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Neuropsychological Rehabilitation

An International Journal

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/pnrh20

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To cite this article: Sophie Fitzgerald, Fergus Gracey, Emma Trigg & Niall Broomfield (2022): Predictors and correlates of emotionalism across acquired and progressive neurological conditions: A systematic review, Neuropsychological Rehabilitation, DOI: 10.1080/09602011.2022.2052326

To link to this article: https://doi.org/10.1080/09602011.2022.2052326

Published online: 24 Mar 2022.

NEUROPSYCHOLOGICAL REHABILITATION
https://doi.org/10.1080/09602011.2022.2052326

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Predictors and correlates of emotionalism across acquired and progressive neurological conditions: A systematic review

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ABSTRACT

Emotionalism can develop following a range of neurological disorders; however the aetiology of emotionalism is still unclear. To identify anatomical, neuropsychological and psychological predictors and correlates of emotionalism across neurological disorders: stroke, Parkinson's disease, multiple sclerosis, traumatic brain injury, Alzheimer's disease, vascular dementia and amyotrophic lateral sclerosis. To explore if these predictors and correlates of emotionalism differ across neurological disorders. A comprehensive systematic search was completed of four databases: MEDLINE, CINAHL Complete, PsycINFO and EMBASE. Methodological quality was assessed using the Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies and each study was graded according to the level of evidence using the Scottish Intercollegiate Guidelines Network. Fifty papers (participants $N = 1922$) were included. 25 studies were rated as "Fair," 21 "Good" and 4 "Poor." The review identified predictors and correlates found in several neurological disorder such as bulbar networks, serotonergic pathways, genetics and female gender. Multiple studies across diseases (stroke, MS, ALS) indicate emotionalism is associated with cognitive impairment, especially frontal deficits. Due to the disproportionate number of studies identified across neurological disorders, it is difficult to draw definitive answers. Further research is required across neurological disorders to explore similarities and differences in anatomical, neuropsychological and psychological predictors and correlates.

ARTICLE HISTORY
Received 30 March 2021
Accepted 7 March 2022

KEYWORDS
Emotionalism; Predictor; Correlate; Systematic review; Neurological disorders

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Systematic Review Registration ID: CRD42020159413

Introduction

Emotionalism, also known as emotional incontinence, pseudobulbar affect (PBA), emotional lability, pathological laughing and crying or involuntary emotional expression disorder (IEED) is a condition that arises following a range of neurological disorders, including multiple sclerosis, amyotrophic lateral sclerosis (ALS), traumatic brain injury (TBI) and stroke (Schiffer & Pope, 2005). The term emotionalism will be used for this review. Emotionalism produces a lessening of the ability to control emotional expression (House et al., 1989). It is characterized by episodes of uncontrollable crying or laughter, not under usual control and which are disproportionate or inappropriate to the social context (Ahmed & Simmons, 2013). Crying episodes are more common, with approximately 82% of individuals with emotionalism following a stroke experience crying episodes only and 2% experience laughing episodes only (Calvert et al., 1998).

Emotionalism may lead to negative consequences in terms of social and occupational functioning, such as a reduction in work productivity or activities of daily living, potentially increasing the burden which already exists due to the primary neurological disorder (Colamonico et al., 2012). Individuals with emotionalism have higher Barthel Index scores (Choi et al., 2013) and a higher degree of disability (Choi-Kwon et al., 2012). Research has found emotionalism can lead to embarrassment, increased levels of distress and social withdrawal (Wortzel et al., 2008). Additionally, emotionalism may interfere with rehabilitation and could cause a lack of willingness to engage with services (Allman, 1991; Sacco et al., 2008).

The prevalence of emotionalism varies considerably across neurological disorders, dependent on the criteria and terminology used. A systematic review and meta-analysis of 15 post-stroke emotionalisms (PSE) prevalence studies found 17% of stroke survivors suffer from PSE acutely, 20% at 6 months and 12% beyond 6 months (Gillespie et al., 2016). Research has found a prevalence rate for emotionalism in patients with multiple sclerosis to be between 10% and 46.2% (Vidović et al., 2015). Additionally, in a sample of patients with TBI, the prevalence of emotionalism was between 5% and 11% and approximately 49% in a sample of patients with ALS (Parvizi et al., 2006; Zeilig et al., 1996).

Emotionalism has been found to be co-morbid with psychiatric disorders, with research suggesting an increased likelihood for depression in individuals with emotionalism (Tang et al., 2004). Emotionalism is also under-recognised and can be mis-diagnosed for depression due to the co-occurrence of both disorders (Wortzel et al., 2008) and because of the tearful aspects central to both. An important difference is noted for depression, whereby affect is proportionate and consistent with prolonged feelings of sadness and hopelessness. In contrast, crying or laughing episodes associated with emotionalism are usually brief, subjectively uncontrollable and could be triggered by an emotional

event rather than an individual's mood (Cummings et al., 2006; Poeck, 1969). Therefore, although emotionalism and mood disorders can be co-morbid, they are different clinical entities in terms of duration and context and require different treatment strategies (Colamonico et al., 2012).

Despite the high prevalence of emotionalism across neurological disorders, the aetiology of emotionalism and underlying mechanisms remains unclear. The release hypothesis proposes that emotionalism occurs as a result of disrupted cortical inhibition to the upper brainstem centre and the release of the lower bulbar nuclei (Wilson, 1924). Other theories suggest disruptions of neurotransmitters such as serotonin or dopamine may lead to changes in emotional expression (Rabins & Arciniegas, 2007). More recently, a gate control theory proposes that damage to the corticobulbar/cerebellar pathways that regulate motor control and co-ordination of emotional expression or lesions in the frontal lobes may contribute to the development of emotionalism (Parvizi et al., 2009). Due to the limited understanding of the mechanisms of emotionalism, a systematic review is required to explore mechanisms associated with the onset and maintenance of emotionalism across neurological disorders, which could help to enhance theoretical understanding and shape clinical practice.

Multiple methods have been used to investigate the pathophysiology of emotionalism. Earlier theories or hypotheses of the pathophysiology of emotionalism were based on post-mortem studies (Bede & Finegan, 2018). More recent theories have deployed in vivo investigation methods, including neuroimaging techniques, electrophysiological responses studying event-related potentials and exploration of neurochemistry (Floeter et al., 2014). The development of more modern technology has enabled further investigations of biological predictors and correlates of emotionalism and to validate previous theories or propose alternative hypotheses.

There is a lack of reviews specifically investigating the aetiology of emotionalism, with only a few published to date. A narrative review of emotionalism explored an overview of PSE, characterized by crying and/or laughing episodes following a stroke in terms of epidemiology, pathophysiology, clinical features and therapeutic options (Girotra et al., 2018). Additionally, a literature review of the epidemiology and pathophysiology of emotionalism was progressed (King & Reiss, 2013). However, these reviews have only provided an overview and lacked a predefined protocol and not completed quality checks or assessment of bias, which highlights the methodological limitations of previous reviews meaning the results/conclusions may not be reliable or valid. Furthermore, these reviews have not explored emotionalism across neurological disorders to enable a greater understanding of this condition.

This systematic review is the first to examine emotionalism across neurological disorders investigating anatomical, neuropsychological and psychological predictors and correlates. This review is important to provide further knowledge, which could inform clinical practice and treatment whereby education

could be provided to clients and families about emotionalism. Therefore, this review is clinically important to help contribute to the development of a model to guide medical and psychological assessment, prevention and management of emotionalism across neurological disorders.

Objectives

The systematic review aimed to explore the following questions:

(1) What are the anatomical, neuropsychological and psychological predictors and correlates of emotionalism across neurological disorders: stroke, Parkinson's disease, multiple sclerosis, TBI, Alzheimer's disease, vascular dementia and ALS?
(2) Do anatomical, neuropsychological and psychological predictors and correlates of emotionalism differ across neurological disorders?

Methods

Protocol and registration

The systematic review protocol was registered with PROSPERO: International prospective register of systematic reviews (Registration ID CRD42020159413) outlining rationale, aims, search strategy and data synthesis plans. The review conforms to the guidelines outlined by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement (PRISMA; Moher et al., 2009).

Eligibility criteria

For this review the eligibility and inclusion criteria were outlined using the PICOS (Participants, Interventions, Comparisons, Outcomes and Study design) framework (Tacconelli, 2010). For this review, "comparisons" was not applicable due to the type of review questions. Due to the breadth of study designs included in this review, "intervention" was extended to "independent variable" to include interventions, predictors or correlates. Articles were included for review if they met the following eligibility criteria below.

Participants

Inclusion criteria

- Studies of emotionalism with adults (18 years or over) with a neurological disorder; stroke, Parkinson's disease, multiple sclerosis, TBI, Alzheimer's disease, vascular dementia and ALS
- No restrictions on time since onset of emotionalism.

Exclusion criteria

- Any neurological disorder not included in the inclusion criteria.

Independent variable – Intervention, predictors or correlates

For this review, predictors were defined as variables used in regression analyses that provide information on an associated dependent variable regarding a particular outcome (Salkind, 2010) and correlates were defined as a measure of the strength of the relationship/association between two variables (Bobko, 2001).

Inclusion criteria

- Biological variables (anatomical, neuropsychological)
- Psychological variables.

Outcome

Inclusion criteria

- Measure of emotionalism such as standardized Kim's criteria (Kim & Choi-Kwon, 2000), House's criteria (House et al., 1989), Center for Neurological Study – Lability Scale (CNS-LS; Moore et al., 1997), Pathological Laughing and Crying Scale (PLACS; Robinson et al., 1993), interviews or self-report questionnaires.

Study design and publication type

Inclusion criteria

- Quantitative studies
- Cross-sectional studies
- Observational
- Cohort studies
- Case-control.

Exclusion criteria

- Qualitative studies
- Reviews
- Dissertations
- Unpublished "grey" literature
- Studies not published in English language.

Context

No limits in terms of context. Studies across different settings such as hospital, residential nursing home, supported living and independent living in the community were included.

Information sources

A comprehensive systematic search of MEDLINE, Cumulative Index to Nursing and Allied Health Literature (CINAHL Complete), PsycINFO and EMBASE databases were completed for this review.

Search strategy

Boolean operators (OR, AND) were used to search each neurological disorder ("participant") with the search terms for emotionalism ("outcome") individually. For example, stroke OR "cerebr* accident" OR "cva" OR "apoplexy" AND emotionalism OR "emotional lability" OR "emotional dysregulation" OR "involuntary emotional expression disorder" OR "involuntary crying" OR "involuntary laughing" OR "lability of mood" OR "pathological laughing" OR "pathological crying" OR "pseudobulbar affect" OR "emotional incontinence" OR "pathological display of affect" OR "inappropriate laughing" OR "inappropriate crying." It was decided not to include search terms for predictors and correlates ("independent variable") as this resulted in a limited number of results in the pilot search whereby studies could be unintentionally missed or this could increase bias where certain independent variables were selected.

Keywords and Medical Subject Headings (MeSH; Rogers, 1963) were also used when completing the search strategy for each neurological disorder such as "Stroke" [Mesh].

Once the searches were completed, the title and abstracts were screened according to eligibility criteria. If a decision for eligibility was not able to be made at the title and abstract screening stage due to insufficient information, the full article was reviewed. Following this, the full texts of identified studies were further screened with reasons for exclusion noted. Reference lists of studies were hand-searched to check if any potential studies were not captured by the search strategy. A total of 25% of papers were checked by a second independent reviewer, a trainee clinical psychologist at the title and abstract stage and at full-text stage. Any discrepancies were discussed and a final decision was made. See Appendix for the full search strategy for each database.

