

Understanding involuntary emotional expression disorder

Abstract

Involuntary emotional expression disorder (IEED) is a syndrome of disinhibition of emotional expression characterized by uncontrollable episodes of crying or laughing or other emotional displays, without an apparent stimulus to trigger such a response. IEED occurs secondary to a number of neurologic conditions. The cause of IEED is unclear but it is generally thought to result from an injury to the neurologic pathways that control emotional expression. Published estimates place the number of people with IEED at approximately 1.5 million in the United States alone. At-risk populations for IEED include patients with multiple sclerosis, amyotrophic lateral sclerosis, dementias including Alzheimer's disease, Parkinson's disease, stroke and traumatic brain injury. Theories regarding the mechanism of IEED vary, but suggest a dissociation between experienced feelings and motor responses resulting from neurostructural damage. Some theories have implicated the glutamatergic and monoaminergic neurotransmitter systems, which appear to be involved in the regulation of expression of emotions. Symptoms of IEED can be severe and lead to embarrassment, anxiety and depression, and social isolation. Presently no medications have been approved by the FDA for the treatment of IEED. Current treatment focuses on the use of selective serotonin reuptake inhibitors, tricyclic antidepressants, and dopaminergic agents. However, the safety and efficacy of these agents have not been evaluated in large controlled clinical trials. New agents designed specifically for treatment of IEED are in development.

Introduction

Involuntary emotional expression disorder (IEED) is a neurologic condition characterized by uncontrolled or exaggerated episodes of crying or laughing or other emotional displays without an apparent stimulus to trigger such responses.^{1,2} IEED is associated with a number of neurologic conditions. It is considered to be a disorder of disinhibition of emotional expression rather than a disturbance of feeling, and is distinct from mood disorders in which feelings of happiness and sadness can also lead to uncontrollable laughing or crying.³ Characteristics of IEED have been described in the medical literature for more than a century,⁴ but the neuropathologic cause of the disorder remains unclear. There is, however, general agreement that IEED is the result of an injury to the neurologic pathways that control the expression of emotions.⁵

Prevalence estimates place the number of people with IEED at around 1.5 million in the United States alone.⁶ However, given the fact that IEED is a relatively common disorder among patients with various neurologic conditions, its actual prevalence may be higher.⁶ Furthermore, IEED is generally thought to be under-recognized and undertreated because clinicians are unfamiliar with the disorder.⁶ In addition, the language clinicians use to describe disorders of affect and disorders of mood does not clearly distinguish between the two.

Several terms have been previously used to describe IEED, including pseudobulbar affect, emotional lability, emotional incontinence, and pathological laughing and crying. This has led to confusion and inconsistency within the scientific literature,^{6,7} with preferences in terminology tending to vary among clinical specialties. Certain terms used imply a neurological basis for the disorder while others suggest a psychiatric basis. The disorder will be referred to here as IEED, an umbrella term meant to encompass all of the nomenclature historically used to describe this disorder.

At-risk populations

IEED is commonly associated with a number of neurologic diseases, including multiple sclerosis (MS), amyotrophic lateral sclerosis (ALS), Parkinson's disease (PD), dementias including Alzheimer's disease (AD), as well as stroke and traumatic brain injury (TBI) (Table 1). IEED tends to occur in patients with ALS as the disease progresses. However, it does not appear to be related to the duration of the disease, but rather is more common among those patients with symptoms suggestive of bulbar involvement, such as speech and swallowing difficulties.^{2,7} In MS, IEED is more closely associated with the later chronic progressive stages of the disease, and with mental deterioration and physical and neurological disability.¹⁰

Table 1. Prevalence of IEED in selected neurologic conditions

Condition	Patients with IEED (%)
Multiple sclerosis	10 ²
Amyotrophic lateral sclerosis	49 ²
Alzheimer’s disease	39 ⁸
Stroke	34 ⁹
Traumatic brain injury	11 ¹

Clinicians have also observed IEED in patients with AD. One study of 103 consecutive patients with AD of mainly mild-to-moderate intensity of 2-4 years duration found that 40 (39%) of them had IEED.⁸ IEED is also one of the most commonly reported syndromes after a stroke, with prevalence rates of between 11% and 52%.² In one study that evaluated 148 stroke patients at 2 to 4 months post stroke, 50 (34%) patients were found to have IEED.⁹

Similarly, IEED has been reported in patients with TBI. Results of one study of 92 consecutive TBI patients (mainly mild-to-moderate closed head injury) found that 10.9% of patients had IEED during the first year after injury. The study also found that patients with IEED were significantly more depressive, anxious, aggressive, and socially dysfunctional compared with those without IEED.¹ Results of another study of patients with TBI showed IEED was associated with more severe head injuries and closely related additional neurological features that suggested pseudobulbar palsy.²

Other neurologic conditions with which IEED has been associated include Wilson’s disease, syphilitic pseudobulbar palsy, and various encephalitides.²

