A cry for help: Treating involuntary emotional expression disorder

Pharmacotherapy can lessen the impact of uncontrollable laughing or crying

Mrs. R, a 68-year-old retired teacher, is referred to you for suspected mania after a closed head injury from a car accident. The referring physician reports that Mrs. R experienced mild anterograde amnesia that has resolved, but she continues to suffer from “persistent mood swings as evidenced by substantial inappropriate laughter.”

Mrs. R is not manic. Her mood is normal, with a relatively euthymic affect. When asked about her accident or injury, however, she breaks into bouts of laughter that appear to be uncontrollable and last up to several minutes. These episodes include respiratory changes that make her laughter nearly indistinguishable from crying. Mrs. R explains that the episodes occur every time she discusses the accident—regardless of her efforts to prevent them—and complains they are extremely frustrating and embarrassing. She avoids situations that might trigger the episodes.

Patients with involuntary emotional expression disorder (IEED)—a neurologic disorder that manifests as brief bouts of uncontrollable crying, laughing, or both—may appear to have bipolar disorder, schizophrenia, depression, or another psychiatric disorder. Careful evaluation, however, can distinguish IEED from other conditions. Managing the disorder requires an understanding of IEED phenomenology, including:

- neurologic conditions that result in IEED
- underlying pathology
- diagnostic criteria
- effective treatments.

continued

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Treating IEED

Clinical Point
If a patient presents with symptoms that suggest IEED, first determine the neurologic condition that is causing them.

<table>
<thead>
<tr>
<th>Table 1</th>
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<tbody>
<tr>
<td><strong>Neurologic conditions associated with IEED</strong></td>
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<tr>
<td>Amyotrophic lateral sclerosis</td>
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<tr>
<td>Multiple sclerosis</td>
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<tr>
<td>Traumatic brain injury</td>
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<tr>
<td>Stroke</td>
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<td>Alzheimer’s disease</td>
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<td>Frontotemporal dementia</td>
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<td>Parkinson’s disease</td>
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<td>Progressive supranuclear palsy</td>
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<tr>
<td>Multiple systems atrophy</td>
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<tr>
<td>Wilson’s disease</td>
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<tr>
<td>Normal pressure hydrocephalus</td>
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<tr>
<td>Olivopontine cerebellar atrophy</td>
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Source: Reference 7

<table>
<thead>
<tr>
<th>Table 2</th>
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<tbody>
<tr>
<td><strong>Is it IEED? Diagnostic criteria</strong></td>
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<tr>
<td><strong>Presence of brain damage</strong></td>
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<tr>
<td>Episodes of involuntary emotional motor output that:</td>
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<tr>
<td>• represent a change from normal emotional reactivity</td>
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<tr>
<td>• are independent or in excess of provoking stimuli</td>
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<tr>
<td>• result in clinically significant distress or social or functional impairment</td>
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<td><strong>Disorder is not:</strong></td>
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<tr>
<td>• better accounted for by another neurologic or psychiatric disorder</td>
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<tr>
<td>• caused by a physiologic substance</td>
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Source: Reference 1

Brain dysfunction alters affect
IEED was introduced as an inclusive term, replacing previous nomenclature such as pathologic laughing and crying, pseudobulbar affect, affective lability, and emotional incontinence.1

IEED can present as episodes of laughter, as in Mrs. R’s case, but more commonly manifests as bouts of crying. Other presentations include a combination of laughing and crying, but episodic outbursts of other emotions that are out of the patient’s control—such as anger—can be included in this syndrome.2 IEED episodes can lead to embarrassment, frustration, and anger that eventually can affect mood and often cause patients to avoid social interaction.3

IEED can occur in any condition that damages and affects the brain areas critical to emotional motor output (Box 1).4,5 The broad pattern of lesions that can result in IEED stems from many disease states. IEED is often observed in amyotrophic lateral sclerosis (ALS), multiple sclerosis (MS), stroke, and traumatic brain injury. It also may occur in dementia, Parkinson’s disease, and other disorders (Table 1).6

Diagnosis can be elusive
Although IEED is not included in DSM-IV-TR, recently developed diagnostic criteria can help distinguish it from other disorders (Table 2).1 As with DSM-categorized disorders, IEED must result in clinically significant distress or impairment in social or occupational function and must not be better accounted for by another disorder or caused by a physiologic substance.

The patient must present with symptoms caused by brain dysfunction from brain injury or neurodegenerative disease. Underlying brain damage might not be apparent when the patient first presents, but to our knowledge no case of idiopathic IEED has been described. If a patient presents with symptoms thought to be IEED, first determine what underlying neurologic condition is causing the symptoms and optimally manage this disorder.