The final search was conducted on 12th February 2021, therefore only research published up to this point was included in the review.

Data extraction

Once searches were completed, relevant data were extracted from the full papers and summarized. A data extraction template was designed to include a descriptive summary of the studies included in the review (cf. Centre for Reviews and Dissemination, 2008). This included study characteristics; authors, year, country/setting, neurological disorder ("participant"), sample size and makeup, independent variables/predictors/correlates ("independent variable"), measures of emotionalism used ("outcome"), research design ("study"), age range and study findings in relation to the review question, see Table 1.

Due to the significant heterogeneity in how emotionalism was measured and small sample sizes, a narrative synthesis was completed rather than a meta-analysis. The systematic review followed the narrative synthesis framework of Popay et al. (2006) to describe the anatomical, neuropsychological and psychological predictors and correlates of emotionalism across each neurological disorder. The narrative synthesis adopted a textual approach to summarize and explain the findings of the synthesis, explore relationships in the data and assess the robustness of the synthesis.

Assessment of methodological quality

The Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies (QATOCCS; National Heart, Lung and Blood Institute (NHLBI), 2014) was used to rate the methodological quality of the studies. This tool examined researcher bias, sample bias, sample size, time effects, accuracy and reliability of outcome measures, drop-out rates and if confounding variables were accounted for. The tool consists of 14 questions with each element rated using "yes," "no," "cannot determine," "not reported" or "not applicable." Each study was summarized and critically appraised following the rating for each item to provide an overall rating of "good," "fair" or "poor." For each study, if less than seven items were rated yes, this was classed as "poor," seven or above items rated yes this was classed as "fair" and if 10 items were rated as yes or nine with additional reasons such as not applicable this was classed as "good."

A random 25% of papers were independently reviewed by a second-rater, a trainee clinical psychologist, to increase the rigour of the quality ratings. Any discrepancies between ratings were resolved through discussions and a review of the QATOCCS guidance document.

No studies were excluded based on the quality rating, see Table 2.

Assessment of risk of bias

The Scottish Intercollegiate Guidelines Network (SIGN; Miller, 2002) was used to grade each study according to the level of evidence. The grades range from 1++

Table 1. Summary of study characteristics and data extraction.

Authors	Aim	Country /setting	Neurological disorder/s	Total number of participants (*N*) and number in subgroups (*n*)	Mean age (SD)	IV – Predictors or correlates in relation to SR question	Measure of emotionalism	Study design	Findings in relation to SR question
Anatomical variables									
Lebert et al. (1994)	Examine the relationship between hemispheric asymmetry and DAT-specific emotionalism using SPECT	France – Outpatient	Alzheimer's disease	*N* = 34 Emotionalism *n* = 8 Non-emotionalism *n* = 26	71.4 ± 10.8	Hemispheric asymmetry	Semi-structured interview with participant and carer and carer questionnaire	Cross-sectional	Frontolateral asymmetry indices were significantly lower in emotionalism-positive group compared with emotionalism-negative group
Liu et al. (2017)	Examine the global spontaneous brain activity in individuals exhibiting PLC after stroke	China – Hospital	Stroke	*N* = 36 PLC *n* = 12 Non-PLC *n* = 12 Healthy control *n* = 12	57.42 ± 5.71	ALFF and ReHo	PLACS	Case-control	ALFF in the right anterior cingulate cortex, middle temporal gyrus, parahippocampal gyrus and bilateral medial prefrontal cortex was significantly greater and ALFF in the left precentral gyrus and right superior frontal gyrus was significantly lower with patients with PLC ReHo in the left inferior temporal gyrus, middle temporal gyrus and bilateral anterior cingulate cortex was significantly greater and ReHO in the left precentral gyrus, superior frontal gyrus/supplementary motor area and right inferior parietal lobule was significantly lower with patients with PLC In patients with PLC ALFF in the right anterior cingulate cortex/ medial prefrontal cortex and parahippocampal gyrus was significantly greater and the left cerebellum posterior lobe was significantly lower Patients with PLC ReHo in the right anterior cingulate cortex/ medial prefrontal cortex and inferior temporal gyrus was significantly greater and the left dorsolateral prefrontal cortex was significantly lower
Kim et al. (2012)	Investigate whether the 5-HTT and 5-HTR2a genes are associated with PSEI independently and/or interactively	Korea – Hospital	Stroke	*N* = 276 PSEI *n* = 37 Non-PSEI *n* = 239	64.8 ± 10.3	Polymorphisms of 5-HTT and serotonin 2a receptor (5-HTR2a) genes	Participants and caregivers asked specified questions using Kim's criteria	Cross-sectional	Patients with PSEI were more likely to have an anterior stroke location (borderline statistical significance) Patients with PSEI had a significantly higher frequency of the 5-HTTLPR 5 allele compared with those without PSEI The association between 5-HTTLPR genotype and PSEI strengthened progressively with an increasing number of 5 alleles and remained significant in patients with 5/5 genotype
Haiman et al. (2008)	To characterize the electrophysiological activity and the brain structures involved in response to subjectively significant and neutral auditory stimuli, to indicate whether PBA in MS patients is limited to the motor system or involves other cortical areas associated with emotional and sensory processing	Israel – MS Clinic	Multiple sclerosis	*N* = 33 Emotionalism *n* = 11 Non-emotionalism *n* = 11 Healthy controls *n* = 11	46.6 ± 9.6	Electrophysiological activity and brain structures	CNS-LS	Case-control	Significantly distinct activation in MS with emotionalism group in the vicinity of the somatosensory and motor areas in response to neutral stimuli and at pre-motor and supplementary motor areas in response to subjectively significant stimuli Subjectively significant and neutral stimuli evoked higher current density in MS and emotionalism group
Andersen et al. (1993)	To investigate the effects of the selective serotonin reuptake inhibitor citalopram on uncontrolled crying	Denmark – Hospital	Stroke	*N* = 13 crying only	58.5	Citalopram	Semi-structured interview	Double-blind placebo-controlled	Number of daily crying episodes decreased by at least 50% in all cases during citalopram treatment compared with patients during placebo treatment The effects were rapid and pronounced in 11 patients (73%)
Prokšelj et al. (2014)	Determine platelet 5-HT concentration in AD patients with or without aggression or IEED	Slovenia	Alzheimer's disease	*N* = 49 IEED *n* = 16 Aggressive behaviour *n* = 14 Controls *n* = 19	79.3 ± 4.5	Platelet 5-HT concentrations	PLACS	Cross-sectional	Platelet 5-HT concentrations were significantly lower (2.9 times and 2.6 times) in patients with Alzheimer's Disease and co-existing IEED compared to control and patients with aggressive behaviours
MacHale et al. (1998)	Investigate the relation between lesion location and psychiatric illness after stroke	Edinburgh – Hospital	Stroke	*N* = 55 Emotionalism *n* = 26	66	Lesion location	Short emotionalism questionnaire as defined in the	Part of an RCT study	Patients with lesions in the right anterior region had a higher frequency of emotionalism at the time of psychiatric assessment when compared with any other region

				Non-emotionalism $n = 29$			Oxfordshire Community Stroke Project		
Haiman et al. (2009)	To assess the effects of DM/Q by comparing the electrophysiological activity and the brain structures involved in MS patients with PBA before and after administration of DM/Q	Israel – MS Clinic	Multiple sclerosis	$N = 12$ PBA $n = 6$ Healthy controls $n = 6$	48.6 ± 9.5	Brain activity and cortical structures	CNS-LS	Case-control	Comparisons between PBA-Pre DM/Q treatment and post-treatment indicated distinct activations in areas involved in emotional processing and high-level and associative visual processing in response to neutral stimuli Distinct activations in areas involved in emotional processing in response to subjectively significant stimuli
Tang et al. (2004)	To examine the frequency of PSEI according to two sets of diagnostic criteria and to determine the clinical and radiological correlates of PSEI in a cohort of Chinese stroke survivors	Hong Kong – Hospital	Stroke	$N = 84$ PSEI $n = 15$ Non-PSEI $n = 69$	69	Radiological correlates	Psychiatric interviews based on Kim's criteria	Cross-sectional	PSEI was associated with a younger age, previous TIA, total National Institute of Health Stroke Scale and cortical infarcts Cortical infarcts were independent predictors of PSEI
Morris et al. (1993)	To determine the frequency of emotional lability in this population and to identify factors associated with this condition	New Zealand – Hospital	Stroke	$N = 66$ EL $n = 12$ Non-EL $n = 54$	70 ± 11	Lesion location	Psychiatric assessment based on House's criteria	Cross-sectional	Marginally higher frequency of EL among patients with left hemisphere lesions than those with right hemisphere lesions Frequency of EL increased from more posterior to more anterior brain regions, a significant association that was apparent in both hemispheres Single lesions located in anterior regions of the cerebral hemispheres had four times the odds of EL than lesions located elsewhere
Brown et al. (1998)	To explore the effectiveness of fluoxetine in the treatment of post-stroke emotionalism	UK – Hospital	Stroke	$N = 19$ Emotionalism $n = 9$ Controls $n = 10$	61.4 ± 8.6	Fluoxetine	Semi-structured interview and modification of Lawson and MacLeod rating scale	Double-blind placebo-controlled	A clinically significant improvement in participants who received fluoxetine treatment compared to the placebo group
Floeter et al. (2014)	To determine the prevalence and characteristics of pseudobulbar affect in patients with primary lateral sclerosis and amyotrophic lateral sclerosis and to test the hypothesis that damage of inputs to the cerebellum, leading to cerebellar dysfunction is associated with PBA	America – Clinics	PLS and ALS	$N = 47$ PBA $n = 22$ Non-PBA $n = 25$	56.9 ± 7.1	Clinical variables and white matter tracts	Psychiatric interview with family	Cross-sectional	ALSFRS-R score and finger-tapping rates were significantly lower for patients with PBA, suggesting more impaired motor function Patients with PBA had increased mean diffusivity of white matter tracts underlying the frontotemporal cortex, the transverse pontine fibres and the middle cerebellar peduncle
Choi et al. (2018)	To examine the relationship between sex hormones and post-stroke emotional disturbances in patients with a history of stroke especially AP and EI and to investigate whether statins affect sex hormone levels or the presence of post-stroke AP/EI	Korea – Medical Centre	Stroke	$N = 40$ EI $n = 16$ Non-EI $n = 24$	61.6 ± 11.3	Hormone levels (testosterone)	Interviews with patients and caregivers	Prospective observational pilot	Total testosterone levels were significantly lower in the AP/EI group Testosterone was independently associated with the presence of AP/EI
Tang et al. (2009a)	To assess the relationship between MBs and PSEI in stroke survivors	Hong Kong – Acute Stroke Unit	Stroke	$N = 519$ PSEL $n = 74$ Non-PSEL $n = 445$	65.6 ± 9.9	Number and location of microbleeds	Psychiatric interviews based on Kim's criteria	Case control	Patients with PSEL group were more likely to have microbleeds in the thalamus as a whole, its anterior and paramedian territories and a higher number of microbleeds in the entire brain Multivariate analysis indicated microbleeds in the thalamus and MMSE were significant independent predictors of PSEL
Ghaffar et al. (2008)	To address the pathogenesis of PBA using quantitative MRI brain analyses in multiple sclerosis patients with and without PBA	Canada – Outpatient	Multiple sclerosis	$N = 28$ PBA $n = 14$ Non-PBA $n = 14$	46.6 ± 9.8	Lesion volume	Screened using Poeck's definition	Case-control	Those with PBA showed discrete differences in hyperintense lesion volume in five regions: right medial inferior frontal, right inferior parietal, left medial inferior frontal and left inferior parietal. Brainstem hypointense lesion volume was also significantly higher in PBA group A Logistic regression model identified brainstem hypointense, left inferior parietal hyperintense and left and right medial inferior frontal hyperintense lesion volumes accounted for 70% of the variance when it came to explaining the presence of PBA
Murai et al. (2003)	To clarify whether differences in serotonin neurotransmission explain the differences between PC patients with unilateral cerebral lesions and non-PC patients with similar lesions	Germany – Stroke Unit	Stroke	$N = 15$ PC $n = 6$ crying only Non-PC $n = 9$	60.2 ± 11	SERT densities	CNS-LS	Pilot	Midbrain/pons [I]β-CIT binding ratios of the PC group were significantly lower than those of the non-PC group

(*Continued*)

Table 1. Continued.

