

Behaviour, physiology and experience of pathological laughing and crying in amyotrophic lateral sclerosis

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Pathological laughing and crying is a disorder of emotional expression seen in a number of neurological diseases. The aetiology is poorly understood, but clinical descriptions suggest a disorder of emotion regulation. The goals of this study were: (i) to characterize the subjective, behavioural and physiological emotional reactions that occur during episodes of pathological laughing and crying; (ii) to compare responses during these episodes to those that occur when emotions are elicited under standard conditions (watching sad and amusing emotional films, being startled); and (iii) to examine the ability of patients with this disorder to regulate their emotions under standardized conditions. Twenty-one patients with pathological laughing and crying due to amyotrophic lateral sclerosis and 14 with amyotrophic lateral sclerosis but no pathological laughing and crying were studied. Emotional measures included self-reported emotional experience, video recordings of facial reactivity and peripheral physiological responses (skin conductance, heart rate and somatic activity). Nineteen of the 21 patients with histories of pathological laughing and crying had at least one episode in the laboratory that they agreed constituted pathological laughing or crying (a total of 56 episodes were documented). Compared with viewing sad and amusing films, the episodes were associated with greater facial and physiological activation. Contrary to many clinical descriptions, episodes were often induced by contextually appropriate stimuli and associated with strong experiences of emotion that were consistent with the display. When instructed to regulate their facial responses to emotion-eliciting films, patients with pathological laughing and crying showed impairments compared with patients who did not have a history of this disorder. These findings support the idea that pathological laughing and crying represents activation of all channels of emotional responding (i.e. behavioural, physiological and subjective). Furthermore, they support previously advanced theories that, rather than being associated with general emotional hyperreactivity, this disorder may be due to dysfunction in frontal neural systems that support voluntary regulation of emotion.

Keywords: behavioural neurology; pseudobulbar affect; affective neuroscience; amyotrophic lateral sclerosis

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Introduction

Pathological laughing and crying is a dramatic disorder of emotional expression caused by neurological disease (Dark *et al.*, 1996; Zeilig *et al.*, 1996; Schiffer and Pope, 2005). The syndrome is characterized by uncontrollable outbursts of laughing and/or crying that are usually described as inconsistent with the emotions the patient feels (Poeck, 1969; Parvizi *et al.*, 2009). When describing their episodes, patients often portray themselves as crying without being sad or laughing without being amused, and as having little ability to stop an episode once it has begun (Poeck, 1969; Gallagher, 1989; Arciniegas, 2005). Pathological laughing and crying is thought to be triggered by a range of stimuli, including non-specific or neutral stimuli that would normally not produce such powerful emotional reactions (Poeck, 1969). Pathological laughing and crying can significantly decrease quality of life. For example, episodes can be highly embarrassing (e.g. laughing at a funeral) and, accordingly, many patients with the disorder curtail their social activities (Lieberman and Benson, 1977).

Pathological laughing and crying occurs in many neurological settings (e.g. multiple sclerosis, dementia, epilepsy), but it is probably most common in amyotrophic lateral sclerosis (Ironside, 1956; Gallagher, 1989; Dark *et al.*, 1996; Zeilig *et al.*, 1996; Schiffer and Pope, 2005). The close association between pathological laughing and crying, and neurological disease implicates disruption in brain systems involved in generating and/or regulating emotional expression; however, the exact mechanism by which neurological injury causes pathological laughing and crying is not understood.

One factor that has impeded progress in understanding pathological laughing and crying is the absence of clear agreed upon criteria for identifying the disorder. For example, different relationships between emotional displays and subjective emotional feelings in pathological laughing and crying have been described, with some authors reporting an absence of association between display and feeling (Poeck, 1969; Gallagher, 1989; Minden and Schiffer, 1990), others reporting that the feelings are appropriate to the display but inappropriate in magnitude (House *et al.*, 1989; Dark *et al.*, 1996) and others indicating that both of these relationships are possible (Arciniegas, 2005; Schiffer and Pope, 2005; Wortzel *et al.*, 2008; Parvizi *et al.*, 2009). The definitional issues and disparate findings raise the concern that different investigators may be studying different disorders.

Research on pathological laughing and crying could be advanced if episodes were directly assessed and systematically characterized. This would yield a more precise description and possibly improved criteria, and also provide an opportunity to investigate specific hypotheses about aetiology. Modern affective science offers approaches for reliable elicitation and measurement of emotions, and for assessment of emotion regulation that can be used to study pathological laughing and crying (Gross, 1998; Levenson *et al.*, 2008). Of course, there are challenges in studying pathological laughing and crying in the laboratory, including the unpredictability of episodes and the lack of

knowledge about standardized manipulations that would induce episodes on demand.

The goal of the present study was to examine episodes of pathological laughing and crying and emotional reactions to standard emotional stimuli under controlled laboratory conditions, using careful assessment of subjective, behavioural and physiological emotional responses. The study addresses several questions: (i) can episodes of pathological laughing and crying be reliably elicited in a laboratory environment and, if so, under what conditions?; (ii) when episodes occur, what are the attendant physiological changes and how do they relate to subjective feelings of emotion?; (iii) how do the emotional reactions in episodes of pathological laughing and crying differ from emotional reactions that occur under 'normal' emotional circumstances?; and (iv) is pathological laughing and crying associated with a measurable deficit in the ability to regulate emotion under normal emotional circumstances?

To address these questions, we studied two groups of patients with amyotrophic lateral sclerosis: one with a history of pathological laughing and crying and the other with no history of the disorder. Using patients with amyotrophic lateral sclerosis enabled us to study pathological laughing and crying in its most common pathophysiological setting and to maximize the neurological comparability of the groups.