To be considered IEED, the patient’s symptoms must represent a change from his or her normal emotional reactivity. When interviewing patients and their families, compare the patient’s current emotional reactivity with that from when he or she was free of all disease symptoms. Such considerations are important because a patient may have a life-long condition in which he or she is prone to emotional displays—such as essential crying—that is distinct from IEED.8

Symptoms must be incongruent with or in excess of the person’s underlying mood and independent or in excess of the provoking stimulus. Inappropriateness of the emotional response is the hallmark of IEED.
**Box 1**

**IEED: A consequence of brain pathology**

Damage to the descending inputs to the pontomedullary area once referred to as the faciorespiratory center is most likely to result in release of bulbar function and, subsequently, involuntary emotional expression disorder (IEED). Therefore, because of the progressive upper motor neuron degeneration associated with amyotrophic lateral sclerosis (ALS), nearly 50% of ALS patients will eventually demonstrate pathological affect. The lesions that can result in IEED are diffuse, however, and have been described in a review of IEED neuroanatomy as including a cortico-limbic-subcortico-thalamo-ponto-cerebellar network. Single lesions to white matter structures—such as the internal capsule—and gray matter structures—such as the thalamus, hypothalamus, basal ganglia, cerebellum, and several cortical locations—have been associated with IEED. Bilateral lesions are more likely to produce the disorder than single lesions.

With such varied neuroanatomic substrates, predicting the underlying neurochemical pathology of IEED is difficult. Among the neurotransmitters considered in IEED pathology and treatment are serotonin, glutamate, and dopamine. The sigma-1 receptor system may also play a role.

**IEED episodes** have characteristic clinical features (*Table 3*). They are brief—lasting seconds to minutes—and sudden in onset and conclusion. Episodes are likely to be stereotyped in severity and presenting type within patients, as well as in the triggering stimulus or set of stimuli. For example, patients often experience episodes when asked about the syndrome. In severe cases, patients experience episodes with any interpersonal contact. Some characteristics support—but are not essential for—an IEED diagnosis:

- **Autonomic symptoms**, such as flushing of the face and increased salivary production during episodes
- **Pseudobulbar signs**, such as increased jaw jerk, exaggerated gag reflex, dysarthria, and dysphagia
- **Other emotional outbursts**.

**CASE CONTINUED**

**Reaching a diagnosis**

After thoroughly interviewing Mrs. R, you exclude mood disorders such as depression or bipolar disorder. The paroxysmal, episodic nature of her emotional outbursts and the consistency of the eliciting stimulus, suggest IEED.

**Distinguishing IEED from depression.**

Physicians may be quick to diagnose a patient with consistent, recurrent crying as having a depressive disorder. In IEED, the patient’s family commonly (and inappropriately) will confirm this misperception, even if the patient claims otherwise. The hallmark distinctions between depression and IEED are:

- **Duration of crying**
- **Associated mood state**.

Major depressive disorder (MDD) is a persistent change in a patient’s mood lasting weeks to months, accompanied by feelings of guilt, helplessness, hopelessness, and worthlessness, apathy, and anhedonia. IEED is paroxysmal, with uncontrollable changes in affect without a corresponding sudden mood change. Patients may report mood changes during episodes, but between episodes return to an euthymic affect.

Patients who suffer from MDD, however, are not excluded from an IEED diagnosis. In 1 small study, almost one-half of patients with IEED also had major depression. Differentiating these syndromes—even in patients who suffer from both—is important to ensure proper management and patient and

**Table 3**

**Characteristics of IEED episodes**

<table>
<thead>
<tr>
<th>Paroxysmal, sudden onset with rapid offset</th>
<th>Brief (up to several minutes)</th>
<th>Stereotyped across patients (may manifest in similar fashion from patient to patient)</th>
<th>Stereotyped within patients (episodes often have similar type, severity, and eliciting stimuli)</th>
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Table 4

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<th>IEEED: Evidence for antidepressants</th>
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<td>Drug</td>
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<tr>
<td><strong>Tricyclics</strong></td>
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<tr>
<td>Amitriptyline</td>
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<tr>
<td>Nortriptyline</td>
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<tr>
<td><strong>Selective serotonin reuptake inhibitors</strong></td>
</tr>
<tr>
<td>Citalopram</td>
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<tr>
<td>Fluoxetine</td>
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<tr>
<td>Paroxetine</td>
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<td>Sertraline</td>
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IEED: involuntary emotional expression disorder; PLACS: Pathological Laughing and Crying Scale

family understanding of the condition. Lastly, although IEEED is not a mood disorder, the embarrassment and frustration it causes can change a patient’s mood over time.

