



Pseudobulbar affect and stroke

Historical Background

Pseudobulbar affect is the original term used to describe uncontrollable episodes of laughing or crying. Patients present with an incongruity between the loss of voluntary facial movement and the unimpaired reflexive facial movements associated with spontaneous laughing or crying. Pseudobulbar palsy was first described by Lépine¹ as a lower cranial nerve palsy (i.e., inability to swallow, move the tongue, articulate, forcefully close the eyes) induced by supranuclear lesions (corticobulbar or corticopontine pathway) resulting from bilateral strokes. However, clinicians later recognized that most cases of uncontrollable laughing and crying were not associated with bilateral upper motor neuron lesions. Therefore, the term pseudobulbar affect was replaced with the more general term, pathological laughing and crying.² Pathological laughing and crying also has been referred to as pathological emotions, emotional lability, emotional incontinence, and emotionalism.³⁻⁶

The phenomenon of laughing and crying out of proportion to the underlying feelings of sadness or happiness was recognized by clinicians in the late 19th century as a common manifestation of acquired brain damage, especially stroke.⁷ However, pathological laughing and crying has been observed in a variety of neurological diseases, including multiple sclerosis, traumatic brain injury, amyotrophic lateral sclerosis, central pontine myelinolysis and hypoxic encephalopathy.⁸

Diagnosis and assessment

Poeck⁹ proposed that the diagnosis of pathological laughing and crying should be based on the existence of four characteristics: 1) response triggered by nonspecific stimuli; 2) lack of relationship between affective change and the observed expression; 3) absence of corresponding change in mood during or

lasting beyond the actual laughing and crying; 4) no voluntary control of facial expression. Although Poeck described the symptoms of pseudobulbar affect, other investigators have emphasized the absence of connection between the expression of emotion and the underlying emotional state as the central characteristic of this condition.¹⁰ The result is a lack of agreement about definitive clinical criteria for the diagnosis of pathological laughing and crying.

Investigators also have failed to agree on a method to clinically assess this disorder. Some investigators have used clinical judgment to evaluate the degree of emotional incontinence while others have counted the number of recorded episodes of crying or laughing over a specified time period.^{11,12} The only scale developed to quantify the severity of symptoms is the Pathological Laughing and Crying Scale (PLACS).¹⁰ This scale is composed of 8 questions related to laughing and 8 questions related to crying on a 4-point scale. Questions include "have the crying episodes been controllable by you?" and "have the crying episodes been in excess of feelings of sadness?" In 67 stroke patients rated by experienced clinicians as having pathological emotions, a score of 13 or greater on the PLACS had a sensitivity of 88%, specificity of 96%, and positive predictive value of 83%. PLACS ratings correlated well with patient reports and family observations from 28 subjects ($r = 0.86$). Prevalence studies of the clinical and neuroanatomic correlates of pathological laughing and crying have come mainly from studies of stroke survivors. **Table 1** lists the studies that have been conducted on pathological laughing and crying in patients with stroke. Based upon the aggregate of studies that have examined pathological emotions in stroke survivors, the estimate of the prevalence of pathological emotions following stroke is 14.9%.

However, investigators have estimated the range from 7% in a community study of patients one year following stroke¹³ to 48.5% among patients with acute stroke.¹⁴

Clinical correlates

Although the mechanisms of pathological laughing and crying remain unknown, there have been a number of interesting correlations observed between the clinical presentation and neuropathology. Poeck⁹ reviewed the pathology reports of 30 patients with pathological crying and concluded that a lesion in the supra nuclear motor pathways was a sufficient, but not necessary, condition for this disorder. Morris et al.¹⁵ found pathological emotion in 12 of 66 patients was associated with frontal or temporal lesions in either hemisphere (35% versus 11%, odds ratio 4.4, 95% CI 1.1-19.9). Andersen et al.¹² examined the pathological correlates in 12 patients divided into three groups based upon the frequency of crying episodes. The group with the most frequent episodes had relatively large bilateral pontine lesions without hemispheric infarction. The intermediate group had relatively large bilateral anterior hemisphere lesions involving the basal ganglia or periventricular structures, and the least effected group had large unilateral subcortical lesions. In a study of 25 outpatients, Kim et al.¹⁶ found that lenticulo capsular lesions were associated with pathological emotions. In a study of 127 patients with acute stroke, Tang¹⁷ found that both depression and cortical infarctions were associated with pathological emotions. In the largest recorded study, Calvert et al.¹⁸ found that among 448 patients with acute stroke, 101 had pathological emotions (21.5%) associated with the existence of depression (38% with depression and pathological emotions, compared to 18% with only depression). Using logistic regression, pathological emotions also were associated with ideas of reference and irritability. Finally, in 145 patients at 6 months following stroke, MacHale et al.¹⁹ found that pathological emotionalism occurred in 18% and was associated with the existence of depression (i.e., 62% with pathological emotionalism and depression versus 11% with only depression, $P < .001$). Pathological emotions were also associated with right anterior lesions (OR = 5.3 95% CI 1.2=22.9, $P = .03$).

Treatment studies

In addition to the numerous studies that have described the prevalence of poststroke pathological emotions, there are four double-blind, placebo-controlled treatment trials and a total of 7 reports assessing treatment of this condition (**Table 2**). In 1993, Robinson et al.¹⁰ compared nortriptyline ($n=14$) and placebo ($n=14$) among patients approximately 8-12 months since stroke. There were no significant differences in age, gender, race, socioeconomic status, previous stroke or time since stroke. After 4 and 6 weeks ($P = .008$), patients treated with nortriptyline (75 mg weeks 3-4, 100 mg weeks 5-6) had significantly lower pathological laughing and crying based upon PLACS scores than the placebo group.

