of laterality of movement control (alluded to above, and codified in handedness) in main-

taining the stream of conscious awareness is becoming clearer. The activating neuronal aggregate devoted to voluntary movements (otherwise called the command center in the major hemisphere) has been recently the subject of an investigation based on a review of the literature and my own data. This ensemble mediates interlimb coordination, guaranteeing the existence of a cohesive self in a brain consisting of two hemispheres. It is only when this asymmetrical interhemispheric relationship is disturbed, such as in surgical callosotomy, Marchiafava-Bignami disease, and traumatic or vascular callosotomy, that the cohesion is lost forever. Cases of ictal automatism, as mentioned above, are instances representing temporary disruption of this cohesion. All references cited indicate that only when the activating moiety (within the major hemisphere) is involved in the epileptogenesis will the person lose consciousness, as the disruptive process is conveyed to the remaining hemisphere via the callosum. Epileptic activity generated within the minor hemisphere is the source of automatisms only, as mentioned above. It cannot be generalized because the callosal traffic for movement is one-way only. This recently described anatomy forms the neural basis for handedness.⁶ One of its manifestations is the melody lead of the piano players that has been known to musicologists for more than a century. The reason for the delay of all effectors on the left side (in right handers) is the time taken for the command in the major hemisphere to reach the motor cortex on the right via the callosum.

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References

1. Devinsky O, Mesad, S, Alpers K. Non-dominant hemisphere lesions and conversion nonepileptic seizures. *J Neuropsychiatry Clin Neurosci* 2001; 13:367-373
2. Serafetinides EA, Hoare RD, Driver MV. Intracarotid sodium amobarbitone and cerebral dominance for speech and consciousness. *Brain* 1965; 88:107-130.
3. Serafetinides, EA, Falconer MA. Speech disturbances in temporal lobe lesions: A study in hundred epileptic patients submitted to anterior temporal lobectomy. *Brain* 1963; 86:333-346
4. Ebner A, Dinner DS, Noachtar S, Luders H. Automatism with preserved responsiveness: A lateralizing sign in psychomotor seizures. *Neurology* 1995; 45:61-64
5. Karlov VA, Selitskii GV, Sviderskaya NE: The trigger role of the left cerebral hemisphere in the generalization of epileptic activity. *Neurosci Behav Physiol*. 1993; 23:280-289
6. Derakhshan I. In defense of the sinistrals: Anatomy of handedness and the safety of prenatal ultrasound. *Obstet Gynecol* 2003; 21:209-212

In Reply

SIR: Dr. Derakhshan accurately summarizes the literature on temporal lobe seizures and impairment of verbal consciousness and speech automatism. Verbal consciousness is impaired by dominant temporal lobe seizures and automatic speech (resulting from preserved dominant speech cortex) occurs most often with nondominant temporal lobe seizures. However, our study concerned nonepileptic conversion seizures.

I strongly disagree with his assertion that one should never diagnose conversion symptoms or conversion disorder in a patient with a "neurological" disorder. Indeed, there is

extensive literature suggesting that patients with structural brain lesions (e.g., tumor, stroke, multiple sclerosis, trauma) or neurophysiological disorders such as epilepsy have an increased incidence of conversion disorder.¹⁻⁴ I would also disagree about any data on lateralized ictal motor automatisms and hemispheric dominance. Rather, partial seizures with lateralized ictal motor automatisms usually start from the ipsilateral hemisphere.⁵

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References

1. Barry E, Krumholz A, Bergey GK, et al. Nonepileptic posttraumatic seizures. *Epilepsia*. 1998;39:427-31
2. Eames P. Hysteria following brain injury. *J Neurol Neurosurg Psychiatry* 1992;55:1046-1053
3. Caplan LR, Nadelson T. Multiple sclerosis and hysteria. *JAMA* 1980;243:418-421
4. Devinsky O, Mesad S, Alper K. Hemisphere lesions and conversion nonepileptic seizures. *J Neuropsychiatry Clin Neurosci* 2001;13:367-73
5. Chee MW, Kotagal P, Van Ness PC, et al. Lateralizing signs in intractable partial epilepsy: blinded multiple-observer analysis. *Neurology* 1993;43:2519-25

Depression, Insomnia, and Memory Loss in a Patient With Chronic Intoxication by Inorganic Mercury

SIR: Conditions of chronic poisoning by inorganic mercury (hydrargyrisms) have been described in persons who habitually handle this material. Besides the physical symptoms, the patients present important neuropsychiatric features because the central nervous system (CNS) is the main target of mercury¹⁻⁵.