Authors	Aim	Country /setting	Neurological disorder/s	Total number of participants (*N*) and number in subgroups (*n*)	Mean age (SD)	IV – Predictors or correlates in relation to SR question	Measure of emotionalism	Study design	Findings in relation to SR question
Andersen et al. (1994)	To correlate the severity of post-stroke PC with lesion size and location as demonstrated by MRI paying particular attention to brain areas involved in serotonergic neurotransmission	Denmark	Stroke	*N* = 12 crying only	51.5	Lesion location	Based on clinical judgement	Double-blind placebo-controlled trial	Those classed as clinically most severe pathological crying had relatively large bilateral pontine lesions without lesions in the hemispheres Intermediate group had bilateral central hemispheric lesions Clinically least affected group had mainly unilateral subcortical lesions
Kim (2002)	Investigate the factors related to PSEI including detailed lesion location	Korea – Medical Centre	Stroke	*N* = 25 EI *n* = 13 Non-EI *n* = 12	58.5	Lesion location – lower (L) level and upper (U) level	Assessment	Prospective	At the L level, the lesions of EI-present patients were more localized dorsally than those of PSEI-absent patients The right-sided lesions were significantly more frequent in the PSEI-present group than PSEI-absent group at this level At the U level, the difference between groups was not distinct Lesions involving mainly the globus pallidus, dorsally located lesions were more often associated with PSEI than ventrally located ones
Hübers et al. (2016)	To explore the pathogenesis of PLC by exposing ALS patients to simultaneously presented visual and auditory stimuli, which were either emotionally congruent or incongruent	Germany – Neurology Department	ALS	*N* = 20 PBA *n* = 10 Controls *n* = 10	64 ± 12.2	Physiological parameters (heart rate, galvanic skin response, activity of facial muscles)	CNS-LS	Case-control	Group-differences in electrophysiological data were explained by frontal cortex functioning as expressed by the ECAS score: EMG activity of the orbicularis ois muscle, the orbicularis oculi muscle, a non-significant trend for heart rate and GST between the two musical conditions
Christidi et al. (2018)	To examine the neuroanatomical substrate of PLC in ALS without dementia by simultaneously evaluating grey matter and white matter changes in ALS patients with and without PLC	Greece	ALS	*N* = 81 PLC *n* = 56 Healthy controls *n* = 25	60.43 ± 10.06	Grey matter and white matter	CNS-LS	Case-control	ALS-PLC patients showed decreased grey matter volume in left orbitofrontal cortex, frontal operculum and putamen and bilateral frontal poles compared to ALS non-PLC ALS-PLC patients had decreased fractional anisotropy in left cingulum bundle and posterior corona radiata White matter abnormalities were additionally detected in white matter associative and ponto-cerebellar tracts
Burns et al. (1999)	To assess whether a selective serotonin reuptake inhibitor is effective in treatment of stroke-associated lability of mood	UK – hospital	Stroke	*N* = 28 crying only	73.4 ± 9.1	Sertraline	Interviewer rated participants using House criteria	Double-blind placebo-controlled trial	Statistically significant improvements in lability score, tearfulness significantly diminished after 2 weeks and remained significantly lower throughout the trial Independent association for the improvement in tearfulness with length of time since stroke and score on the Frenchay aphasia battery
Luhoway et al. (2019)	To explore the relationship between posterior fossa lesions and PLC in people with MS	England and Canada – MS Clinics	Multiple sclerosis	*N* = 77 PLC *n* = 22 Non-PLC *n* = 55	39.3 ± 11	Posterior fossa lesions	CNS-LS	Retrospective	A significant inverse relationship was identified for patients with MS and without evidence of depression such that fewer posterior fossa lesions on automated magnetic resonance imaging was associated with the presence of PLC
Kim and Choi-Kwon (2000)	To correlate the location of stroke with post-stroke depression and emotional incontinence	Korea – Outpatient	Stroke	*N* = 148 PSEI *n* = 50 Non-PSEI *n* = 98	62 ± 9	Lesion location, demographic variables and characteristics	Assessment with patients and relatives	Prospective cohort	Female gender, ischaemic stroke and severe motor dysfunction were found to be related to PSEI Anterior cortical stroke was more associated with PSEI than was the posterior cortical lesion
Lopez et al. (2001)	To examine the hypothesis that depression, emotional lability and apathy in AD patients are associated with cortical-subcortical dysfunction	America – Research Centre	Alzheimer's disease	*N* = 8 EL *n* = 1 Controls *n* = 7	84	Cortical-subcortical dysfunction – (rel-CBF)	Psychiatric assessment	Part of a longitudinal study	Patient with EL showed decreased re-CBF in the anterior cingulate and dorsolateral prefrontal cortices, bilaterally, and in the left basal ganglia. Showed increased rel-CBF in the right middle temporal area
Tateno et al. (2004)	To examine the clinical correlates and course of PLC following TBI	America – Hospital and Clinics	TBI	*N* = 103 PLC *n* = 34 Non-PLC *n* = 69	30.4 ± 11.5	Neuropsychiatric assessment variables and severity and localization of brain injury	PLACS	Longitudinal cohort	Patients with PLC had a greater frequency of frontal lobe injury than patients without PLC Significant difference between PLC group and non-PLC group in frequency of diffuse lesions At three months after TBI, there was a significant difference in the frequency of frontal lobe lesions between patients with and without PLC

									Logistic regression analysis showed lateral aspect of left frontal lobe was associated with the presence of PLC
Ko et al. (2018)	To investigate whether TPH2 gene polymorphisms were associated with PSEI	Korea – Medical Centre	Stroke	*N* = 383 PSEI *n* = 41 Non-PSEI *n* = 342	60 ± 10	TPH2 genes, NIHSS and lesion location	Interview based on Kim's criteria	Secondary analysis	PSEI was associated with high NIHSS score at admission and severe mRS score at 3 months TPH2 SNP rs4641528 differed significantly between patients with and without PSEI. TT homozygote of rs4641528 was less common in patients with PSEI PSEI was associated with NIHSS score at admission and with TPH2 rs4641528 allele carriers
Starkstein et al. (1995)	To examine the prevalence and correlates of pathological affect	Argentina	Alzheimer's disease	*N* = 103 Pathological crying *n* = 26 Pathological mixed *n* = 14 Non-PBA *n* = 63	72.5 ± 7.1	Neuroradiological variables and neurological findings	PLACS	Cross-sectional	Patients with mixed pathological affect had a significantly larger left lateral ventricle than patients with either pathological affect crying or no pathological affect Patients with pathological laughing or crying had a significantly longer duration of illness and significantly higher anosognosia scores
Neuropsychological variables									
Hanna et al. (2016)	Determine the association between PLC and CI in an MS cohort	Canada – Cognitive Clinic	Multiple sclerosis	*N* = 153 PLC *n* = 58 Non-PLC *n* = 95	45.6 ± 8.1	Characteristics and MACFIMS performance variables	CNS-LS	Retrospective cohort	CNS-LS was found to be significantly correlated with years of education. CNS-LS scores were negatively correlated with performance on the COWAT, BVMTR immediate recall, BVMTR delayed recall, PASAT, DKEFS card sort, DKEFT card sort description and Stroop score Comparing non-PLC group to the PLC group a difference was identified on the COWAT, CVLT2-IR, CVLT2-DR
McCullagh et al. (1999)	Explore a possible role for the prefrontal cortex in the syndrome of PLC using novel neuropsychological measures to probe its functional integrity	Canada – Clinic	ALS	*N* = 28 PLC *n* = 10 Non-PLC *n* = 8 Healthy controls *n* = 10	63.5 ± 6.7	WCST and novel "Gambling task" psychometric variables	Poeck's criteria	Case-control	PLC group made significantly more total errors on the WCST than either the non-PLC or healthy controls group. A trend in the same direction was found for perseverative errors WSCT total errors predicted the presence or absence of PLC with 75% accuracy
Feinstein et al. (1999)	To explore a putative role for the prefrontal cortex in the pathogenesis of PLC	Canada – Outpatient	Multiple sclerosis	*N* = 24 PLC *n* = 11 Non-PLC *n* = 13	43.7 ± 8.3	Cognitive indices	PLACS	Case-control	PLC group generated significantly less words on the COWAT while also taking significantly longer to perform the Stroop test A trend was found for PLC patients to make more (total) errors on the WCST
Feinstein et al. (1997)	To define associated neurological, emotional and cognitive correlates of PLC	Canada – Outpatient	Multiple sclerosis	*N* = 24 PLC *n* = 11 Controls *n* = 13	43.7 ± 8.3	WAIS subtests	PLACS	Case-control	Patients with PLC had lower performance and full-scale but not verbal, IQ scores on the WAIS-R PLC group were more impaired on a single verbal subscale, namely Arithmetic, and on two of the performance tasks, namely Digit Symbol and Picture Arrangement Significant differences were identified on the Digit Backwards scores
Patel et al. (2018)	To describe the neuropsychiatric correlates of self-reported PBA symptom severity	America – tertiary care Centre	Parkinson's disease, ALS and aPD	*N* = 108 PBA *n* = 31 Non-PBA *n* = 77	PD 63.39 aPD 68.08 ALS 62.01	Characteristics and MoCA scores	CNS-LS	Cross-sectional	PBA patients were significantly younger than PBA negative patients in the aPD and ALS groups CNS-LS score was significantly related to younger age and education and corrected lower MoCA scores for participants in the aPD group but not for the other clinical groups
Fitzgerald et al. (2018)	To determine the prevalence of pseudobulbar affect and assess its association with disability and symptom severity	America – MS Registry	Multiple sclerosis	*N* = 8136 PBA *n* = 133 Non-PBA *n* = 8003	56.9	MS symptoms, cognitive impairment and characteristics	CNS-LS	Retrospective Cohort	PBA group tended to be younger, non-white and have less education and income compared with non-PBA group Those with PBA had on average greater disease severity across a range of symptoms PBA was associated with increased odds of moderate vs mild self-reported cognitive impairment in multivariate models Multivariate models adjusted for depression severity identified PBA was associated with increased odds of severe vs mild self-reported impairment in cognition, fatigue, hand function, vision, sensory and spasticity domains

(*Continued*)

Table 1. Continued.

