

Case Report of Mesial Temporal Sclerosis With Seizures and Psychosis: An Interface Between Psychiatry and Neurology

Sir: Psychiatric disorders can co-occur with seizure disorders but can also be secondary to structural lesions in the brain. These lesions are directly responsible for both the epileptic focus and psychiatric symptoms. Psychoses associated with seizures are among those of major concern to both psychiatrists and neurologists.¹ Psychosis and seizure disorders associated with structural lesions represent an area of interface between neurology and psychiatry that requires careful coordination of information and treatment. With early diagnosis, quality of life could be improved by optimizing treatment.

Case report. Ms. A is a 48-year-old woman from Guyana who was brought to the hospital in September 2005 by her home health aide secondary to her behaving in a disorganized manner, including yelling, cursing, throwing belongings out of the window, walking into traffic, praying in the middle of the street, making little sense verbally, and hearing voices of God and her dead sister. She was fearful of people being after her, looking at her, and plotting against her and expressed poor sleep and appetite.

Ms. A was reported to have a 20-year history of psychiatric symptoms and poorly controlled seizures. She described a 3-year history of domestic violence by her husband consisting of repeated head trauma with loss of consciousness before her first seizure episode at the age of 26. The patient reported that the initial seizure occurred while she was cooking; she fell on the stove and sustained burns on her face, head, and right hand, resulting in amputation of her middle finger secondary to the severity of the burns. A few months after this event, she experienced her first psychiatric symptoms, recalled as depression and psychosis.

The patient has had many psychiatric hospitalizations with poor symptom control and many hospitalizations secondary to poorly controlled seizures, all at different institutions. The patient had not been diagnosed with mesial temporal sclerosis (MTS) until this hospitalization and had not been previously scanned with magnetic resonance imaging (MRI) of the brain with contrast, nor had there been coordination between psychiatry and neurology.

The patient experienced her seizure episodes as starting focally with repetitive jerky movements of the right shoulder, which then progressed to a generalized convulsion with a duration of 2 to 4 minutes. Her aura included a funny sensation in the stomach, unusual smells, a motionless stare, and ideas of reference (words picked up from the television giving her premonition of bad things that would happen to her). The postictal period was characterized by mental confusion, memory lapses, episodes of urinary incontinence, and tongue biting.

During the course of hospitalization, Ms. A was talking without making sense and was acting irrationally, such as spitting in a cup, staring, and trying to drink it; and throwing water at the ceiling and saying, "There is a fly up there." She would sit in the lounge in a bizarre posture, talking to herself and to her dead sister. She was religiously preoccupied, holding a picture of Lord Shiva and praying most of the day. She was elated, hearing voices of God and her sister, and was delusional, saying that she could heal ill people. Her electroencephalogram (EEG) results were normal, but MRI

showed abnormal signal and volume loss within the left amygdala and hippocampus compatible with MTS.

Phenytoin, carbamazepine, valproic acid, and gabapentin had been used, in monotherapy or polytherapy (doses unknown), to treat Ms. A's seizures, with inadequate response. She continued to have 7 or 8 complex partial seizures per month, with secondary generalization. She had also received haloperidol, risperidone, and citalopram (doses unknown) in the past, for psychiatric symptoms.

On the fourth day of inpatient psychiatry admission, Ms. A had a seizure. Neurology consultation was requested, and an MRI was done. After the neurology evaluation, Ms. A was placed on treatment with 600 mg/day of oxcarbazepine and 300 mg/day of lamotrigine, which were subsequently increased to 900 mg/day and 400 mg/day, respectively, during clinic follow-ups. Her psychiatric symptoms were treated with olanzapine 7.5 mg/day and trazodone 50 mg/day. With this new combination of drugs, her seizure episodes decreased to 2 or 3 per month.

Currently, Ms. A is experiencing clusters of aura every day without seizures. Her home health services have been increased to 24 hours a day, 7 days a week. Her progress is being closely monitored to see if her seizures and psychiatric symptoms can be controlled pharmacologically without a need for surgical intervention.

Mesial temporal sclerosis is the most common pathological entity associated with refractory temporal lobe epilepsy (TLE); it is seen in as many as 60% to 80% of cases.² The etiology of MTS is still not fully understood. However, there is now considerable evidence, from both animal and clinical studies, showing that MTS is not only the cause of seizures, but also the result of seizures.³ Postictal or anoxic hippocampal damage is usually bilateral. Infiltrating gliomas cause enlargement rather than volume loss of hippocampus. There was no evidence of cortical dysplasia. Therefore, these diagnoses were excluded in this patient.