**Recommended treatment**

**Education.** In our experience, education is critical to help patients and family members understand IEEED and deal with embarrassment and other normal reactions they may experience. Explain that these emotional displays are not manic or psychotic episodes but periods of motor dyscontrol caused by a neurologic condition. Teach them to cope with IEEED by:
- identifying and avoiding stimuli that provoke IEEED episodes
- ignoring the episodes and continuing with usual activities.

**Antidepressants** are first-line pharmacotherapeutic agent for IEEED. Studies and case reports have shown efficacy for tricyclic antidepressants (TCAs) such as nortriptyline and selective serotonin reuptake inhibitors (SSRIs) such as fluoxetine (Table 4).²⁻⁶

These agents have IEEED-specific therapeutic effects through a mechanism independent of their antidepressant action. In patients with IEEED and depression, antidepressants may resolve IEEED while depression remains refractory.²⁻⁶ Potential drawbacks include anticholinergic effects with TCAs and sexual and gastrointestinal side effects with SSRIs. Nevertheless, these agents are the optimal first-line therapy for IEEED among currently available options.

**Other agents.** Small studies have investigated other agents, but the data are insuffi-
Box 2

2 scales for measuring IED treatment efficacy

Among scales that measure involuntary emotional expression disorder (IED) severity, 2 have been used in studies of IED therapeutic efficacy (see Related Resources): 12,20

• Pathological Laughing and Crying Scale (PLACS) developed by Robinson et al 12 is an interviewer-administered, 18-item tool that has been validated in IED patients with stroke, 12 dementia, 22 and traumatic brain injury. 23

• 7-item Center for Neurologic Study-Lability Scale (CNS-LS) is a self-report measure that has been validated in IED patients with amytotrophic lateral sclerosis 24 and multiple sclerosis. 25

Although these scales have been used primarily for research, you can use them clinically to establish a baseline severity and gauge treatment efficacy. Improved scores generally correlate with successful treatment; if a patient fails to show adequate response on 1 of these scales, consider changing treatment.

CASE CONTINUED

Effective pharmacotherapy

After diagnosing IED, you start Mrs. R. on sertraline, 50 mg/d. She experiences a nearly immediate reduction in the number of daily IED episodes. As a result, she feels more comfortable engaging in social activities. We recommend using pharmacologic therapy for IED. Patients who have the presence of underlying brain damage, IED patients likely require treatment for other chronic or progressive conditions. Choose first-line therapy based on the patient’s medication regimen and comorbid conditions, as well as the drug’s side-effect profile.

 cent to warrant recommendations for clinical practice. One study found that the novel antidepressant mitrazapine improved symptoms in 2 patients who did not respond to SSRIs. 17 In another study, levodopa therapy resulted in improvement in 10 of 25 patients. 18

A combination dextromethorphan and quinidine (DM/Q) is being evaluated for IED. This compound has demonstrated efficacy in IED patients with ALS 19 and MS 20 and is in Phase III clinical development. DM/Q is thought to be a potent activator of the sigma-1 receptor system as well as an N-methyl-D-aspartate antagonist. 21

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Effective pharmacologic intervention can greatly improve patients’ quality of life.19,20 Use scales that measure IEED severity to gauge treatment effectiveness (Box 2).21,19,20,22-25 Because treatment failure is a realistic possibility,17 you may need to try a variety of agents to determine which regimen provides the greatest efficacy and therapeutic effects.

References

Related Resources
• Involuntary emotional expressive disorder (for healthcare professionals). www.ieed.org/hp.

Drug Brand Names
- Amitriptyline · Elavil, Endep
- Citalopram · Celexa
- Dextromethorphan/quinidine · Zenxia
- Fluoxetine · Prozac
- Levodopa · Larodopa
- Mirtazapine · Remeron
- Norbuproprion · Aventyl
- Paroxetine · Paxil
- Sertraline · Zoloft

* IN PHASE II DEVELOPMENT

Disclosures
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Dr. Cummings is a consultant to Acadia Pharmaceuticals, Astellas Pharma, Avanir Pharmaceuticals, Cephalon, CoMentis, Eisai, Eli Lilly and Company, EnVivo Pharmaceuticals, Forest Pharmaceuticals, Janssen, LP, Lundbeck, Merck, Merz Pharma, Myriad, NeuroChem, Novarti, Ono Pharmaceutical Co., Pfizer Inc, and sanofi-aventis. He is a speaker for Eisai, Forest Pharmaceuticals, Janssen, LP, Lundbeck, Merz Pharma, Novartis, and Pfizer Inc.

Bottom Line
Inappropriate emotional response is a hallmark of involuntary emotional expression disorder (IEED). If a patient’s symptoms suggest IEED, determine the neurologic condition that is causing the symptoms and optimally manage that disorder. Pharmacotherapy with tricyclic antidepressants or selective serotonin reuptake inhibitors can improve patients’ symptoms and quality of life.