Neuropathologic features and clinical presentation

IEED is a syndrome of disinhibition of affect caused by an underlying neurological condition involving neurostructural damage that leads ultimately to a disconnection or lack of close coordination between feeling and motor responses (Figure 1).⁶ Its precise pathophysiology and the neuropathologic basis for the disorder remain unclear.⁵ Theories regarding the cause of IEED vary. In his classic 1924 paper, SA Kinnear Wilson hypothesized that the cause of IEED was a loss of cerebral control due to bilateral corticobulbar motor tract lesions that resulted in the disruption of neural networks leading to involuntary laughing and crying.¹¹

More recently, Parvizi et al proposed an alternative hypothesis for the mechanism of IEED, suggesting that it is the result of dysfunctioning circuits involving the cerebellum that influence brainstem nuclei and the cerebral cortex. It is this disruption of the cerebellar modulation of affective display that causes involuntary episodes of emotional expression, such as laughing and crying.³

Although their theories regarding the underlying mechanism of IEED differ, both Wilson and Parvizi seem to suggest that this dissociation between feelings that are experienced and motor responses is the result of neurostructural damage.

Symptoms of IEED can be severe, with persistent and unremitting episodes of involuntary crying or laughing, which

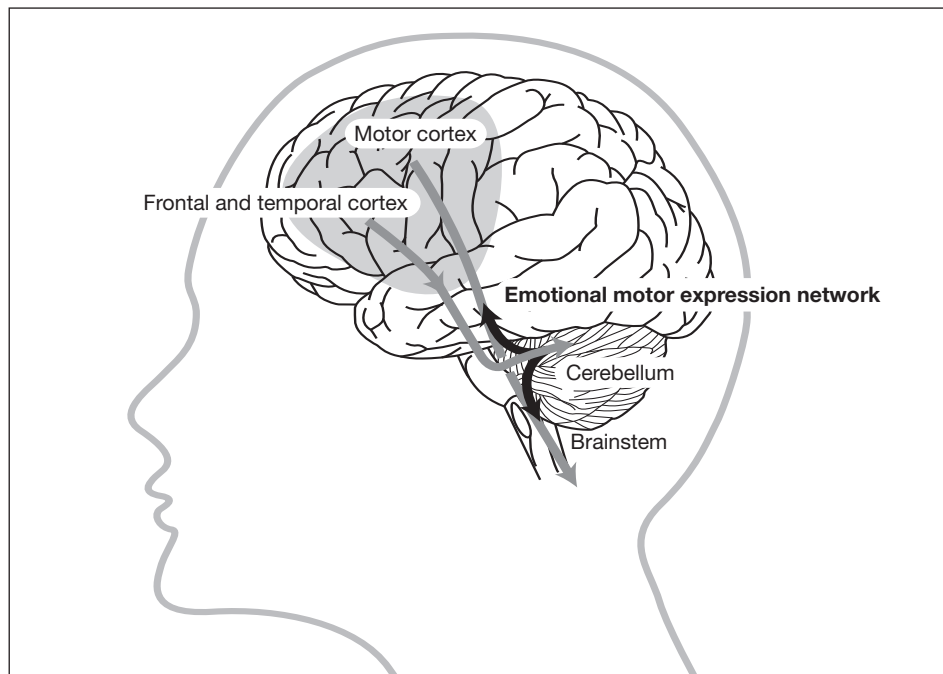


Figure 1. Emotional motor expression network

may in turn lead to embarrassment, anxiety and depression, and social isolation. As a result, IEED can have a significant negative impact on patients, their families and caregivers.⁶

Neurochemistry

The neurochemistry of IEED is not fully understood; however, some studies have implicated the glutamatergic and monoaminergic neurotransmitter systems, which appear to be involved in the regulation of expression of emotions and may be involved in the manifestation of IEED episodes. The hypothesis is that neurologic disease and injuries affect the excitatory action of glutamate, leading to excessive glutamatergic signaling and increased electrical activity in neurons.^{12,13}

Glutamate is the primary excitatory neurotransmitter of the central nervous system,¹⁴ including those networks that regulate emotional affect, and stabilizing or reducing glutamatergic activity may prove useful in the treatment of IEED. Glutamate activity may be regulated through sigma-1 receptor agonists and *N*-methyl-D-aspartate (NMDA) receptors.⁶ Sigma-1 receptor agonists have demonstrated fast onset of action, producing rapid modulation of serotonergic activity in the dorsal raphe nucleus and glutamatergic transmission in the hippocampus,¹⁴ and may be effective in improving the regulation of affect (Figure 2).