The association of psychoses with TLE is reinforced by the presence of frequent complex partial seizures^{4,5} and comorbidity with behavioral changes associated to TLE,^{4,5} both of which were present in the case we have described. Shukla et al.⁶ studied 2 comparable groups of 62 patients with TLE and 90 patients with generalized epilepsy and found a significantly higher incidence of psychosis in patients with TLE.

MRI is the radiological investigation of choice for the evaluation of patients with MTS, since it can identify structural abnormalities. However, other magnetic resonance techniques such as magnetic resonance spectroscopy and functional MRI are also being increasingly used in the diagnosis of MTS.⁷ Periodic repetition of MRI in young patients with a history of psychosis and seizures may be the most prudent step in diagnosing MTS early and improving outcome.

Not all seizures with MTS are medically intractable; 25% of the patients in one study⁸ achieved complete control while receiving medication. Poor seizure control was related to an early age at seizure onset, a history of febrile convulsions, and epileptiform discharges on the EEG.

Surgical resection is the treatment of choice in appropriate candidates who have medically refractory seizures. Approximately two thirds of patients with medically refractory MTS become seizure-free following surgical resection.⁹ As many as 95% of patients with unilateral MTS are seizure-free after surgery.

Mesial temporal lobe sclerosis contributes to a significantly compromised quality of life for many patients.³ Antiepileptic agents offer complete seizure control in some of these patients. However, with the aid of MRI and positron emission tomography scans, patients can now be selected for surgical resection, a procedure that leads to seizure control and improvement in disabling psychiatric symptoms with minimal need for medication. Studies have shown a better long-term outcome in patients with MTS receiving surgical therapy in comparison with medical therapy.¹⁰ Currently, this patient is responding to her regimen. Based on the above evidence, if seizures are not controlled satisfactorily in the future, temporal lobectomy may be an option to improve quality of life by controlling symptoms.

The authors report no financial or other relationship relevant to the subject of this letter.

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Depression or “Proper Sorrows”—Have Physicians Medicalized Sadness?

Levity of heart and neglect of our faults make us insensible to the proper sorrows of the soul. —Thomas a Kempis¹

Sir: Most patients who feel “down in the dumps,” “blue,” or depressed will first see their primary care physician—not a psychiatrist. How that family practitioner or general practitioner

sees the patient’s complaint—ordinary sadness? major depressive episode?—will have momentous implications for the patient’s health and well-being. Now, in their book *The Loss of Sadness*, Allan V. Horwitz and Jerome C. Wakefield argue that “normal sadness . . . has three essential components . . . it is context-specific; it is of roughly proportionate intensity to the provoking loss; and it tends to end about when the loss situation ends . . .”^{2(p16)} Pathological or “disordered” sadness does not conform to these criteria; it occurs without evident cause or context; it is disproportionate to the provoking loss; and it continues long after the loss situation ends. For millennia, the authors argue, symptoms of sadness that were “with cause” were separated from those that were “without cause.” Only the latter were viewed as mental disorders. With the advent of modern (DSM-III) diagnostic criteria, the authors claim, doctors began to ignore the context of the patient’s complaints and focus only on symptoms. Horwitz and Wakefield believe that this “decontextualized” approach has led to a bogus “epidemic” of pseudodepression and overtreatment with antidepressants.

Indeed, the DSM-IV criteria for major depressive disorder deliberately avoid passing judgment on whether a patient’s depressive complaints have been triggered by recent losses, with the exception of bereavement (which, somewhat arbitrarily, is limited to a period of 2 months).³ Nor do the DSM-IV criteria attempt to determine whether the patient’s sadness is proportionate to some putative triggering event. Instead, the criteria focus on symptoms of suffering and/or incapacity, such as inability to concentrate, insomnia, and impaired social-vocational function. These features must be present for at least 2 weeks.³