Also in 1993, Andersen et al.¹² recorded the frequency of episodes of laughing or crying of 16

subjects over 1 week, provided 3 weeks of citalopram (20 mg < age 65, 10 mg >65) or placebo followed by 1 week of washout, obtained a second week of laughing and crying measurements, and concluded with 3 weeks of crossover treatment. All 13 subjects completing the protocol had a greater than 50% reduction in the number of crying episodes, while only 2 patients responded similarly to placebo treatment. Eight patients responded within 24 hours, 3 patients within 3 days and 4 patients after 1 week.

In a study of 9 patients treated with fluoxetine (20 mg) or placebo ($n=10$) over 10 days, Brown et al.²⁰ found that, by day 3, 8 of 9 patients treated with fluoxetine had a greater than 50% reduction in the number of outbursts compared with 2 of 10 patients treated with placebo. Finally, Burns et al.²¹ compared 14 patients treated with sertraline (50 mg) and 14 patients given placebo over 8 weeks. Episodes of tearfulness were significantly decreased in 93% of the sertraline patients after 2 weeks compared with 50% of the placebo group. Combining these 4 double-blind treatment trials, there was a greater than 50% reduction in crying episodes at the end of the trial in 98% of patients receiving active treatment compared with 29.4% among placebo treated patients (Fisher exact $P < .0001$).

In summary, pathological laughing and crying is a frequent problem in patients with stroke. It occurs in about 15% of patients during the acute poststroke period and in approximately 20% of patients some time during the first year following stroke. This is a socially debilitating disorder that may occur as frequently as 100 times a day and last from a few seconds to several minutes. It is associated with the existence of depression in a significant number of cases but can occur independently of depression. The neuroanatomic correlates of pathological emotions have included both unilateral lesions of the basal ganglia, as well as lesions of the brain stem, periventricular structures and frontal or temporal cortex. Four double-blind treatment studies have demonstrated that nortriptyline, fluoxetine, citalopram and sertraline are effective in treating this clinically-important condition. Responses to treatment with fluoxetine, sertraline, and citalopram may occur within 24 hours. The doses used for treatment of this condition are similar to those used for antidepressant treatment, although some patients have been reported to respond to low doses of antidepressants.²² The cause of pathological emotions is unknown, but may involve the disruption of biogenic amine input to both the limbic and descending bulbar motor pathways. Further research is needed to determine the mechanisms of this disorder and to examine the longer-term outcome of this condition with and without treatment.

Table 14. Pathological Emotions Following Stroke

Study	N	Setting	Findings	Clinical Correlates
Murai ²³	15	Acute		Spect, lower serotonin transporter in pPath. cry group
Piamarta ¹⁴	33	Acute	Prevalence 48.5% path. cry, 57.6% depression	
Langhorne ²⁴	311	Acute & Rehab	12% emotionalism	Emotionalism correlated depression
Calvert ¹⁸	448	Acute	21.5% (101) had emotionalism, of 101 with emotionalism, -38% had mood disorder vs 18% without emotionalism	Irritability and ideas of reference associated with emotionalism
MacHale ¹⁹	55	Acute	Single lesion, 18% of depressed had emotionalism	
Allman ²⁵	30	Rehab	All had emotionalism, no subtypes found	
Tang ¹⁷	127	Acute	17.9% had emotionalism	Logistic regression: Hx of depression and cortical infarct associated with emotionalism
Kim ²⁶	25	Outpatient		Lesions < 2 cm, Lenticulocapsular stroke, 52% associated with globus pallidus (dorsal) lesion
Choi-Kwon ²⁷	70	Acute	34% had emotionalism 3 months post-stroke, resolved by 2 years	
Kim ¹⁶	148	Outpatient	34% emot. (18% MDD)	Frontal lenticulocapsular lesion associated with emotionalism
House ²⁸	128	Acute	15% emot at 1 month, 11% emot. at 1 year	
Andersen ²²	211	Acute	14% acute, 11% at 1 year, (19% overall)	
Morris ¹⁵	66	Acute	18% emotionalism	
Robinson ¹⁰	67	Acute	25% emotionalism	
Burvill ¹³	42 with MDD at 4 mo.	Community	7% (of 42) with emotionalism at 12 months.	

Overall estimate of prevalence of emotionalism is 14.9%.



*-Studies that contributed to overall estimate of prevalence of emotionalism
 Table 2. Treatment of Pathological Emotions following Stroke

Study	N	Weeks of Treatment	Rx type	Methodology	Results
Robinson* ²⁹	28	6 weeks	Nortriptyline vs. placebo	Double blind	Nortriptyline > placebo at weeks 4 & 6
Brown* ²⁰	19	10 days	Fluoxetine vs placebo	Double blind	Diminished tearfulness Fluoxetine > placebo
Burns* ²¹	28	8 weeks	Sertraline vs. placebo	Double blind	50% reduction in emotionalism Sertraline > placebo
Andersen* ¹²	13	9 weeks	Citalopram vs. placebo	Double blind Cross-over	Citalopram > placebo. all citalopram vs. 2 placebo patients had decreased crying
Sloan ³⁰	6 (5 stroke)	1 week	Fluox open label		All improved
Ramasubbu ³¹	1	4 weeks	Lamotrigine		Recovered
Derex ³²	1	8 weeks	Paroxetine		Recovered
Mukand ³³	2	Unknown	Sertraline		Both recovered

Using 3 double-blind studies: 35 of 37(94.6%) treated patients improved vs 12 of 38(31.6%) placebo patients improved. Fisher's exact test $P \leq .0001$

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