Authors	Aim	Country /setting	Neurological disorder/s	Total number of participants (*N*) and number in subgroups (*n*)	Mean age (SD)	IV – Predictors or correlates in relation to SR question	Measure of emotionalism	Study design	Findings in relation to SR question
Psychological variables									
Eccles et al. (1999)	To determine whether patients with emotionalism differed from patients without emotionalism in their psychological reactions to stroke or in the coping strategies reported	UK – Hospital	Stroke	*N* = 65 Emotionalism *n* = 19 Non-emotionalism *n* = 46	71.8	IES and MASS items	Interview	Cross-sectional	Association between emotionalism and the impact of events subscales intrusion and avoidance. Association between emotionalism and the mental adjustment to stroke scale subscales helplessness/hopelessness and anxious preoccupation
Calvert et al. (1998)	To identify psychological symptoms, other than those that define emotionalism which are associated with the condition	UK	Stroke	*N* = 448 Emotionalism *n* = 101 Non-emotionalism *n* = 347	68.5	Psychological variables	Standardized set of questions	Interview data from an RCT study	Multivariate logistic regression identified irritability and ideas of reference were associated with emotionalism
Mixed variables									
Wei et al. (2016)	Evaluate PSD and PSEI at different stages to correlate their symptoms with lesion location, coping styles and other variables	China – Hospital	Stroke	*N* = 378 PSEI *n* = 40 Non-PSEI *n* = 328	61.3 ± 9.4	Lesion location, coping styles and characteristics	Interview based on Kim's criteria	Longitudinal cohort study	Patients with both motor and sensory dysfunctions were more susceptible to PSEI at admission compared to individuals with pure motor or sensory dysfunction Avoidance, acceptance-resignation and low objective support were predisposing factors for PSEI Anterior cortex, pons and midbrain infarction, bilateral lesion location, severe white matter change, avoidance and acceptance-resignation were all significant risk factors associated with PSEI 3 months later Multivariate analysis indicated PSEI at admission was associated with acceptance-resignation, whereas it was related to anterior cortex infarction and acceptance-resignation 3 months later
Choi-Kwon et al. (2012)	To investigate the characteristics and prevalence of post-stroke depression and post-stroke emotional incontinence and the factors related to these conditions at admission and 3 months after stroke	Korea – Medical Centre	Stroke	*N* = 508 PEI *n* = 48 Non-PEI *n* = 460	63.2 ± 10.3	5-HTTLPR, number of tandem repeats within intron 2 (Stin2VNTR), social support and lesion location	Interview based on set criteria	Longitudinal cohort	At admission lesion location (basal ganglia, corona radiata and internal capsule), presence of microbleeds and NIHSS score were related to PSEI Lesion location, motor dysfunction at admission, mRS score and low social support were related to PSEI 3 months after stroke Significant difference in the genotype frequencies of Stin2 VNTR polymorphism at 3 months after stroke between patients with and without PSEI. Stin2 10/10 and 12/10 genotypes more common among patients with PSEI Multivariate logistic regression indicated lesion location (pons and midbrain) was the only independent factor associated with PSEI at admission, whereas mRS score, Stin2 VNTR and low social support were independently associated with PSEI at 3 months after stroke
Choi et al. (2013)	To investigate the association of post-stroke emotional incontinence with various psychiatric symptoms and quality of life independent of potential covariates	Korea – Hospital	Stroke	*N* = 432 PSEI *n* = 51 Non-PSEI *n* = 381	64.6 ± 10	Sociodemographic and clinical variables	Patients and caregivers interviewed based on Kim's criteria	Secondary analysis	PSEI group were significantly more likely to have a previous history of stroke, higher NIHSS and lower BI scores
Wang et al. (2016)	To study the clinical features of and to identify the factors associated with PSPLC, to correlate PSPLC with lesion location and to analyse the difference between patients with and without pseudobulbar signs	China – Hospital	Stroke	*N* = 112 PSPLC *n* = 56 Non-PSPLC *n* = 56	62.4 ± 6.8	Characteristics, cognitive impairment, lesion location	PLACS	Retrospective case-control	Lesion located at the pons was related to PSPLC. PSPLC was independently related to pontine lesion PSPLC group had a higher frequency of bilateral lesions PSPLC was significantly related to Mild Cognitive Impairment Significantly more patients had at least two strokes in the last two years in the group with PSPLC with pseudobulbar signs Percentage of patients with severe neurological deficits at the onset of PLC was higher in the group with pseudobulbar signs. Those with PLC and pseudobulbar signs showed lesions with both bilateral basal ganglia plus bilateral subcortical white matter than those without pseudobulbar signs

Tang et al. (2009b)	To assess the relationship between executive functions, PSEI, and frontal and basal ganglia infarcts in stroke survivors	China – Research Clinic	Stroke	*N* = 78 PSEI *n* = 39 Controls *n* = 39	63.8 ± 8.7	MRI variables, executive function, location of acute infarcts	Psychiatric interviews based on Kim's criteria	Case-control	PSEI group had significantly more infarcts in the frontal and/or basal ganglia. There was a trend whereby the involvement of the middle cerebral artery territory was more frequent in PSEI group PSEI group had significantly lower Chinese Frontal Assessment Battery scores A significant correlation between frontal infarct and severity of PSEI (.420)
Vidović et al. (2015)	To determine the prevalence of pseudobulbar affect in patients with MS and to analyse the link between PBA and patient age, sex, clinical course of MS, disease duration and degree of disability	Croatia – Inpatient	Multiple sclerosis	*N* = 79 PBA *n* = 33 Non-PBA *n* = 46	48.7 ± 10.96	Age, sex, clinical course of MS, disease duration and degree of disability	CNS-LS	Cross-sectional	Those with PBA showed a significantly higher female predominance
Petracca et al. (2009)	To examine the frequency and clinical correlates of IEED in Parkinson's disease	Argentina – Hospital	Parkinson's disease	*N* = 131 IEED *n* = 22 crying only Non-IEED *n* = 109	63.8 ± 9.6	Parkinson's disease-related variables	PLACS	Cross-sectional	Patients with IEED had greater severity of Parkinson's disease compared with non-IEED patients; higher unified Parkinson's Disease Rating Scale salivation, axial rigidity, bradykinesia and gait disturbance scores
Siddiqui et al. (2009)	Examine whether PBA was associated with mood disturbances, motor disability, disease stage and quality of life	America – Movement Disorder Centre	Parkinson's disease	*N* = 719 PBA *n* = 37 Non-PBA *n* = 682	64.8 ± 12.2	Diagnosis, medication, VAMS score, severity of Parkinson's disease	Modified University of Florida Pseudobulbar affect screening questionnaire	Cross-sectional	Increased prevalence of PBA as PD/Parkinsonism patients approached higher levels of disability – stage 2
Phuong et al. (2009)	To examine frequency and correlates of IEED in PD using both the CNS-LS and new IEED diagnostic criteria, examine the overlap between IEED and depression, determine the discriminant validity of the CNS-LS in PD against a diagnostic interview applying the new IEED diagnostic criteria	America – Clinical and Medical Centres	Parkinson's disease	*N* = 193 IEED *n* = 100 Non-IEED *n* = 93	65.8 ± 10.7	Clinical variables and GDS-15	CNS-LS	Cross-sectional	Univariate analysis found female sex was associated with increasing CNS-LS score
Thakore and Pioro (2017)	To examine the prevalence, associations and course of PBA in ALS, explore associations if any, that differentiate laughter from crying in PBA and examine the relationship of PBA and depression	America – Clinical Centre	ALS	*N* = 735 PBA *n* = 209 Non-PBA *n* = 526	60.8	Population characteristics and ALS related variables	CNS-LS	Exploratory observational study	PBA was significantly associated with female gender, bulbar onset, lower ALSFRS-R score and more rapidly progressive disease Female gender, lower bulbar and gross motor ALSFRS-R sub-scores, lower age and shorter disease duration significantly increased odds of PBA. Model has an acceptable goodness of fit and predicts the presence of PBA with 74%
Andersen et al. (1995)	To explore possible relationship between post-stroke PC and depression	Denmark – Hospital	Stroke	*N* = 211 PC 1-month *n* = 24 PC 6 months *n* = 16 PC 1-year *n* = 33	69	Lesion site, lesion size, intellectual impairment, BI and Motricity Index	Interview	Longitudinal cohort	Patients with PC were significantly more physically impaired (BI and Motricity Index) PC was correlated to intellectual impairment at 6- and 12-months post-stroke but not at 1 month Lesion size were significantly larger in patients with PC
Foley et al. (2016)	To estimate the prevalence of PBA and examine the relationship between PBA symptoms and other clinical correlates	America – Nursing Home	Alzheimer's disease, stroke, Parkinson's disease, multiple sclerosis	*N* = 804 PBA *n* = 72 Non-PBA *n* = 732	79.6 ± 12.6	Demographic characteristics	CNS-LS	Retrospective observational	Patients with PBA symptoms were significantly more likely to be female compared to those without PBA
Tortelli et al. (2016)	To investigate using both a self-reported questionnaire and clinical examination the prevalence of pseudobulbar affect and define the ALS clinical phenotype associated with PBA at onset	Italy – Population based registry	ALS	*N* = 132 PBA *n* = 45 Non-PBA *n* = 87	62	Clinical phenotypes	CNS-LS	Prospective cross-sectional	PBA group was characterized by shorter disease duration from symptom onset, onset-diagnosis interval (ODI) and lower ALSFRS-R bulbar sub-score In patients with MS for less than two years, pathological CNS-LS was associated with a shorter ODI and lower ALSFRS-R bulbar sub-score
House et al. (1989)	To estimate the prevalence of emotionalism after stroke, to assess its relation with other mood disorders, and to identify clinical variables with which its associated	England – Stroke Register	Stroke	*N* = 112 One-month *n* = 13 Six months *n* = 25 12 months *n* = 12	NR	Intellectual function and lesion location	Psychiatric assessment based on standardized questions	Longitudinal cohort study	Patients with emotionalism at one and six months had more intellectual impairments. At one month a significant trend for patient with emotionalism to show larger lesions Lesions in the left frontal and temporal regions were associated with emotionalism at six months Significant association at 12 months between emotionalism and anterior lesion locations

(*Continued*)

Table 1. Continued.