Materials and Methods

Participants

Thirty-five patients with motoneuron disease, including amyotrophic lateral sclerosis and progressive lateral sclerosis, were recruited from the University of California San Francisco Amyotrophic Lateral Sclerosis Centre to participate in a study session at the Berkeley Psychophysiology Laboratory (<http://ist-socrates.berkeley.edu/~ucbpl/index.html>). Diagnoses were made according to established criteria (Pringle *et al.*, 1992; Brooks *et al.*, 2000). Subjects were identified as having pathological laughing and crying or not using a cut-off score of 13 or higher on the Centre for Neurological Study-Lability Scale (Moore *et al.*, 1997; Smith *et al.*, 2004), which is usually collected as part of the standard assessment at University of California San Francisco, or by clinical history if Centre for Neurological Study-Lability Scale scores were not available. Exclusion criteria included brain tumour, stroke and major depression. Prior studies have indicated that up to 50% of patients with amyotrophic lateral sclerosis show some level of cognitive impairment or dementia (Lomen-Hoerth *et al.*, 2003). Subjective emotional experience is an important component of emotional reactions and its role in pathological laughing and crying is unclear. Thus, we excluded individuals with frank dementia based on a clinical interview of the patient and an informant (if available) to ensure that self-reports would be as reliable as possible. Prior studies have also suggested that pathological laughing and crying in amyotrophic lateral sclerosis is associated with bulbar symptomatology (Ironside, 1956; Gallagher, 1989; Zeilig *et al.*, 1996). Thus, for each participant, we determined via chart review whether there was evidence of

bulbar symptomatology (tongue fasciculations, tongue slowness or weakness and dysarthria) at the time of study and at disease onset. Participants were offered \$30 for their participation.

Assessment: screening session

Prior to their laboratory session, patients participated in screening sessions at the University of California, San Francisco Amyotrophic Lateral Sclerosis Centre, in their homes or by phone. This screening session was used to verify that the patients diagnosed with pathological laughing and crying endorsed having episodes of uncontrollable emotion consistent with pathological laughing and crying, and that those without the disorder did not. The session was also used to identify topics and stimuli that, in patients' opinions, might produce episodes of pathological laughing and crying.

Assessment: laboratory session

After informed consent (using a form approved by the Committee for the Protection of Human Subjects at the University of California, Berkeley, which included the information that the session would be videotaped) patients filled out questionnaires including the Centre for Neurological Study-Lability Scale and the Beck Depression Inventory (Beck *et al.*, 1961). They were then brought into an experimental suite where they were seated and physiological monitoring devices were attached. The session included three types of assessments: (i) an interview; (ii) a series of standardized film stimuli; and (iii) an acoustic startle.

Interview

The session began with a 30–40 min interview designed to learn about the patient's episodes of pathological laughing and crying. For patients who described a history of the disorder, the interview included questions about the types of episodes (e.g. laughing, crying and both) and the contexts in which they occur. If a provocative topic or trigger was identified in the screening session, it was utilized in the interview as a stimulus for possibly provoking an episode of pathological laughing and crying. For patients not endorsing a history of pathological laughing and crying, the interview included questions asking about recent events during which they had experienced very strong emotions.

Standardized emotional stimuli

Following the interview, patients participated in a series of trials in which they watched 2–5 min film clips chosen to elicit specific emotions relevant to pathological laughing and crying, including sadness and amusement. Subjects were alone when watching films that were presented on a colour television monitor. Each trial began with a 1 min baseline period during which subjects watched a black 'X' on a featureless background and were told to relax. This was followed immediately by the film clip, and then a 1 min post-film baseline period during which subjects watched a blank screen. After each film, a self-report questionnaire was administered, as described below. In total, all patients viewed 10 films in the same order. For this report, we will focus on the analysis of six film stimuli with sad and amusing emotional content, which were thought to be most relevant to pathological laughing and crying.

Two films were presented under passive viewing conditions and four were presented along with instructions designed to invoke emotion regulation (Gross, 1998).

For passive viewing, subjects watched an amusing film (a satirical commercial from the television show 'Saturday Night Live') and a sad film (a clip from the movie 'The Champ'). Before each film, subjects were instructed simply to watch the film. Four other films were used to examine two types of regulation strategies. Two films, one amusing (another satirical commercial) and the other sad (clip from the movie '21 Grams'), were shown after suppression instructions, where subjects were told to 'hide your feelings' and to 'pretend that someone is watching you and you do not want them to be able to tell that you are feeling anything about the film'. Two more films, one amusing (skit from 'Saturday Night Live') and one sad (clip from the film 'Terms of Endearment'), were shown after reappraisal instructions, where subjects were told to 'adopt a detached and unemotional attitude' and to 'try to think about what you are seeing in such a way that you feel less emotion'.

Acoustic startle

One trial began with a 60 s period of attending to an 'X' on the television screen followed by an unwarned presentation of a 115 dB, 100 ms burst of white noise delivered using hidden speakers located directly behind the participant's head. This trial was used to assess low-level emotional reactivity.

Apparatus and measurement of emotional reactivity

We assessed three major aspects of emotional reactivity: subjective emotional experience, facial behaviour and physiological responding.

Subjective emotional experience

Two kinds of ratings were obtained: retrospective self-reports of emotional valence (positive–negative) and of particular emotions were collected after completion of the films and episodes of pathological laughing and crying, and continuous ratings of emotional valence were obtained during the films. After each film, the researcher entered the room where participants were sitting and asked them to rate the overall valence of their emotions during the film (scale of 0 to 8 with 0 = very negative, 4 = neutral and 8 = very positive) and the overall intensity (scale of 0–8, with 0 = no emotion and 8 = strongest emotion ever felt) of each of the following specific emotions: amusement/humour, anger, contentment, compassion, disgust, enthusiasm/excitement, fear, sadness, surprise and poignancy. If, at any time, the patient had a strong emotional event that was potentially an episode of pathological laughing and crying, they were asked a series of open-ended questions: (i) 'Did you just have an episode of emotion that was difficult to control?' (ii) 'Could you please describe what happened?' (iii) 'Did anything trigger the episode?' and (iv) 'How did you feel during the episode?'. They were then asked to rate the emotions they felt during the episodes using the scales described above. If a patient did not answer yes to the first question, further questions were not asked. In patients who

experienced many episodes, repeated self-reports were impractical and were discontinued after the first few episodes. Self-report was collected at least for the first episode of each type (laughing/crying) in each patient.