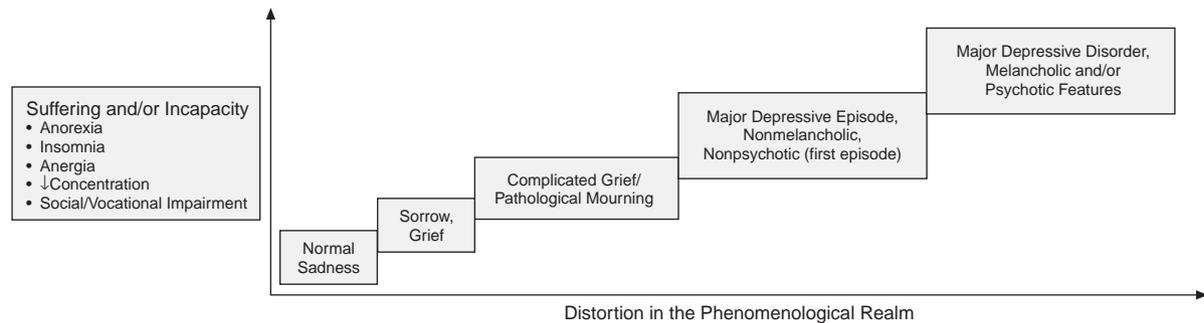
There are compelling reasons why DSM-IV has not adopted the Horwitz-Wakefield thesis. First, their thesis implies that it is fairly easy to determine whether someone with depressive complaints is reacting to a loss that has triggered the depression. Experienced physicians know this is rarely the case. A patient who suffered a stroke one month ago may appear tearful, lethargic, and depressed. Does this represent normal sadness in reaction to a psychological blow, or disruption of mood-regulating monoamine pathways in the brain? Or (more likely), is it a combination of both?

Second, Horwitz and Wakefield want to distinguish evolutionarily appropriate, adaptive “loss responses” from reactions representing malfunction of these loss mechanisms. Thus, they opine that someone “. . . who becomes deeply depressed after the death of a pet goldfish . . .” is exhibiting an “overly sensitive, disproportionate loss response [mechanism] . . .,” barring what they call “special circumstances.”^{2(p18)} To the physician, this conclusion may seem both arbitrary and value laden. Would a patient who becomes deeply depressed after the death of his golden retriever also be exhibiting a disproportionate loss response?

Perhaps most troubling is the implication by Horwitz and Wakefield that the presence of a recent major loss somehow makes it more likely that the person’s depressive symptoms will run a benign, time-limited course. To my knowledge, there are no controlled, prospective studies showing that, in a patient who otherwise meets full DSM-IV criteria for major depressive disorder, the presence of a recent loss reliably predicts a benign course. Neither does the presence of a recent loss mean that antidepressants are necessarily inappropriate (as Horwitz and Wakefield acknowledge). Indeed, work by Zisook and colleagues⁴ has shown that antidepressants may be helpful in patients with major depressive symptoms occurring shortly after the death of a loved one.

Finally, there is a dimension of depression with which neither the DSM-IV nor the Horwitz-Wakefield thesis comes to

Figure 1. The Depressive Continuum



grips—the realm of “felt experience” or *phenomenology*. Generally, when we experience sorrow, we are capable of feeling intimately connected with others. In contrast, when we experience severe depression, we typically feel outcast and alone. Sorrow, to use Martin Buber’s terms, is an *I-Thou* experience,⁵ whereas clinical depression is a morbid preoccupation with *me*. (William Styron, in *Darkness Visible*, describes depressed individuals as having “their minds turned agonizingly inward.”⁶) When we experience ordinary grief, we usually feel that, someday, it will end. In contrast, severe depression envelops us in the gloom of *permanence*. Dr. Leston Havens observes that in depression, “. . . the future is lost, and the past becomes fixed, immovable, bad, the place of irredeemable mistakes.”⁷ Indeed, the depressed individual often feels that time itself is slowed. This observation has been verified using computerized time-estimation tasks.^{8,9} Finally, unlike sorrow, severe depression often produces extreme self-deprecation or self-loathing, sometimes of delusional proportions.

Unipolar depression—which must be carefully distinguished from bipolar depression¹⁰—is best understood as lying on a continuum of dysphoric mood states (Figure 1). As we move up the vertical axis, we find increasing suffering and/or incapacity, e.g., impairment in sleep, appetite, energy, concentration, and social-vocational function. As we move from left to right along the horizontal axis, we find increasingly severe distortions in the phenomenological realm. If the patient’s suffering and/or incapacity are great, and there is severe distortion in the phenomenological realm, the question of a recent external trigger becomes moot: *the patient must be treated*. Yes, sadness is a normal part of life, as are “proper sorrows.” And, yes, normal sadness should not be “medicalized,” but neither should suffering and incapacity be “normalized” at the expense of treating a potentially lethal disorder.

Dr. Pies reports no financial affiliation or other relationship relevant to the subject of this letter.

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Correction

In the letter to the editor “Diagnosis of Nonorganic Monoplegia With Single-Pulse Transcranial Magnetic Stimulation” by Spyros N. Dettoreos, M.D., Ph.D., and colleagues (*Prim Care Companion J Clin Psychiatry* 2008;10[5]:414), an author’s name was incorrect. The fourth name in the byline should be Elissaios Karageorgiou, M.D., without a middle initial.

The online version of the letter has been corrected.

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