Cognitive evaluations of individuals with hydrargyrisms show disturbances that persist over the years, even after interruption of exposure to mercury¹⁻⁴. Insomnia is a symptom that also persists as a sequelae⁵. Here, the case of a patient with depression, insomnia, and recent memory loss related to the chronic intoxication by inorganic mercury is discussed.

Case Report

About 5 years ago, a 45-year-old patient without personal or familial history of psychiatric disorders started to work in a lamp factory, where he handled inorganic mercury. Some 6 months after daily contact with the metal, he started to present with gingival hemorrhage, headache, tremors of the extremities, loss of the recent memory, insomnia, and severe depression (lack of pleasure, social withdrawal, psychomotor retardation, depressive mood, feelings of worthlessness and inappropriate guilt, irritability). Even exhibiting such a condition, the patient continued to perform the same function for 1 more year. In this way, his symptoms became more intense. After a high metal dosing in his urine (only at that moment he was submitted to this exam), 105 mg/L (nl: 25mg /L), the patient was dismissed from work. Subsequent to withdrawal from exposure, the physical symptoms disappeared; however, the neuropsychiatric symptoms continued. For 3 years, the patient remained without medical care, and he was then referred to our outpatient unit. At that time, the patient did not show detectable levels of mercury in his urine. As the patient exhibited significant depressive symptoms, he was administered sertraline. While his changes of mood improved, the dose of antidepressant was increased until it reached 250 mg/day. With this dose, the patient no

longer presented with depression; however, recent memory impairment and the insomnia persisted.

Comment

Diagnosis of hydrargyrisms for this patient seems unquestionable, taking into account the characteristics of the symptoms (physical and neuropsychiatric) and mercury dosing in his urine. Further evidences are the onset of the symptoms after the exposure to inorganic mercury, worsening related to the time of exposure, and improvement of the physical symptoms soon after interruption of the exposure. Nevertheless, the neuropsychiatric symptoms continued, even after exposure ended and mercury levels in the urine became normal. This phenomenon suggests that neuropsychiatric symptoms associated with poisoning by mercury are not restricted to the acute stage of intoxication but persist as sequelae¹⁻⁵.

With antidepressant drug treatment, the patient presented remission of the depression symptoms. Notwithstanding remission of the depressive condition, insomnia and loss of memory did not improve with the use of the antidepressant. The continuation of these symptoms in this situation minimizes the possibility that they may be the outcome of the depression disorder, thus memory loss and insomnia seem to be related to the chronic poisoning by mercury in this case.

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References

1. O'Carroll RE, Masterton G, Dougall N, et al: The neuropsychiatric sequelae of mercury poisoning: the Mad Hatter's disease revisited. *Br J Psychiatry* 1995; 167:95-98
2. Soleo L, Urbano ML, Petrera V, et al: Effects of low exposure to inorganic mercury on psychological performance. *Br J Ind Med* 1990; 47:105-109
3. Powell TJ: Chronic neurobehavioral effects of mercury poisoning on a group of Zulu chemical workers. *Brain Inj* 2000; 14:797-814
4. Tirado V, Garcia MA, Moreno J, et al: Neuropsychological disorders after occupational exposure to mercury vapors in El Bagre (Antioquia, Colombia). *Rev Neurol* 2000; 31:741-742
5. Rossini SRG, Reimão R, Lefèvre BH, et al: Chronic insomnia in workers poisoned by inorganic mercury: psychological and adaptative aspects. *Arq Neuropsiquiatr* 2000; 58(1):32-38