During films, patients provided a continuous rating of their affect by adjusting a rating dial that traversed a 180° arc, with 0° = very negative, 90° = neutral and 180° = very positive (Gottman and Levenson, 1985). Patients were instructed to adjust the dial as often as necessary so that it reflected their feelings on a continual basis.

Facial behaviour

Facial behaviour was recorded using a hidden, remotely controlled video camera. Two coders trained in the Emotional Expressive Behaviour coding system (Gross/Levenson system) (Gross and Levenson, 1993), and blinded to the pathological laughing and crying versus non-pathological laughing and crying diagnoses, were employed to code selected sections of the laboratory session in 1-s bins (selection process described below). This system quantifies 10 types of facial activity associated with emotion (happiness/amusement, disgust, fear, confusion, interest, anger, surprise, sleepy, sadness and neutral) using a 4-point scale (0 = none to 3 = strong). For each second, raters identified the dominant emotion and indicated its severity. Inter-rater agreement for this technique has been established at 0.81 (Gross and Levenson, 1993, 1997).

Physiological responding

Continuous recordings of several channels of autonomic physiology were measured using a previously described system and set of procedures (Sturm *et al.*, 2008). For this analysis, we focused on heart rate (represented as interbeat interval), skin conductance level and general somatic activity, because they sample three systems (cardiovascular, electrodermal, somatic) that are important in emotional responding.

Data reduction and analysis

The dataset for each patient was reduced in dimension by identifying episodes of pathological laughing and crying, and corresponding portions of films. Summary variables were then calculated for each of the defined periods. In addition to describing episodes of pathological laughing and crying in terms of their triggers and their subjective, behavioural and physiological characteristics, we designed two formal analyses to address hypothesis-driven questions. (i) Based on clinical descriptions of pathological laughing and crying, we hypothesized that episodes would differ from 'normal' emotional reactions, with higher levels of facial (and possibly physiological) reactivity and lower levels of subjective emotional experience. To address this, we adopted a within-subject design to compare the emotional reactivity in patients during episodes with their reactivity during films; and (ii) because pathological laughing and crying is described as a disorder of uncontrolled emotion, we hypothesized that patients with pathological laughing and crying would have impaired emotional regulation. To address this, we designed a group comparison of reactivity during films between patients with pathological laughing and crying and

non-pathological laughing and crying patients under the passive viewing and regulation conditions.

Identifying episodes of pathological laughing and crying

We used facial behaviour and self-report to identify episodes of pathological laughing and crying. An episode was defined as a strong display of laughing or crying lasting at least 10 s. Potential episodes were first located by having raters screen all 150 h of video from the sessions to identify any events of any length where strong emotions were displayed. Then, raters coded the type and intensity (0 = none to 3 = strong) of emotion in 1-s bins beginning 1 min before and ending 1 min after the event. Intensity of coded emotion had to reach a level of three for at least 10 s to be defined as an episode of pathological laughing and crying. For each episode, we then checked the self-report ratings collected during the session to ensure that it had been endorsed as an episode of abnormal, uncontrolled emotion. If not, the episode was not included for analysis. We analysed the first 30 s after the onset, and calculated reactivity as the differences between the mean facial reactivity, interbeat interval, skin conductance level and general somatic activity during episodes and the 30 s baseline period before the episodes. For patients experiencing multiple episodes, we used only the first episode (regardless of type) such that each patient contributed only once to the analysis.

Identifying emotional 'hot spots' during films

To standardize the periods of time being compared between episodes of pathological laughing and crying and films, and to ensure that episodes of pathological laughing and crying would be compared with the portions of the films eliciting the strongest emotions, we identified the 30 s portion of each film clip with the strongest emotional content. This 'hot spot' was determined using the rating dial data collected from non-pathological laughing and crying patients. For the amusing film, we used the first 30 s of the period during which the non-pathological laughing and crying patients rated themselves as feeling the most positive. For the sad film clip, we used the first 30 s during which these patients rated themselves as feeling the most negative. These periods were analysed with the same approach as in pathological laughing and crying, using the 30 s periods preceding the onsets of the films as baselines.

Physiological composite

To reduce the number of measures used for primary hypothesis testing, we created a physiological composite score of interbeat interval, skin conductance level and general somatic activity. First, Z-scores were generated with respect to the mean and standard deviation (SD) of each specific channel across all time points, conditions and patients. The Z-scores were subsequently averaged across channels to generate the composite score. Note that, (i) interbeat interval raw data were inverted so that larger values would represent increased activation similar to skin conductance level and general somatic activity; and (ii) startle physiology was treated separately because the bin size was 10 s rather than 30 s of maximal reactivity.

Hypothesis 1: within subject analysis of pathological laughing and crying versus films

Using a linear model (ANOVA), reactivity during episodes of pathological laughing and crying was compared with reactivity during the emotionally similar film (e.g. laughing episode versus amusing film, crying episode versus sad film) within subjects who had episodes of pathological laughing and crying. The models included emotion type (amusement, sadness) and context (episode, film) as repeated measures. Only the passively viewed films were included because unregulated emotion is the most appropriate 'normal' context to compare episodes. For subjective emotional experience, we compared the valence and intensity of feelings during the episodes and films as rated on the post-episode and post-film questionnaires. We also followed-up on these findings by examining the intensity of individual emotions. For facial behaviour, we used the emotion with the highest cumulative rating over the first 30s during episodes of pathological laughing and crying and film hot spots. Physiological responses were compared based on the Z-score composite.