Authors	Aim	Country /setting	Neurological disorder/s	Total number of participants (*N*) and number in subgroups (*n*)	Mean age (SD)	IV – Predictors or correlates in relation to SR question	Measure of emotionalism	Study design	Findings in relation to SR question
McGrath (2000)	To identify possible causal factors of emotionalism	England – Inpatient	TBI	*N* = 82 Emotionalism *n* = 43 crying only Non-emotionalism *n* = 39	46.76	Lesion location and psychological variables	Structured interview	Retrospective design	Patients with left anterior lesions compared with those with visible lesions in other parts of the brain showed a significant association with emotionalism at one, six and 12 months Significant correlations were obtained between emotionalism-tearfulness ratings and ratings for other interview items: sadness, frustration, fear and worry Independent variables which predicted crying behaviour were female gender and focal damage to the right cerebral hemisphere

Notes: 5-hydroxytryptamine (*5-HT*); ALS Functional Rating Scale-Revised (*ALSFRS-R*); Amplitude of low frequency fluctuation (*ALFF*); Amyotrophic Lateral Sclerosis (*ALS*); Anger Proneness (*AP*); Atypical Parkinson Disease (*aPD*); Barthel Index (*BI*); Center for Neurological Study – Lability Scale (*CNS-LS*); Controlled Oral Word Association Test (*COWAT*); Dementia of Alzheimer's type (*DAT*); Dextromethorphan/Quinidine (*DM/Q*); Emotional Lability (*EL*); Electromyography (*EMG*); Geriatric Depression Scale (*GDS-15*); Impact of Events Subscales (*IES*); Involuntary Emotional Expression Disorder (*IEED*); Pathological Laughing and Crying (*PLC*); Pathological Laughter and Crying Scale (*PLACS*); Post-stroke Emotional Incontinence (*PSEI*); Post-stroke Emotionalism Laughing (*PSEL*); Post-stroke Pathological Laughing and Crying (*PSPLC*); Primary Lateral Sclerosis (*PLS*); Pseudobulbar affect (*PBA*); Mental Adjustment to Stroke Scale (*MASS*); Minimal Assessment of Cognitive Function in MS (*MACFIMS*); Montreal Cognitive Assessment (*MoCA*); Mini-Mental State Examination (*MMSE*); Multiple Sclerosis (*MS*); National Institutes of Health Stroke Scale (*NIHSS*); Polymorphism of the Serotonin Transporter Protein (*STin2VNTR*); Regional homogeneity (*ReHo*); relative regional Cerebral Blood Flow (*rel-CBF*); Serotonin Transporter (*5-HTT*) Serotonin transporter (*SERT*); Serotonin transporter protein (*5-HTTLPR*); Traumatic Brain Injury (*TBI*); Tryptophan hydroxylase 2 (*TPH2*); Visual Analogue Mood Scales (*VAMS*); Wechsler Adult Intelligence Scale (*WAIS*); Wisconsin Card Sort Test (*WCST*).

Table 2. Quality assessment ratings using the QATOOCS.

Criteria	Lebert et al. (1994)	Liu et al. (2017)	Hanna et al. (2016)	Kim et al. (2012)	Haiman et al. (2008)	Andersen et al. (1993)	Wang et al. (2016)	Prokšelj et al. (2014)	MacHale et al. (1998)	Haiman et al. (2009)	Tang et al. (2009a)	Tang et al. (2004)
1. Clear research question?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2. Study population defined?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
3. Participation rate at least 50%?	CD	CD	CD	CD	CD	CD	CD	CD	Yes	CD	CD	Yes
4. Inclusion and exclusion criteria prespecified?	Yes	CD	Yes	Yes	Yes	CD	Yes	NR	Yes	Yes	Yes	Yes
5. Sample size justification?	No	No	No	No	No	No	No	No	No	No	No	No
6. Exposure(s) of interest measured prior to the outcome?	No	No	Yes	No	No	Yes	No	No	Yes	Yes	Yes	Yes
7. Timeframe between measures sufficient?	Yes	Yes	Yes	Yes	Yes	CD	Yes	Yes	Yes	Yes	Yes	Yes
8. Different levels of the exposure?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
9. Exposure measures clearly defined?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
10. Exposure(s) assessed more than once?	No	No	No	No	No	Yes	No	No	No	No	No	No
11. Outcome measures clearly defined?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
12. Outcome assessors blinded?	No	No	No	No	No	Yes	No	Yes	Some	No	Yes	Some
13. Follow-up loss under 20%?	NA	NA	NA	NA	NA	Yes	NA	NA	NA	NA	NA	NA
14. Measurement of confounding variables?	NR	NR	Yes	NR	NR	NR	NR	Yes	Yes	Yes	NR	NR
Quality rating	*Fair*	*Poor*	*Good*	*Fair*	*Fair*	*Good*	*Fair*	*Fair*	*Good*	*Good*	*Good*	*Good*

Criteria	Morris et al. (1993)	House et al. (1989)	Wei et al. (2016)	Brown et al. (1998)	Petracca et al. (2009)	Floeter et al. (2014)	Siddiqui et al. (2009)	Christidi et al. (2018)	Phuong et al. (2009)	Thakore and Pioro (2017)	Choi et al. (2018)	Tang et al. (2009b)	Ghaffar et al. (2008)
1. Clear research question?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2. Study population defined?	Yes	Yes – details in previous study	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes
3. Participation rate at least 50%?	Yes	Yes	CD	CD	CD	CD	Yes	CD	Yes	Yes	Yes	CD	NR
4. Inclusion and exclusion criteria prespecified?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
5. Sample size justification?	No	No	No	No	No	No	No	No	No	No	No	No	No
6. Exposure(s) of interest measured prior to the outcome?	Yes	Yes	Yes	Yes	Yes	Some	No	Yes	No	No	No	Yes	Yes
7. Timeframe between measures sufficient?	Yes	Yes	CD	CD	Yes	Yes	No	Yes	No	CD	CD	Yes	Yes
8. Different levels of the exposure?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	NA	Yes	Yes
9. Exposure measures clearly defined?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
	No	Yes	Yes	Yes	No	No	No	No	No	No	No	No	No

(*Continued*)

Table 2. Continued.

Criteria	Morris et al. (1993)	House et al. (1989)	Wei et al. (2016)	Brown et al. (1998)	Petracca et al. (2009)	Floeter et al. (2014)	Siddiqui et al. (2009)	Christidi et al. (2018)	Phuong et al. (2009)	Thakore and Pioro (2017)	Choi et al. (2018)	Tang et al. (2009b)	Ghaffar et al. (2008)
10. Exposure(s) assessed more than once?													
11. Outcome measures clearly defined?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
12. Outcome assessors blinded?	Some	No	No	Yes	Yes	Yes	No	No	Yes	No	No	Yes	No
13. Follow-up loss under 20%?	NA	Yes	Yes	Yes	NA	NA	NA	NA	NA	NA	NA	NA	NA
14. Measurement of confounding variables?	Yes	NR	NR	NR	NR	NR	Yes	Yes	NR	Yes	Yes	NR	NR
Quality rating	*Good*	*Good*	*Good*	*Good*	*Good*	*Good*	*Fair*	*Good*	*Fair*	*Fair*	*Fair*	*Good*	*Fair*

Criteria	Murai et al. (2003)	Andersen et al. (1994)	Tateno et al. (2004)	Hübers et al. (2016)	McCullagh et al. (1999)	Feinstein et al. (1999)	Kim (2002)	Andersen et al. (1995)	Luhoway et al. (2019)	Kim and Choi-Kwon (2000)	Choi-Kwon et al. (2012)	Ko et al. (2018)
1. Clear research question?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2. Study population defined?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
3. Participation rate at least 50%?	NR	NR	CD	CD	CD	CD	CD	CD	CD	CD	No	Yes
4. Inclusion and exclusion criteria prespecified?	Yes	CD	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
5. Sample size justification?	No	No	No	No	No	No	No	No	No	No	No	No
6. Exposure(s) of interest measured prior to the outcome?	Yes	Yes	Some	No	No	No	Yes	Yes	CD	Yes	Yes	Yes
7. Timeframe between measures sufficient?	CD	CD	CD	CD	CD	CD	Yes	Yes	CD	Yes	Yes	CD
8. Different levels of the exposure?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
9. Exposure measures clearly defined?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
10. Exposure(s) assessed more than once?	No	No	Yes	No	No	No	No	Yes	No	No	Yes	No
11. Outcome measures clearly defined?	Yes	CD	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
12. Outcome assessors blinded?	No	No	No	No	No	No	No	No	No	No	No	No
13. Follow-up loss under 20%?	NA	NA	Yes	NA	NA	NA	NA	Yes	NA	NA	Yes	NA
14. Measurement of confounding variables?	CD	CD	No	NR	Yes	NR	NR	NR	Yes	NR	Yes	Yes
Quality rating	*Fair*	*Poor*	*Good*	*Poor*	*Fair*	*Poor*	*Fair*	*Good*	*Fair*	*Fair*	*Good*	*Good*

Criteria	Starkstein et al. (1995)	Feinstein et al. (1997)	Foley et al. (2016)	Tortelli et al. (2016)	Patel et al. (2018)	Vidović et al. (2015)	Fitzgerald et al. (2018)	Choi et al. (2013)	Lopez et al. (2001)	Eccles et al. (1999)	Calvert et al. (1998)	McGrath (2000)	Burns et al. (1999)
1. Clear research question?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2. Study population defined?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
3. Participation rate at least 50%?	CD	CD	CD	CD	Yes	CD	CD	NR	CD	Yes	NR	Yes	Yes
4. Inclusion and exclusion criteria prespecified?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
5. Sample size justification?	No	No	No	No	No	No	No	No	No	No	No	No	No
6. Exposure(s) of interest measured prior to the outcome?	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes
7. Timeframe between measures sufficient?	Yes	Yes	CD	CD	CD	CD	Yes	Yes	Yes	CD	CD	CD	CD
8. Different levels of the exposure?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	Yes
9. Exposure measures clearly defined?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
10. Exposure(s) assessed more than once?	No	No	No	No	No	No	No	No	No	No	No	No	Yes
11. Outcome measures clearly defined?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
12. Outcome assessors blinded?	Yes	No	No	No	No	No	No	No	No	No	No	No	Yes
13. Follow-up loss under 20%?	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	No
14. Measurement of confounding variables?	NR	CD	NR	NR	Yes	NR	NR	Yes	NR	NR	Yes	NR	NR
Quality rating	*Fair*	*Fair*	*Fair*	*Fair*	*Good*	*Fair*	*Fair*	*Good*	*Fair*	*Fair*	*Fair*	*Fair*	*Good*

for high-quality meta-analyses with a very low risk of bias to 4 for expert opinion and formal consensus. This tool examines the quality of evidence whereby the greater weight is given to studies that have controlled for biases or design limitations.

Results

Study selection

Initial searches of the databases generated 3238 studies, with a total of 1342 studies once duplicates were removed. The titles and abstracts of the studies from the search results were reviewed for eligibility and studies were excluded if they did not meet the criteria (1203 studies). A total of 139 studies were reviewed at the full-text stage and reasons for excluding studies were recorded. Following eligibility checking a total of 50 studies were regarded as eligible for the review. See Figure 1 for the PRISMA flow chart displaying the process of identifying a final selection of studies to be included.

Study characteristics

The characteristics of the studies were extracted and have been outlined according to the PICOS criteria below.

Participants

A total of 1922 participants with emotionalism were included in the studies across all the papers. Of these participants 48% had a diagnosis of stroke, 12% ALS, 18% multiple sclerosis, 4% TBI, 6% Parkinson's disease, 8% Alzheimer's disease and 4% mixed with no breakdown of diagnoses. No studies were identified as appropriate that included participants with vascular dementia. Across the 50 studies, the mean age of participants with emotionalism was 63.87 years.

The majority of studies had small sample sizes, whereby the largest sample had 209 unique participants (Thakore & Pioro, 2017) and the smallest sample had one participant (Lopez et al., 2001) with emotionalism. The mean sample size was 38 participants.

Studies were conducted across 17 different countries. The largest number of studies were conducted in Europe ($N = 18$) followed by 15 studies in Asia. Nine studies were completed in America, five in Canada, two in South America and one in New Zealand.