Ziprasidone-Induced Pisa Syndrome after Clozapine Treatment

SIR: Pleurothotonus or Pisa syndrome is a rare dystonia, which was first described by Ekbom and co-workers in the early 1970s.¹ The development of Pisa syndrome is most commonly associated with prolonged treatment with typical antipsychotics. However, the illness has also been reported, although less frequently, in patients who are receiving other medications (e.g., cholinesterase inhibitors and antiemetics), in those not receiving medication (idiopathic Pisa syndrome), and in those with neurodegenerative disorders. Drug-induced Pisa

syndrome develops predominately in females and older patients with organic brain disorder.² It sometimes occurs following the addition of another antipsychotic drug to an established regimen of antipsychotics, or it insidiously arises in antipsychotic-treated patients for no apparent reason. Recently, this adversity has been associated with atypical antipsychotics, such as clozapine, sertindole, olanzapine, and risperidone.³ Clinical characteristics suggest that the underlying pathophysiology of drug-induced Pisa syndrome is complex. A dopaminergic-cholinergic imbalance or serotonergic or noradrenergic dysfunction may be implicated.² Pisa syndrome during ziprasidone therapy has not been documented in the literature. Herein, we present a case of ziprasidone-induced Pisa syndrome.

A 38-year-old female patient with schizophrenia (meeting DSM-IV criteria) developed side effects (sedation, weight gain, salivation) during clozapine treatment (275 mg/day). Because of the persisting side effects, the clozapine therapy was discontinued, and ziprasidone, 20 mg twice daily, was started. After 2 weeks, the ziprasidone dose was increased to 40 mg twice daily. On day 18, the patient developed acute truncal dystonia, with predominantly unilateral distribution that led to a left-sided lean and backward rotation, classically referred to as the Pisa syndrome. Ziprasidone was reduced to 20 mg twice daily at day 20 and discontinued on day 24, without improvement in motor abnormality. Successively, treatment with amisulpride began (day 21, 50 mg; day 24, 100 mg). Blood tests, an electroencephalogram, and a tomography (CT) of the brain revealed no abnormal findings. After an additional 14 days, the patient began responding to withdrawal;

and symptoms disappeared.

A constellation of putative risk factors for development of Pisa syndrome was found in this case: female gender and previous treatment with typical and atypical neuroleptics (the medical history revealed an approximately 9-year-long previous treatment with typical and atypical neuroleptics). We hypothesize that clozapine medication that was subsequent to a long treatment with typical neuroleptics led to dopaminergic hypersensitivity. In the cortices of rat brains, ziprasidone and clozapine are capable of increasing dopamine (DA) release⁴, and ziprasidone is an agonist at the 5-HT_{1A} receptor, which is believed to occur pre- and postsynaptically.⁵ These mechanisms might play a role in our patient, and we recommend cautious use of neuroleptic drugs in patients with risk factors.

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References

1. Ekbom K, Lindholm H, Ljungberg I: New dystonic syndrome associated with butyrophenone therapy. *Z Neurol* 1972; 202:94-103
2. Suzuki T, Matsuzuka H: Drug-induced Pisa syndrome (pleurothotonus): epidemiology and management. *CNS Drugs* 2002; 16(3):165-174
3. Stübner S, Padberg F, Grohmann R, Hampel H, Hollweg M, Hippius H, Möller HJ, Rüter E: Pisa syndrome (pleurothotonus): report of a multicenter drug safety surveillance project. *J Clin Psychiatry* 2000; 61:569-574

4. Rollema H, Lu Y, Schmidt AW, Spores JS, Zorn SH: 5-HT_{1A} receptor activation contributes to ziprasidone-induced dopamine release in the rat prefrontal cortex. *Biol Psychiatry* 2000; 48:229–237
5. Barnes NM, Sharp T: A review of central 5-HT receptors and their function. *Neuropsychopharmacology* 1999; 38:1083–1152