Hypothesis 2: analysis of response to films in patients with pathological laughing and crying and those without

Using a linear model (ANOVA) reactivity to films was compared across diagnoses. The models included diagnosis as a between subject factor, and emotion type (amusing, sad) and viewing context (passive viewing, suppression, reappraisal) as within-subject factors. The primary focus of hypothesis testing was on a main effect of group. However, when any variables/factors showed statistically significant interactions with diagnostic group, the group effects were evaluated conditional on those variables. In the absence of significant interactions, the interaction term(s) were dropped from the model and a simpler model only including the associated main effects was used to quantify main effects.

Acoustic startle

As the primary facial response to the acoustic startle develops very rapidly (Davis *et al.*, 1982; Sturm *et al.*, 2006), a 2-s period after the startle stimulus was used to analyse facial reactivity. Physiological responding occurs more slowly, and so reactivity was calculated using the 10s after the startle with the 10s prior to the startle used as the baseline.

Not every patient contributed to every analysis. For comparisons of episodes of pathological laughing and crying to film viewing, only patients who had episodes of pathological laughing and crying could be included. In addition, there was one patient with pathological laughing and crying whose physiology data for film watching were lost due to computer error. One non-pathological laughing and crying subject and three subjects with pathological laughing and crying did not contribute skin conductance level data due to taking medications that interfere with skin conductance level, calibration errors and becoming

disconnected from sensors. Four participants ($n = 1$, non-pathological laughing and crying; $n = 3$, with pathological laughing and crying) were wheelchair bound and did not contribute to the general somatic activity data. The startle task was not performed on one patient with pathological laughing and crying. Two participants with pathological laughing and crying did not undergo the regulation trials. Centre for Neurological Study-Lability Scale data were available for 24 patients (12 pathological laughing and crying and 12 non-pathological laughing and crying) and Beck Depression Inventory data were available for 28 patients (16 pathological laughing and crying and 12 non-pathological laughing and crying).

Demographic and clinical variables were compared using *t*-tests for continuous variables and Fisher's exact tests for binary measures. Hypothesis testing was performed at a nominal statistical level of $\alpha = 0.05$. All analyses were conducted in Statistical Package for the Social Sciences v17 (<http://www-01.ibm.com/software/analytics/spss/>).

Results

Participants

Thirty-five patients with amyotrophic lateral sclerosis were enrolled: 21 with pathological laughing and crying and 14 without the disorder. There were no statistically significant differences between the groups in age, proportion of males or mean Beck Depression Inventory score (Table 1). In the group with pathological laughing and crying, 33% of participants had bulbar symptoms at the onset of amyotrophic lateral sclerosis as opposed to 0% in the non-pathological laughing and crying group ($P < 0.05$). Bulbar symptoms were present at the time of study in 95% of patients with pathological laughing and crying versus 64% of non-pathological laughing and crying patients ($P < 0.05$).

Characterization of episodes of pathological laughing and crying in the laboratory

Nineteen of the 21 patients with pathological laughing and crying had episodes in the laboratory. A total of 116 events (54 crying, 62 laughing) were induced. The majority ($n = 74$) occurred during the interview portion, with the rest occurring before, after or during films. Detailed self-report was available for 56 of these events, and every event in a patient with a history of pathological laughing and crying was endorsed as an episode of uncontrolled emotion similar to what they were experiencing in daily life. In the 14 non-pathological laughing and crying patients, there were only four events (in two patients) meeting our criteria for possible pathological laughing and crying, but the patients reported that these were normal reactions similar to what they would have had in the past. These subjects were kept in the non-pathological laughing and crying group. Among the patients with pathological laughing and crying, seven had at least one laughing and one crying episode, eight had only crying and four had only laughing.

Table 1 Demographics and clinical features across diagnostic groups

	Pathological laughing and crying (n = 21)	Non-pathological laughing and crying (n = 14)	Test statistics
Age (SD)	54.48 (10.28)	59.21 (11.17)	$t(33) = 1.29, P = 0.21$
Males	16	11	$P = 1.00$, Fisher's exact test
CNS-LS (SD)	19.67 (4.60); n = 12	7.92 (1.62); n = 12	$t(22) = -8.35, P < 0.01$
BDI (SD)	11.19 (5.31); n = 16	8.00 (5.75); n = 12	$t(26) = -1.52, P = 0.14$
Bulbar onset	33% (7/21)	0% (0/14)	$P = 0.027$, Fisher's exact test
Bulbar involvement	95% (20/21)	64% (9/14)	$P = 0.028$, Fisher's exact test

BDI = Beck Depression Inventory; CNS-LS = Centre for Neurological Study-Lability Scale.

Table 2 Intensities for various emotions during episodes of pathological laughing and crying

	Laughing episode, mean (SD)		Crying episode, mean (SD)	
	Self-report (n = 8)	Facial behaviour (n = 10)	Self-report (n = 8)	Facial behaviour (n = 9)
Amusement/humour	5.88 (2.03)	77.50 (10.91)	0 (0)	0 (0)
Sadness	0 (0)	0 (0)	5.63 (2.67)	74.33 (17.45)
Anger	0 (0)	0 (0)	1.25 (1.9)	0 (0)
Disgust	0.13 (.354)	0 (0)	0.38 (.74)	0 (0)
Fear	0.13 (0.35)	0 (0)	3.5 (3.02)	0 (0)
Surprise	0.88 (1.25)	0 (0)	1.50 (1.85)	0 (0)
Contentment	4.25 (1.83)	NA	0.75 (2.12)	NA
Enthusiasm/excitement	4.12 (3.04)	NA	0.50 (1.41)	NA
Compassion	1.75 (2.49)	NA	4.5 (3.07)	NA
Poignancy	0.86 (2.27)	NA	3.75 (3.151)	NA
Confusion	NA	0 (0)	NA	0 (0)
Interest	NA	0 (0)	NA	0 (0)
Sleepy	NA	0 (0)	NA	0 (0)

Reactivity in episodes

Episodes of pathological laughing and crying were associated with high levels of self-reported emotion. The mean emotional intensity was 5.75 (SD 0.54, range 0–8) for laughing episodes and 6.13 (SD 0.76) for crying episodes. Furthermore, the specific emotions reported were appropriate to the display (Table 2). The three most intense emotions during laughing episodes were amusement/humour, contentment and enthusiasm/excitement. The three emotions showing the highest intensity during crying episodes were sadness, compassion and poignancy. In terms of facial behaviour, the emotion with the highest rating for laughing episodes was amusement, and for crying episodes, the emotion with the highest rating was sadness (Table 2).