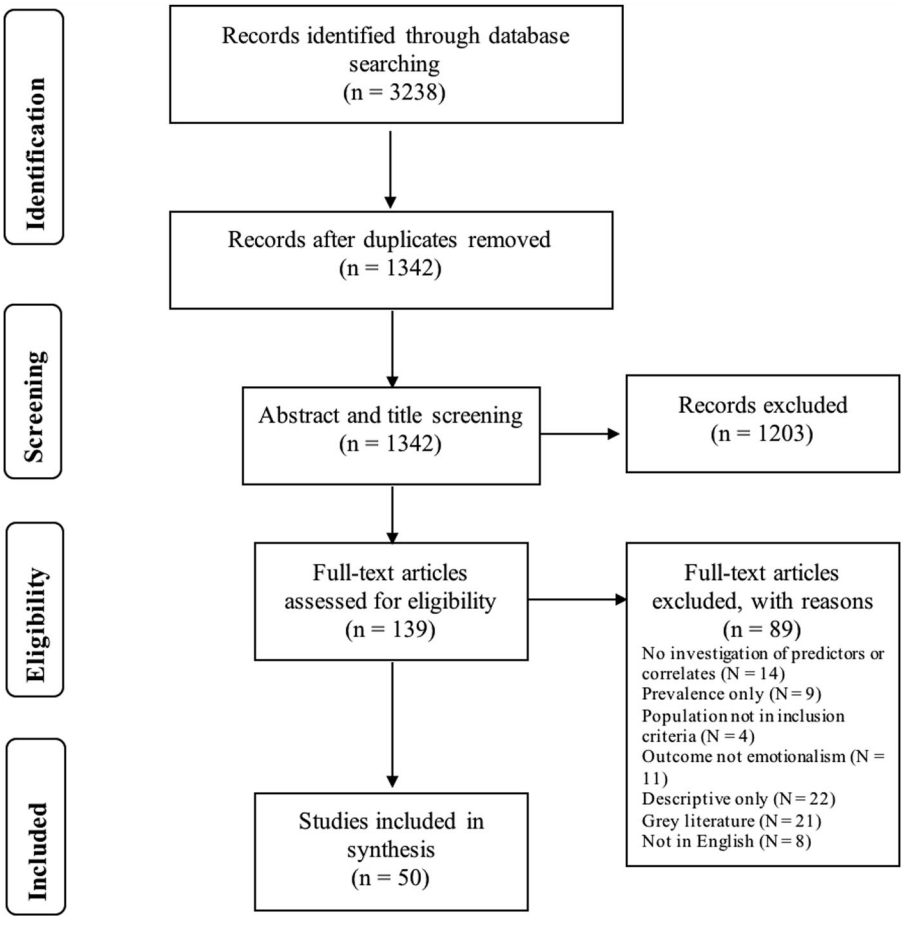

Figure 1. Flowchart displaying the process of identifying studies for inclusion in the review.

Predictors and correlates

Demographic and disease characteristics, anatomical, neuropsychological and psychological factors were investigated as possible predictors and correlates of emotionalism across neurological disorders. Anatomical factors were the most commonly explored across studies and included lesion location, number of lesions, lesion size, white matter changes and alleles/genes. Neuropsychological factors were only investigated in stroke, multiple sclerosis and ALS. Additionally, only five studies explored psychological factors in a sample of stroke participants.

The majority of studies ($N = 43$) included participants with mixed episodes of emotionalism and did not differentiate between crying only or laughing only episodes of emotionalism and associations of predictors and correlates. Seven studies included samples of participants with crying only episodes of emotionalism (Andersen et al., 1993, 1994, 1995; Burns et al., 1999; McGrath et al., 2000;

Murai et al., 2003; Petracca et al., 2009) when investigating correlates and predictors.

Outcome

Emotionalism was measured using a range of methods. The majority of studies ($N = 14$) used the Center for Neurological Study – Lability Scale (CNS-LS; Moore et al., 1997). This is a self-report questionnaire, comprising seven questions across two subscales of laughter and labile tearfulness. The Pathological Laughing and Crying Scale (PLACS; Robinson et al., 1993) was used by eight studies. This is an interviewer-rated instrument, which consists of 16 items that are scored from zero (rarely or not at all) to three (frequently).

Eleven studies completed assessments for emotionalism using a psychiatric interview based on Kim's criteria ($N = 7$; Kim & Choi-Kwon, 2000). Three conducted a psychiatric assessment using pre-defined criteria (Choi-Kwon et al., 2012; House et al., 1989; Lopez et al., 2001) and two studies (Burns et al., 1999; Morris et al., 1993) used House's criteria (House et al., 1989).

Of the remaining studies, two studies (Ghaffar et al., 2008; McCullagh et al., 1999) screened patients using Poeck's criteria (Poeck, 1969), one study used the modified University of Florida PBA Screening Questionnaire (Siddiqui et al., 2009), one study used a short emotionalism questionnaire (MacHale et al., 1998) and one study assessed emotionalism based on clinical judgement (Andersen et al., 1994).

Design

The majority of included studies had cross-sectional designs ($N = 13$) or case-control designs ($N = 11$). Two included studies were part of an RCT (Calvert et al., 1998; MacHale et al., 1998) and four were from a double-blind placebo-controlled trial (Andersen et al., 1993, 1994; Brown et al., 1998; Burns et al., 1999).

A longitudinal cohort design was implemented by five studies (Andersen et al., 1995; Choi-Kwon et al., 2012; House et al., 1989; Tateno et al., 2004; Wei et al., 2016) and one study was part of a longitudinal study (Lopez et al., 2001). Six studies were retrospective (Fitzgerald et al., 2018; Foley et al., 2016; Hanna et al., 2016; Luhoway et al., 2019; McGrath, 2000; Wang et al., 2016), three were prospective (Choi et al., 2018; Kim, 2002; Kim & Choi-Kwon, 2000).

Risk of bias within studies

Quality assessment

The QATOCCS was completed for studies that were observational, cohort and cross-sectional in design, see Table 2. The majority of studies ($N = 25$) were

rated as "Fair," 21 studies were rated as "Good" and 4 studies were rated as "Poor" (Andersen et al., 1994; Feinstein et al., 1999; Hübers et al., 2016; Liu et al., 2017). All the studies had clearly stated the research question and all but one study (Thakore & Pioro, 2017) had defined the study population sample. Additionally, all studies had clearly defined the exposure (predictors and correlates) and outcome (emotionalism) measures with the exception of one study where it was not possible to determine if the outcome measure was clearly defined (Andersen et al., 1994).

All the studies included in this review had elements of risk of bias and no studies were excluded from this review based on the quality assessments.

Level of evidence

The Scottish Intercollegiate Guidelines Network grading system (SIGN; Miller, 2002) was used to examine the level of evidence for each study. When grading the level of evidence, the ratings from the QATOCCS were considered. For this review, the level of evidence ranged from "2++" for high-quality case-control or cohort studies with a very low risk of confounders or bias, "2+" for well-conducted case-control or cohort studies with a low risk of confounders or bias or "2−" for case-control or cohort studies with a high risk of confounders or risk. Only one study was classified as "3" for non-analytic studies, including case reports. Overall, the majority of the studies fell in the "2++" and "2+" level of evidence.

Results of individual studies

Demographic and disease characteristics predictors and correlates

Overall, female gender was associated with emotionalism for participants with stroke, multiple sclerosis, TBI, ALS and Parkinson's disease (Foley et al., 2016; Kim & Choi-Kwon, 2000; McGrath, 2000; Phuong et al., 2009; Thakore & Pioro, 2017; Vidović et al., 2015). However, Kim (2002) found no relationship between gender and emotionalism in participants following a stroke. This study included 25 participants with emotionalism and was rated "fair" in terms of methodological quality, with the participation rate not able to be determined, which could decrease the power of the study. Lower education level (Fitzgerald et al., 2018; Hanna et al., 2016) and non-white ethnicity (Fitzgerald et al., 2018) were identified as predictors of emotionalism in a cohort of participants with multiple sclerosis.

Additionally, a correlation between emotionalism and a younger age was reported for participants with stroke and ALS (Tang et al., 2004; Thakore & Pioro, 2017). Patel et al. (2018) similarly found emotionalism was significantly correlated with a younger age for individuals with ALS but no difference was identified for individuals with Parkinson's disease. This study had a fairly small

sample size with only 31 participants with emotionalism, whereas Thakore and Pioro (2017) included 209 participants with emotionalism.

Studies exploring predictors of emotionalism and stroke reported an association between a previous history of stroke (Choi et al., 2013; Tang et al., 2004), motor and sensory dysfunction (Choi-Kwon et al., 2012; Kim & Choi-Kwon, 2000; Wei et al., 2016), higher NIHSS scores (Choi et al., 2013; Choi-Kwon et al., 2012; Ko et al., 2018; Tang et al., 2004), higher BI score (Andersen et al., 1995; Choi et al., 2013) and mRS score (Choi-Kwon et al., 2012; Ko et al., 2018).

Disease characteristics were investigated by only a small number of studies. Shorter disease duration (Tortelli et al., 2016) and rapidly progressive disease (Thakore & Pioro, 2017) in participants with ALS, greater disease severity in participants with multiple sclerosis (Vidović et al., 2015) and longer illness duration in participants with Alzheimer's disease (Starkstein et al., 1995) were associated with emotionalism. Furthermore, a higher level of disability was associated with emotionalism in participants with Parkinson's disease (Siddiqui et al., 2009).

Anatomical predictors and correlates

Out of the total studies identified for this review, the majority of studies explored anatomical predictors and correlates of emotionalism in participants following a stroke. Therefore, a summary for the reader has been provided according to each neurological disorder.

Stroke

Lesion size was found to be significantly larger in participants with emotionalism post-stroke (Andersen et al., 1995). House et al. (1989) explored predictors longitudinally and revealed an association between larger lesions at one month, lesions in left frontal and temporal regions at 6 months and anterior lesions at 12 months. Additionally, the number of lesions was commonly investigated as a predictor of emotionalism in participants following a stroke, which could be an indication of the extent of damage to the brain. Higher frequency of lesions in the right anterior region at assessment (MacHale et al., 1998), bilateral lesions (Wang et al., 2016) and more lesions in the globus pallidus and dorsally located (Kim, 2002) were predictors of emotionalism. A further study found a significant correlation between more infarcts in frontal and/or basal ganglia and a significant correlation between frontal infarct and severity of emotionalism (Tang et al., 2009b).

Overall, there was a higher number of studies exploring lesion location as a predictor of emotionalism in participants who experienced a stroke. Lesions in the right frontal/anterior region featured more with an association with anterior cortical stroke (Kim & Choi-Kwon, 2000), cortical infarcts (Tang et al., 2004), lesion location at admission (Choi-Kwon et al., 2012; Ko et al., 2018) and at three months (Ko et al., 2018) associated with emotionalism. Evidence reporting

single lesions in the anterior regions of cerebral hemisphere were 4 times the odds of emotionalism than lesions located elsewhere (Morris et al., 1993) and only left anterior lesions were significantly associated with emotionalism at 1, 6 and 12 months (House et al., 1989). Three months post-stroke anterior cortex, pons and midbrain infarction, bilateral lesion location and severe white matter changes were also identified as significant risk factors associated with emotionalism (Wei et al., 2016).

Research also highlighted evidence of further brain areas, specifically the brainstem and posterior structures. Andersen et al. (1994) classified participants with emotionalism in terms of severity. They found those classed as most severe had relatively large bilateral pontine lesions without lesions in the hemispheres, those classed intermediate had bilateral central hemispheric lesions and those classed least affected had mainly unilateral subcortical lesions. Furthermore, Liu et al. (2017) investigated specific brain networks and revealed differences in the amplitude of low-frequency fluctuation and regional homogeneity in the default mode network, sensorimotor network, affective network and cerebellar lobes. However, both these studies were rated as "poor" for methodological quality as authors did not report if participation rate was above 50%, if confounding variables were accounted for and no sample size justification was provided.