Low-affinity NMDA receptor antagonists (uncompetitive) also appear to stabilize the transmission of glutamate, entering the NMDA receptor-associated ion channel quickly and thereby avoiding interfering with normal synaptic activity.¹⁵ By preventing excessive glutamatergic activity, both sigma-1 receptor agonists and uncompetitive NMDA receptor

antagonists may allow for normalized glutamate-mediated excitatory transmission. Further investigation into the glutamatergic hypothesis is required; however, preliminary evidence suggests that the modulatory effects of sigma-1 receptor agonists and low-affinity NMDA receptor antagonists on glutamate activity may prove useful in the treatment of IEED.⁶

Diagnosis

As IEED occurs secondary to other neurologic conditions,⁵ it is necessary to identify the underlying condition before diagnosing IEED.⁶ In the majority of cases, the clinician evaluating the patient will already have diagnosed the primary neurologic condition. However, if a diagnosis of the underlying condition has not been established, the clinician should conduct a complete neurologic exam and possibly treat both the underlying condition and IEED.

Symptoms of IEED may appear similar to symptoms of other conditions. As a result IEED is often misdiagnosed as depression, bipolar disorder, generalized anxiety disorder, personality disorder, and, occasionally, epilepsy.⁶

Two standard rating scales are available to evaluate patients with IEED. The Pathological Laughter and Crying Scale (PLACS), a qualitative scale that measures the severity of IEED, has shown high reliability and has been used to effectively rate IEED in patients with various neurologic conditions.^{1,4} The Center for Neurologic Study-Lability Scale (CNS-LS), a short, easy-to-administer scale used to screen patients for symptoms of lability, has been shown to be effective in evaluating patients with MS and ALS.^{10,16}

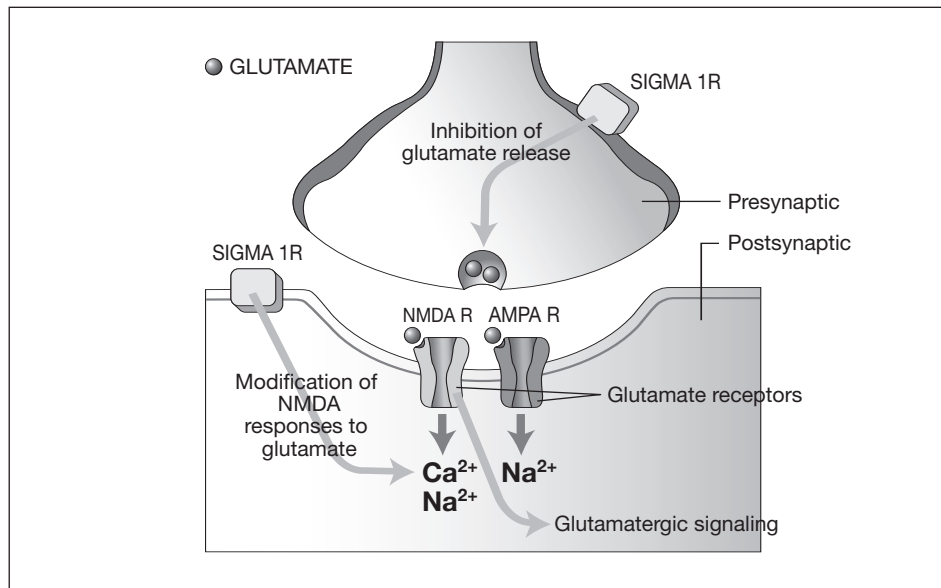


Figure 2. Synaptic activity. AMPA, α -amino-3-hydroxy-5-methyl-4-isoxazolepropionate; NMDA, *N*-methyl-D-aspartate; R, receptor

Both scales may be particularly effective for screening patients with suspected IEED and help clinicians develop a more reliable approach for identification of IEED. These scales are also useful in helping to establish baseline levels of IEED and to monitor the efficacy of treatment of the disorder.⁶ In addition to identifying and quantifying IEED in patients, clinicians need to consider the effects of the disorder on the quality of life of patients and the quality of their relationships with their families or caregivers.⁶ Clinicians are encouraged to informally evaluate the personal and social impact of IEED.

Current treatment options

Presently no medications have been approved by the FDA for the treatment of IEED. Current pharmacologic therapy focuses on the off-label use of selective serotonin reuptake inhibitors (SSRIs), tricyclic antidepressants (TCAs), and, to a lesser extent, dopaminergic agents. However, the safety and efficacy of these agents have not been evaluated in large controlled

clinical trials. New agents designed specifically for the treatment of IEED are needed and are in development.²

Summary

IEED is a syndrome of disinhibition of emotional expression characterized by uncontrollable episodes of crying or laughing or other emotional displays, without an apparent triggering stimulus to provoke such a response. It is closely associated with a number of neurological conditions, including amyotrophic lateral sclerosis, multiple sclerosis, dementias including Alzheimer's disease, Parkinson's disease, stroke, traumatic brain injury, and other disorders. Despite its prevalence, IEED is under-recognized and undertreated. Careful evaluation and diagnosis to distinguish IEED from mood disorders is critical.

New therapeutic approaches are needed in order to reduce the physical, emotional, and social impact of the disorder and improve the quality of life of patients, their families and caregivers.

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