Episode triggers

In open-ended questioning after the episodes, nearly all patients identified specific triggers for events, which appeared to be contextually appropriate for 10 of the 10 crying episodes and eight of the nine laughing episodes (Table 3). The one patient who identified a trigger of unclear emotional significance said that he laughed every time he thought about drinking water, which had become a complicated process for him. There were some

patients who had very frequent bursts of laughing, not all of which had obvious precipitants.

Hypothesis 1: episodes of pathological laughing and crying are larger in terms of behaviour and smaller in terms of subjective experience than 'normal' emotion

There were no statistically significant interactions between episode type (laughing, crying) and context (episodes versus films) in any of the reactivity channels measured; thus, we focused only on direct comparisons ('main effects') of contexts (episodes versus films) using a model without fitted interactions.

The intensity of subjective emotional experience was stronger in episodes than in films [$F(1,13) = 6.02, P = 0.029$, estimated difference of 1.35, 95% confidence interval (CI) 0.16–2.54, Fig. 1A and B]. The mean valence ratings were similar for episodes and films [laughing episodes 6.13 (SD 0.76); amusing films 5.79 (SD 0.32); crying episodes 2.57 (SD 0.82); sad films 2.68 (SD 0.3), estimated mean difference across contexts of 0.54, 95% CI –1.37–1.27]. These valence ratings indicate that on the whole, patients felt

Table 3 Reported triggers

Laughing episodes
Sneezing, when told I should be quiet
Talking about things that make me laugh
Talking about what my mother looks like when she's trying to be stern
Thinking about the comedian Eddie Murphy makes me laugh
Talking about the movie 'Borat'
Talking about myself having a laughing episode in the movies and making a 'hee-haw' laugh
Talking about a scene from the movie 'The Break Up', specifically the line 'Guys in helmets, clubbing each other to Yanni's greatest hits'
Crying episodes
The image of my son playing a touching song on the piano
Talking about the death of a student I taught
Talking about Huskies in the movie 'Eight Below'
Talking about my children missing me in the future
Talking about being at a daughter's friend's wedding
Seeing pictures of my children
Talking about my disability induced by pathological laughing and crying
Talking about a friend who died of amyotrophic lateral sclerosis
Talking about difficulties for my children due to divorce
Thinking about old memories of my dog
Thinking about the Brink's alarm commercial and thinking the fear in the woman's face is my daughter
Being reminded of good times in my life
My wife talking about my situation and diagnosis

positive during laughing episodes and amusing films and negative during crying episodes and sad films.

Facial behaviour was stronger in episodes of pathological laughing and crying than reactions to corresponding films [$F(1,17) = 67.32$, $P < 0.001$, estimated difference of 50.85, 95% CI 37.79–63.91, Fig. 1A and B].

Physiological reactivity was also higher in episodes of pathological laughing and crying than films, regardless of emotion type [$F(1,16) = 35.28$, $P < 0.001$, estimated difference of 1.33, 95% CI 0.86–1.81, Fig. 1A and B].

Hypothesis 2: patients with pathological laughing and crying have deficits in emotion regulation

Several events meeting our criteria for potential pathological laughing and crying were identified during regulation trials, all occurring in patients with pathological laughing and crying. Film trials could not be stopped for formal self-report to document whether these episodes were considered by patients to be pathological laughing and crying (informally, some were endorsed after the trial as pathological laughing and crying and some not). Analyses were conducted both with and without these trials. The primary presentation of results is based on including all trials; the impact of omitting trials with potential episodes is noted.

There was a diagnosis by emotion type by regulation condition interaction for facial reactivity [$F(2,30) = 4.16$, $P = 0.020$], which was also apparent when films containing potential episodes were removed from analysis [$F(2,29) = 3.49$, $P = 0.037$]. Follow-up comparison of estimated differences between groups indicated that facial reactivity was higher in patients with pathological

laughing and crying versus non-pathological laughing and crying for amusing films during suppression (estimated difference of 21.74, 95% CI 4.76–38.67, $P = 0.014$, Fig. 3A). There was also some evidence of a difference across groups for reappraisal during amusing films, but this difference was not statistically significant (estimated difference of 11.41, 95% CI –4.08–24.9, $P = 0.094$). There was no clear difference across groups for passive viewing with a relatively small estimated difference, though the CI was wide (estimated difference of 5.35, 95% CI –9.31–20, $P = 0.46$, Fig. 3A). There were no statistically significant differences for sad films under any conditions, and sad films produced notably smaller responses than amusing films (Fig. 3B).

There were no statistically significant interactions or main effects of interest for subjective emotional experience or physiology, and physiological reactivity to films was relatively low (Figs 2 and 4). For subjective experience, patients with pathological laughing and crying appeared to show slightly more reactivity overall, and this effect approached statistical significance [$F(1,31) = 3.24$, $P = 0.082$, estimated difference of 1.09, 95% CI –0.15 to 2.33]. None of these results changed when potential episodes of pathological laughing and crying were removed from the analyses.