The presence of microbleeds was investigated by several studies. Tang et al. (2009a) found individuals with PSE had a higher frequency of microbleeds in the thalamus as a whole, anterior and paramedian areas and a higher number in the entire brain. Only microbleeds in the thalamus were significant independent predictors of emotionalism however. Furthermore, the presence of microbleeds was associated with emotionalism at admission (Choi-Kwon et al., 2012).

Studies exploring the serotonergic system as a predictor of emotionalism examined this by investigating genes and medication effectiveness. Disruptions to serotonergic pathways or abnormalities were implicated in a number of studies. Kim et al. (2012) found a higher frequency of 5-HTTLPR 5 allele of participants with emotionalism. An association between 5-HTTLPR genotype and PSEI strengthened progressively with an increasing number of 5 alleles and remained significant in participants with 5/5 genotype. Further studies found TPH2 rs4641528 allele carriers were associated with emotionalism at admission (Ko et al., 2018) and STin2 VNTR was one factor associated at 3 months (Choi-Kwon et al., 2012). Administration of Sertraline in participants with crying only episodes of emotionalism (Burns et al., 1999), Fluoxetine (Brown et al., 1998) and Citalopram medicines (Andersen et al., 1993) resulted in significant improvements in emotionalism scores compared with a placebo group. These studies were rated as "good" for methodological quality with clear research questions, exposure measured prior to outcome and well-defined outcome measures.

Two studies rated as "fair" according to QATOCCS found lower total testosterone levels were independently associated with emotionalism (Choi et al., 2018)

and midbrain/pons [I]β-CIT binding ratios were significantly lower in those with crying only episodes of emotionalism (Murai et al., 2003). These were both pilot studies with small sample sizes for participants with emotionalism ($N = <6$), exposure was not measured more than once and researchers were not blinded to outcomes.

Multiple sclerosis

Lesion volume and location were investigated in participants with multiple sclerosis. An inverse relationship for those with emotionalism and without depression was found with fewer posterior lesions associated with emotionalism (Luhoway et al., 2019). Ghaffar et al. (2008) found brainstem hypointense lesion volume was significantly higher in individuals with emotionalism and differences in hyperintense lesion volume in five regions: right medial inferior frontal, right inferior parietal, left medial inferior frontal and left inferior parietal. A Logistic regression model, which accounted for 70% of the variance identified brainstem hypointense, left inferior parietal hyperintense and left and right medial inferior frontal hyperintense lesion volumes in explaining the presence of emotionalism. This further supports the evidence found in stroke patients with damage to brainstem and posterior structures.

Investigations of activations of brain areas in response to emotional and neutral stimuli were explored to identify differences in multiple sclerosis participants with emotionalism. Distinct activations in areas involved in emotional processing, high-level and associative visual processing in response to neutral stimuli (Haiman et al., 2009) and somatosensory and motor areas in response to neutral stimuli and higher current density were revealed (Haiman et al., 2008). This suggests that individuals with emotionalism show greater emotional reactivity to neutral stimuli in certain brain areas compared to individuals without emotionalism.

ALS

Overall, there was evidence of white and grey matter changes in participants with ALS and emotionalism. Evidence of disruptions to the corticobulbar/cerebellar pathways that regulate motor control and co-ordination of emotional expression was highlighted in this review. Floeter et al. (2014) found increased mean diffusivity of white matter tracts underlying the frontotemporal cortex, transverse pontine fibres and middle cerebellar peduncle in individuals with emotionalism. Christidi et al. (2018) found white matter abnormalities in associative and ponto-cerebellar tracts and decreased grey matter volume in the left orbitofrontal cortex, frontal operculum, putamen and bilateral frontal poles. Additionally, they found decreased fractional anisotropy in left posterior cingulum and posterior corona radiata.

Electrophysiological differences were explored to investigate the role of the frontal cortex as expressed by the ECAS score with participants with emotionalism. Hübers et al. (2016) found changes in EMG activity of mimic muscles in

individuals with emotionalism compared with controls. They concluded reduced inhibitory activity in the frontal cortex could explain changes in physiological parameters in relation to emotionalism. However, it should be noted that the methodological quality was rated as "poor" as the predictors were not measured prior to the outcome, the timeframe between measures could not be determined and the authors did not report whether confounding variables were controlled for.

Several studies found an association between bulbar onset, lower bulbar and gross motor ALSFRS-R sub-scores and emotionalism in a sample of participants with ALS (Floeter et al., 2014; Thakore & Pioro, 2017; Tortelli et al., 2016).

TBI

Only one study exploring anatomical predictors in patients with TBI was identified in this review providing evidence of damage to frontal lobes. In a sample of participants with TBI, greater frequency of frontal lobe injury, more diffuse lesions and lateral left frontal lobe were associated with emotionalism (Tateno et al., 2004).

Alzheimer's disease

Studies investigating predictors of emotionalism varied in terms of variables explored in participants with Alzheimer's disease. Lebert et al. (1994) explored cerebral laterality and found frontolateral asymmetry indices were significantly lower in those with emotionalism. Significant differences in anatomical predictors were identified in several studies. Starkstein et al. (1995) found mixed pathological affect had significantly larger left ventricle compared with pathological crying affect or no pathological affect. Additionally, emotionalism was associated with decreased rel-CBF in the anterior cingulate and dorsolateral prefrontal cortices bilaterally and in the left basal ganglia and increased rel-CBF in the right middle temporal area (Lopez et al., 2001).

Further implications of the serotonergic pathways were highlighted with one study which revealed significantly lower (2.9- and 2.6-times) platelet 5-HT concentrations in individuals with emotionalism (Prokšelj et al., 2014).

Neuropsychological predictors and correlates

General intellectual impairments or global functioning were assessed by seven studies with evidence that mild cognitive impairment (MCI) was significantly related to emotionalism in participants who had experienced a stroke (Wang et al., 2016) and MMSE scores were a significant predictor of post-stroke laughter (Tang et al., 2009a). Those with emotionalism were found to have greater intellectual impairments at one and six months following a stroke (House et al., 1989). However, another study found an association between crying only episodes of emotionalism and intellectual impairments at 6- and 12-months post-stroke but no association at 1-month (Andersen et al., 1995).

Participants with emotionalism had lower performance and full-scale IQ scores on the Wechsler Adult Intelligence Scale-Revised (WAIS-R), whereby those with emotionalism were more impaired on a single verbal subscale, on the Digit Symbol and Picture Arrangement tests (Feinstein et al., 1997). Furthermore, emotionalism was associated with increased odds of moderate versus mild cognitive impairments in individuals with multiple sclerosis (Fitzgerald et al., 2018).

A number of studies included measures of executive functioning to explore the cognitive correlates of emotionalism based on the hypothesis executive/inhibitory control might be implicated with emotionalism. The Wisconsin Card Sorting Task (WCST) is a measure of frontal lobe function whereby performance in this task is considered to be sensitive to the dorsolateral prefrontal function and lesions (Berman et al., 1995). Evidence suggested that those with emotionalism and multiple sclerosis generated significantly less words on the Controlled Oral Word Association Test (COWAT), took longer to perform the Stroop test and showed a trend for more total errors on the WSCT (Feinstein et al., 1999). Additionally, those with ALS and emotionalism made significantly more total errors on the WSCT and more perseverative errors (McCullagh et al., 1999). The authors also found that WSCT total errors predicted emotionalism with 75% accuracy. However, this research was rated as "fair" as the participation rate and a sufficient timeframe between the measures were not able to be determined. These studies highlighted deficits in executive functioning but did not state which specific components of executive functioning were associated with greater emotionalism.

Frontal dysfunction was highlighted by a case-control study, which revealed participants with emotionalism had significantly lower Chinese Frontal Assessment Battery Scores (Tang et al., 2009b). Furthermore, evidence found a negative correlation with performance on several cognitive subtests in a sample of patients with emotionalism and multiple sclerosis. Hanna et al. (2016) revealed deficits in verbal fluency (COWAT), visual memory (Brief Visuospatial Memory Test-Revised; BVMTR immediate and delayed recall and California Verbal Learning Test-2 Immediate Recall; CVLT2-IR and California Verbal Learning Test-2 Delayed Recall; CVLT2-DR), slower processing speed (Paced Auditory Serial Addition Test; PASAT) and executive dysfunction (Delis-Kaplan Executive Function System; D-KEFS card sort and card sort description). This study was rated as methodologically "good" for this review as they controlled for variables such as years of education, had clear research questions and variables were clearly defined.

Psychological predictors and correlates

There was limited research exploring psychological predictors and correlates in participants with neurological disorders. In this review, psychological factors were only investigated in a stroke population and the psychological impact

of emotionalism was investigated by several studies. There was evidence that irritability and ideas of reference were associated with emotionalism (Calvert et al., 1998). One study reported associations of emotionalism with the Impact of Events (IES) subscales intrusion and avoidance and the Mental Adjustment to Stroke Scale (MASS) subscales helplessness/hopelessness and anxious preoccupation (Eccles et al., 1999).

Variables such as ways of coping or social support from others were investigated. Low social support was independently related to emotionalism three months after stroke (Choi-Kwon et al., 2012). Wei et al. (2016) found avoidance, acceptance-resignation and low social support were predisposing factors for emotionalism. Additionally, acceptance-resignation and avoidance were associated with emotionalism three months after stroke. Both these studies were rated as methodologically "good" for the purpose of this review with clearly defined research questions, measures and less than 20% follow-up dropout rate.

Additional analysis

As the majority of studies explored anatomical, neuropsychological and psychological predictors and correlates of emotionalism in a stroke population, only tentative comparisons of predictors between neurological disorders were completed. See Tables 3–6, which summarizes findings for all predictors and correlates across the neurological disorders. A number in brackets has been added to indicate the number of times findings have been found in different studies and predictors and correlates have been bolded to indicate these were found across different neurological disorders.

Discussion

Summary of evidence

To date, this is the first systematic review that has provided a comprehensive narrative synthesis of the published research exploring the predictors and correlates of emotionalism across neurological disorders. A total of 50 studies were included in this review and overall the quality ratings of the studies ranged from "good" to "fair." The largest amount of evidence revealed anatomical predictors and correlates of emotionalism across neurological disorders; however, a large majority of these predictors were investigated in only stroke participants. Due to the disproportionate number of studies across neurological disorders, the review provides patterns of predictors and correlates for each disorder and tentatively compares across disorders. Overall, this review identified common predictors and correlates such as bulbar networks, serotonergic pathways, frontal areas, white matter genetics, executive functioning, psychological impact, coping style and female gender as potentially involved in the pathophysiology of emotionalism. This review highlights the need for further high-quality

Table 3. Summary of demographic and disease characteristics predictors and correlates across neurological disorders.

Demographic and disease characteristics	Neurological disorder					
	Stroke	Multiple sclerosis	TBI	Alzheimer's disease	ALS	Parkinson's disease
Previous history of stroke	2					
Higher NIHSS score	4					
Higher BI score	2					
mRS score	2					
Greater disease severity		1				
Higher levels of disability						1
Rapidly progressive disease					1	
Longer illness duration				1		
Shorter disease duration					2	
Motor and sensory dysfunction	2					
Female gender	1	1	1		1	1
Younger age	1	1			1	
Non-white ethnicity		1				
Lower education level		2				

Note: Number indicates how many studies found an association between neurological disorder and predictors and correlates.

research exploring emotionalism across neurological disorders to validate these findings and to enhance theoretical understanding.