Acoustic startle

Estimated differences across groups for reactivity to acoustic startle were very small. There was no statistically significant difference across groups in reactivity to the acoustic startle for any measure, including subjective emotional intensity [$t(32) = -0.37$, $P = 0.971$], valence [$t(32) = 0.264$, $P = 0.794$], physiological reactivity [$t(32) = 0.993$, $P = 0.328$] or facial reactivity {surprise [$t(32) = 0.26$, $P = 0.794$], happiness [$t(32) = -0.73$, $P = 0.942$], fear [$t(30) = 1.58$, $P = 0.123$]}.

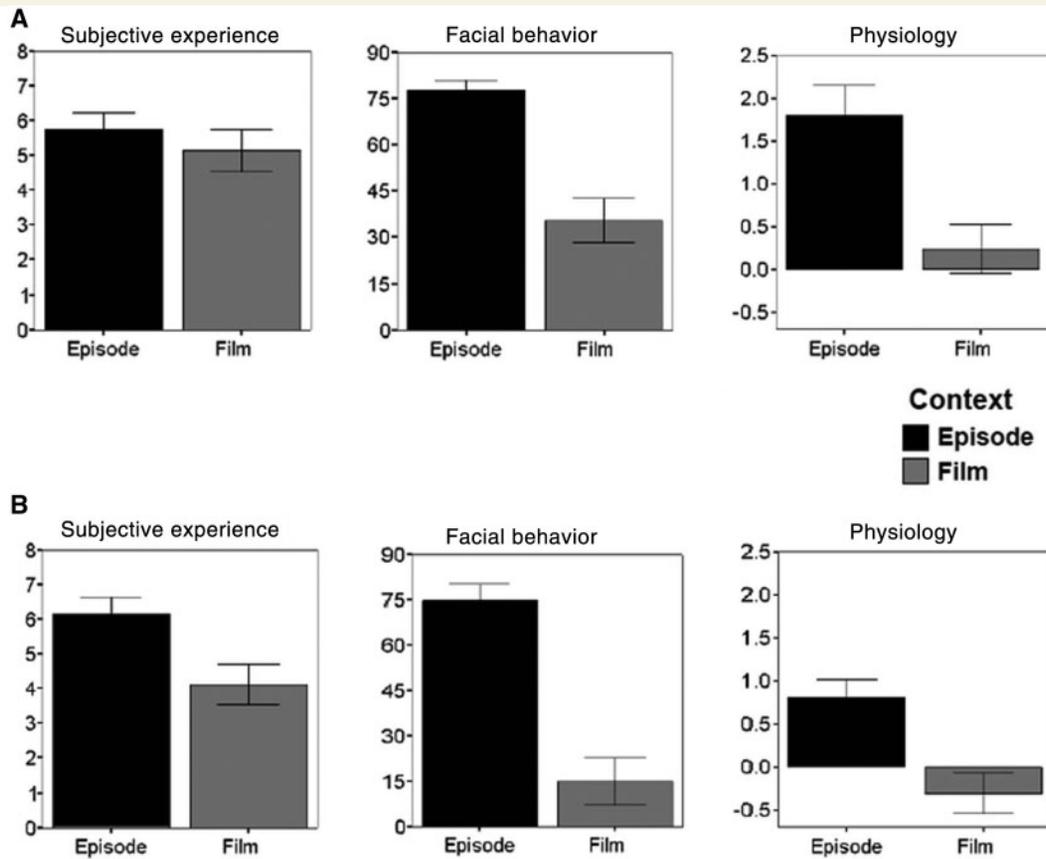


Figure 1 Plots of subjective experience, facial behaviour and physiology in patients with pathological laughing and crying for (A) laughing episodes and amusing films, and (B) crying episodes and sad films. Error bars represent standard errors.

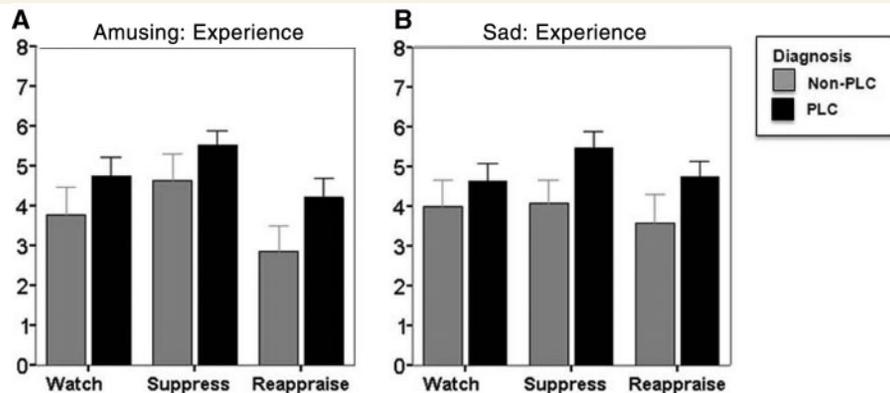


Figure 2 Plots of subjective experience in patients with pathological laughing and crying (PLC) and non-pathological laughing and crying patients in passive viewing, suppression and reappraisal conditions for (A) amusing and (B) sad films. Error bars represent standard errors.

Discussion

This first comprehensive, laboratory-based assessment of pathological laughing and crying allowed us to address several fundamental questions about the nature of the disorder. Results involving episodes of pathological laughing and crying were in some respects consistent with prior clinical observations, but in other ways surprising. Furthermore, direct assessment of emotion

regulation under standardized conditions suggested specific deficits in patients with pathological laughing and crying that support prior theories.

In a sample of 21 patients with a history of pathological laughing and crying, strong emotional outbursts were induced in 19 patients, whereas comparable events occurred in only 2 of 14 subjects with no history of pathological laughing and crying. The fact that objectively identified episodes were induced almost

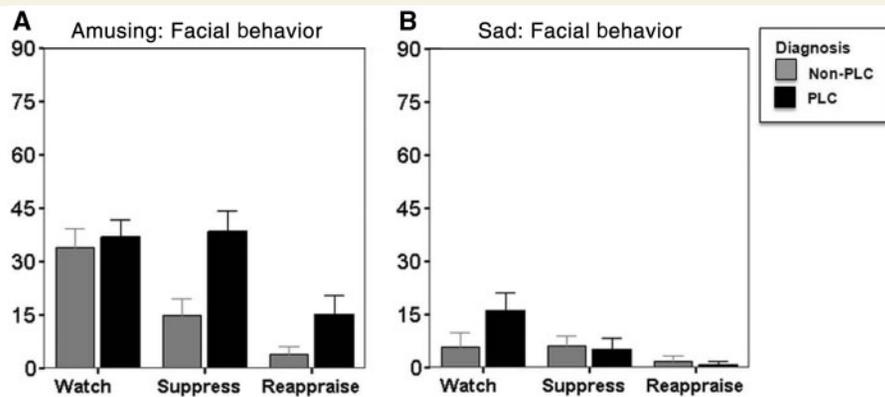


Figure 3 Plots of facial behavior in patients with pathological laughing and crying (PLC) and non-pathological laughing and crying patients in passive viewing, suppression and reappraisal conditions for (A) amusing and (B) sad films. Error bars represent standard errors.

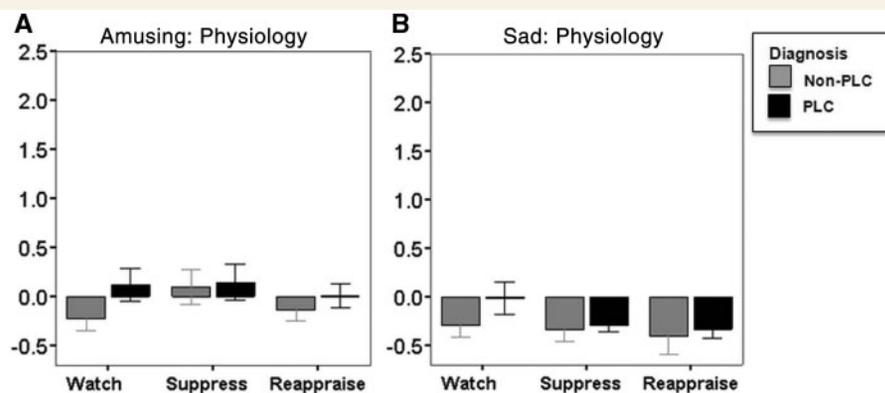


Figure 4 Plots of physiology composite scores in patients with pathological laughing and crying (PLC) and non-pathological laughing and crying patients in passive viewing, suppression and reappraisal conditions for (A) amusing and (B) sad films. Error bars represent standard errors.

exclusively in patients endorsing pathological laughing and crying, along with the fact that these events were confirmed by patients as being similar to those experienced in daily life, indicates that episodes of pathological laughing and crying can be elicited in a laboratory setting. Further, this suggests that the subjective, behavioural and physiological characteristics of these in-laboratory events are representative of the reactivity that occurs during episodes in the community. In most cases, the triggers of episodes of pathological laughing and crying were related to thoughts or stimuli that might induce crying or laughing in anyone, but in these patients the triggers resulted in rapidly developing, high intensity, uncontrollable outbursts. The specificity and reproducibility of these trigger–event relationships were remarkable in that many of the patients identified triggers during pre-session interviews that then induced episodes when they were brought up during the laboratory session. In the case of laughing, there was a greater tendency for episodes to occur without an obvious precipitant, but this is consistent with the psychology of laughing, which can normally occur in a variety of contexts, sometimes seemingly inappropriate (Askenasy, 1987).

As would be expected based on prior clinical descriptions (Poeck, 1969) as well as a single prior EMG study of pathological laughing and crying (Tanaka and Sumitsuji, 1991), facial expressions were stronger during episodes of pathological laughing and crying than during films. Physiological reactions were also stronger in episodes of pathological laughing and crying than films, which was consistent with our hypothesis as well as some prior clinical observations (Wilson, 1924). A finding that was not expected was that episodes were associated with intense reports of subjective emotional experience that were stronger than those induced by films. This finding is notably opposite to the relationship we hypothesized based on much of the pathological laughing and crying literature, which often depicts pathological laughing and crying as being unrelated, or even opposite to how the patient is feeling (Gallagher, 1989; Minden and Schiffer, 1990), although some prior authors have anticipated this finding (Wilson, 1924; Wortzel *et al.*, 2008).

The findings regarding subjective emotional experience merit additional comment. Previous studies have rarely, if ever, systematically collected self-report data immediately after observed

episodes of pathological laughing and crying. In many cases, we found that patients would begin to have a reaction during a pause in conversation, and it was only in directed questioning after the episode that the patient could describe the thoughts that led to it. If careful probing had not been pursued, one could have easily assumed that the events had no psychological precipitant. At the same time, pathological laughing and crying was not associated with a statistically significant increase in depressive symptomatology. This contrasts with some findings in the literature (House *et al.*, 1989), but reinforces the general belief that pathological laughing and crying is not a direct consequence of depression. It is also worth noting that the finding regarding subjective experience might not have emerged if we had included patients with cognitive impairment. Whether the results from our study generalize to patients with cognitive impairment would have to be addressed in other studies, but our results raise concern that studies discussing the relationship between episodes of pathological laughing and crying and subjective feelings could reach inaccurate conclusions in patients with cognitive difficulties. Given its importance for a full understanding of pathological laughing and crying, future studies should make every effort to ensure the validity of self-report data. In patients with speech difficulties, written reports could substitute for verbal reports. Control conditions could be used to help assess the validity of self-reports in cognitively impaired patients.

Our findings suggest that pathological laughing and crying, at least in amyotrophic lateral sclerosis, is much more similar to normal emotion than often depicted (Poeck, 1969), being associated with congruent activity in all major channels of emotional responding, and often being associated with contextually appropriate triggers. This conclusion is consistent with the original description of pathological laughing and crying in the medical literature by Wilson (1924) as well as some more recent descriptions (Wortzel *et al.*, 2008). However, it is also possible that the events occurred spontaneously and were assigned an appropriate feeling state and attributed to specific triggers *post hoc*. This would be consistent with models of emotion which posit that physiological activation is too non-specific to engender particular subjective feelings of emotion, and that subjective feelings are attributed to physiological activation based on the context (Schacter and Singer, 1962). As many of the triggers that produced episodes of pathological laughing and crying in the laboratory session were identified prior to that session, we think this explanation is unlikely. However, additional research will be needed to exclude this possibility.

In response to emotion-eliciting films, we found that the largest difference between patients with pathological laughing and crying and those without occurred during attempts to regulate emotion voluntarily. This finding supports the most prevalent mechanistic hypothesis about pathological laughing and crying, which incorporates the neuroanatomy of emotional processing. Normal emotional processing is dependent on a network of brain regions, including subcortical structures that generate coordinated, often automated emotional responses (e.g. brainstem, hypothalamus, amygdala, striatum), paralimbic structures that link these responses to social and motivational information (e.g. orbitofrontal, ventromedial frontal, ventral anterior cingulate and insular cortices) and dorsal brain regions that mediate voluntary regulation of emotion

(e.g. dorsal anterior cingulate and dorsolateral prefrontal cortices, hippocampus). The interactions between these regions are modulated by neurochemical systems including the serotonergic, dopaminergic and adrenergic systems (see Wortzel *et al.*, 2008 and Rosen and Levenson, 2009 for more detailed descriptions). This complex set of systems provides many pathways where disruption can lead to aberrant emotional reactivity. One particular mechanism that has been suggested to cause pathological laughing and crying is failure of the dorsolateral frontal regions to regulate lower systems in the brainstem, either because of disconnection from the brainstem or dysfunction in these dorsal systems (Wilson, 1924; Wortzel *et al.*, 2008). Functional and structural imaging experiments have indicated that emotion regulation tasks similar to those used in the current study activate dorsal frontal structures (Ochsner and Gross, 2005; Goldin *et al.*, 2008; Welborn *et al.*, 2009; Giuliani *et al.*, 2011; Kanske *et al.*, 2011; Kuhn *et al.*, 2010; Winecoff *et al.*, 2011). Thus, the inability of patients with pathological laughing and crying to use this mechanism for regulation supports the possibility that failure of these dorsolateral frontal-based mechanisms is responsible for pathological laughing and crying, at least in amyotrophic lateral sclerosis.

Some caveats regarding the specificity of our findings should be noted. Suppression and reappraisal are thought to be functionally and possibly anatomically distinct mechanisms of regulation with suppression being associated with a higher metabolic demand (Gross, 1998; Goldin *et al.*, 2008). In our study, only suppression was significantly impaired in pathological laughing and crying. Reactivity during reappraisal showed a similar pattern, with greater reactivity in patients with pathological laughing and crying than non-pathological laughing and crying patients; this difference approached statistical significance. For this reason, it is probably not wise to conclude that the deficits in emotion regulation in patients with pathological laughing and crying are specific to suppression but are likely to extend to other forms of emotion regulation as well.

In contrast to emotion regulation trials, we found that reactivity during passive viewing in patients with pathological laughing and crying did not differ from that of patients without pathological laughing and crying. This provides preliminary evidence that pathological laughing and crying is not a problem of generalized hyperactivity in the emotion systems studied. Similar findings of comparability between patients with pathological laughing and crying and those without in reactivity to the acoustic startle stimulus supports the idea that the basic mechanisms of emotional reactivity mediated by the brainstem are also intact (Koch and Schnitzler, 1997). Having said this, it is important to note that small sample sizes work against our ability to detect group differences, and this was probably reflected in relatively large CIs for some of our estimated differences. In addition, we found no statistically significant difference in reactivity between patients with pathological laughing and crying and those without the disorder for sad films under any conditions, but reactivity to sad films was generally lower than for amusing films, and this may indicate that the sad films we used were not powerful enough to elicit the pathological laughing- and crying-related regulation abnormalities. Finally, our experimental design did not include counterbalancing films across viewing conditions, thus the possibility that differences

between patient groups were specific to individual films rather than specific regulatory conditions cannot be ruled out.

Patients with pathological laughing and crying were significantly more likely to show bulbar signs and/or symptoms at the onset of amyotrophic lateral sclerosis (33%) and near the time of study (95%) than non-pathological laughing and crying patients. This is consistent with traditional neurological teaching (Poeck, 1969), and with prior studies (Ironsides, 1956; Gallagher, 1989; Zelig *et al.*, 1996; Newsom-Davis *et al.*, 1999), and provides further indirect evidence of a frontally-based impairment.

Conclusions

Direct assessment of pathological laughing and crying due to amyotrophic lateral sclerosis in a laboratory setting produced a number of important findings. First, episodes can be reliably induced in the laboratory, but this requires identification of specific triggers derived from sensitive interviewing. Secondly, the triggers and subjective experience associated with pathological laughing and crying are often quite appropriate to the emotional display (although this may be less apparent for laughter). Thirdly, normal reactivity in standard contexts combined with evidence of impaired ability to regulate emotion supports prior theories (Wilson, 1924; Wortzel *et al.*, 2008) that pathological laughing and crying is a disorder of voluntary emotion regulation rather than a state of generalized emotional hyperactivity. Fourthly, there is reason to suspect that damage to frontal brain structures in amyotrophic lateral sclerosis is responsible for pathological laughing and crying in these patients; however, additional studies will be needed to confirm this speculation, to link pathological laughing and crying directly to specific neuroanatomical and neurochemical changes and to determine if these findings generalize to diseases other than amyotrophic lateral sclerosis that cause pathological laughing and crying.

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