Strengths and limitations

Key strengths of this review were the use of a systematic approach, a clear predefined protocol and the inclusion of quality checks or assessment of biases. This meant that the methodological quality of studies could be appraised and researcher bias was less likely, which allowed for the review to summarize the evidence highlighting strengths and limitations of research. Additionally, the review explored predictors and correlates of emotionalism across neurological disorders, which enabled a greater understanding of this condition and for similarities and differences to be tentatively investigated.

This review has a number of limitations. Firstly, due to the significant heterogeneity in how emotionalism was measured and small sample sizes a narrative synthesis was completed rather than a meta-analysis. It has been highlighted that narrative syntheses lack transparency; there is an increased potential for bias and conclusions are based on subjective interpretation (Valentine et al., 2017). To minimize researcher bias, a systematic review protocol was registered before commencing with aims, search strategy, data analysis plan and an assessment to measure the risk of methodological bias in the studies outlined. The review conforms to the guidelines outlined by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement (PRISMA; Moher et al., 2009).

A second limitation was that this review excluded studies not published in English and "grey" literature, which could limit the generalisability of the findings. It has been highlighted that including "grey" literature can minimize

Table 4. Summary of anatomical predictors and correlates across neurological disorders.

	Neurological disorder					
Anatomical	Stroke	Multiple sclerosis	TBI	Alzheimer's disease	ALS	Parkinson's disease
Higher 5-HTTLPR 5 allele	1					
Lower platelet 5-HT concentrations				1		
ALDD and ReHo differences	1					
Lesion location	9					
Higher frequency of lesions	2					
Greater frequency of frontal lobe injury, diffuse lesions			1			
Left hemisphere lesion	1					
Larger lesion size	4					
White matter changes/abnormalities	2				1	
Decreased grey matter volume, fractional anisotropy					1	
Microbleeds	2					
Lower testosterone levels	1					
Ischemic stroke	1					
Lower midbrain/pons [I]β-CIT binding ratios	1					
Pronounced hypoperfusion	1					
STin2 VNTR polymorphism	1					
TPH2 SNP rs4641528	1					
Somatosensory and motor areas		1				
Higher current density		1				
Activation of emotional processing areas		1				
Hyperintense lesion volume differences		1				
Fewer posterior fossa lesions		1				
Lateral left frontal lobe			1			
Larger left lateral ventricle				1		
Damage to right cerebral hemisphere			1			
Bilateral lesions, unilateral lesions, brain cortex and basal ganglia, cortical and subcortical areas			1			
Frontal asymmetry indices lower				1		
Higher anosognosia scores				1		
Rel-CBF levels				1		
Bulbar onset					2	
Lower ALSFRS-R score					2	
EMG activity					1	
Higher unified Parkinson's disease rating scale salivation, axial rigidity, bradykinesia and gait disturbance scores					1	

Note: Number indicates how many studies found an association between neurological disorder and predictors and correlates.

the effects of publication bias and provide a more balanced understanding of the evidence (McAuley et al., 2000). Also, the inclusion criteria for this review included a number of neurological disorders; however, the majority of studies focused on predictors of emotionalism in participants following a stroke, whereby there was limited research focusing on the other neurological disorders. For example, only three studies were identified that explored predictors in a sample of participants following a TBI and no studies investigated predictors and correlates in participants with vascular dementia. Therefore, further analysis of the results to compare predictors of emotionalism across neurological disorders was completed tentatively.

Table 5. Summary of neuropsychological predictors and correlates across neurological disorders.

	Neurological disorder					
Neuropsychological	Stroke	Multiple sclerosis	TBI	Alzheimer's disease	ALS	Parkinson's disease
Intellectual impairment	2					
Mild Cognitive Impairment/Increase odds of moderate cognitive impairment	1	1				
Lower performance and full-scale IQ scores		1				
MMSE	1					
Lower Chinese Frontal Assessment Battery Scores	1					
Negatively correlated with COWAT, BVMTR items, PASAT, DKEFS card sort,		1				
CVLT2-IR and CVLT2-DR		1				
Less words generated on COWAT and more total errors		1				
Longer to perform Stroop test		2				
WSCT total errors and more preservative errors					1	

Note: Number indicates how many studies found an association between neurological disorder and predictors and correlates.

Additionally, the range of study designs varied with the majority of studies using a cross-sectional or case-control design and only a few RCT's. RCT's have high internal validity, minimize the risk of bias by controlling for confounding variables and participants are randomized, which allows for causation to be explored (Booth & Tannock, 2014). In contrast, cross-sectional studies measure exposure and outcome at the same time whereby it is difficult to derive causal relationships (Wang & Cheng, 2020). The conclusions drawn from this review acknowledge that causation is difficult to determine and highlight the need for further RCT studies or longitudinal studies that use appropriate sampling and controls to be completed in the future.

The methodological quality of each study was rated using the QATOCCS. In this review, there was variation in the overall ratings, with the majority of the studies rated as "good" or "fair" and a few studies rated as "poor." For this review, a total of 25% of studies were rated by a second independent rater. As only 25% of studies were reviewed independently, this increases the risk of bias with ratings based on the interpretation of the rater.

A further limitation included the wide-ranging methods used in studies to measure emotionalism across neurological disorders. Some studies measured emotionalism based on clinical judgement or criteria assessed by a physician, which could increase bias and potential error whereby this is based on subjective interpretation. A number of studies used the Pathological Laughter and Crying Scale (PLACS; Robinson et al., 1993) or the Center for Neurological Study – Lability Scale (CNS-LS; Moore et al., 1997), which has been shown to have good test-retest reliability. However, both of these are non-stroke-specific measures and have limitations as they are not derived based on

Table 6. Summary of psychological predictors and correlates across neurological disorders.

	Neurological disorder					
Psychological	Stroke	Multiple sclerosis	TBI	Alzheimer's disease	ALS	Parkinson's disease
Avoidance	2					
Acceptance-resignation	1					
Low social support	2					
Irritability	1					
Ideas of reference	1					
Intrusion	1					
Helplessness/ hopelessness	1					
Anxious preoccupation	1					

Note: Number indicates how many studies found an association between neurological disorder and predictors and correlates.

consensus diagnostic criteria, do not have cut-off scores to determine emotionalism caseness and it is not possible to calculate sub-scale scores for separate components of emotionalism. The differences in how emotionalism was classified in the studies identified for the current systematic review might influence the associations revealed by the studies as emotionalism may/may not have been detected correctly. The latest development of a new measure of emotionalism following stroke Testing Emotionalism After Recent Stroke – Questionnaire (TEARS-Q; Broomfield et al., 2020) has shown high internal consistency and diagnostic accuracy of tearful episodes, which could address the limitations highlighted by this review.

Interpretation of findings

The findings from this review will be discussed further in relation to each predictor and/or correlate across the neurological disorders.

Demographic and disease characteristic predictors and correlates

Evidence suggested that female gender (Foley et al., 2016; Kim & Choi-Kwon, 2000; McGrath, 2000; Phuong et al., 2009; Thakore & Pioro, 2017; Vidović et al., 2015) and a younger age (Patel et al., 2018; Tang et al., 2004; Thakore & Pioro, 2017) were associated with emotionalism in participants with stroke, multiple sclerosis and ALS. However, not all research controlled for confounding variables, which increases the risk of bias and could limit the generalisability of these findings. This research highlights important factors clinicians may consider in clinical practice whereby further support to aid the prevention of emotionalism or psycho-education to help with treatment could be offered to individuals who are younger or female.

Interestingly, demographic and stroke-specific characteristic predictors and correlates suggested strong evidence for the association between emotionalism and history of previous strokes (Choi et al., 2013; Tang et al., 2004), higher NIHSS score (Choi et al., 2013; Choi-Kwon et al., 2012; Ko et al., 2018; Tang et al., 2004), motor and sensory dysfunction (Choi-Kwon et al., 2012; Kim & Choi-Kwon, 2000; Wei

et al., 2016), higher BI score (Andersen et al., 1995; Choi et al., 2013) and mRS score (Choi-Kwon et al., 2012; Ko et al., 2018). These factors could highlight the general severity of the stroke and the extent of damage to brain areas, which is consistent with the neuropsychological findings of an association between emotionalism and poorer intellectual functioning. However, this highlights a threshold effect whereby the greater the degree of cognitive deterioration, the more likely it will be that areas specific to emotionalism will be implicated, so research needs to control for this.

Anatomical predictors and correlates

The findings summarized in this review support previous theories and hypotheses about the mechanisms of emotionalism that have been proposed. An early theory of the pathophysiology of emotionalism proposed emotionalism may be due to disruptions to the cortical inhibition to the upper brainstem centre and release of the lower bulbar nuclei (Wilson, 1924). This review offers support for this theory with an association between lesions located at the pons and PSPLC identified with pontine lesion independently related to PSPLC in participants following a stroke (Wang et al., 2016).

Furthermore, there was a considerable amount of research included in this review that supported the gate control theory highlighting the role of the cerebellum in the modulation of emotion and cerebellar pathways or lesions from the motor, frontal and temporal lobes to the brainstem (Parvizi et al., 2009). The research found individuals with emotionalism had increased mean diffusivity of white matter tracts underlying the frontotemporal cortex, the transverse pontine fibres and the middle cerebellar peduncle following a stroke (Floeter et al., 2014). Also, the left cerebellum posterior lobe was significantly lower for ALS individuals with emotionalism (Liu et al., 2017). Additionally, there was a greater frequency of frontal lobe injury and a difference in the frequency of frontal lobe lesions in individuals with emotionalism following a TBI (Tateno et al., 2004).

These anatomical findings highlight the possible involvement of the frontostriatal network, which consists of both bulbar and frontal inhibition (Wiecki & Frank, 2013). Furthermore, frontal-subcortical circuits which mediate motor activity and behaviour in humans could be implicated (Tekin & Cummin, 2002). The frontal-subcortical circuits link specific areas of the frontal cortex to the basal ganglia and thalamus. In this review, lesions to brain areas involved in these networks/circuits have been highlighted across neurological disorders. This emphasizes important possible mechanisms of emotionalism which could help enhance theoretical understanding of emotionalism and extend clinicians understanding. However, further research is required to validate these findings.

Disruptions of neurotransmitters such as serotonin or dopamine have been hypothesized to lead to changes in emotional expression (Rabins & Arciniegas, 2007). Selective serotonin reuptake inhibitors (SSRI's), which increase the synaptic availability of serotonin were found to show improvements in crying only episodes of emotionalism and mixed episodes of emotionalism (Andersen

et al., 1993; Brown et al., 1998; Burns et al., 1999). Additionally, midbrain/pons [I]β-CIT binding ratios of serotonin transporter densities were significantly lower in stroke participants with crying only episodes of emotionalism (Murai et al., 2003). These studies included in this review suggested the role of serotonergic pathways in the pathophysiology of emotionalism and supports the neuroanatomical evidence discussed in this review of different brain areas which are intimately involved in the production of serotonin or have functions strongly modulated by serotonin as indicated by more dense occurrence of serotonin receptors. The serotonergic circuits in the brain have a large set of 5-HT receptors in the substantia nigra, the hippocampal formation, the hypothalamus, the amygdala, the striatum, and the frontal cortex (Charnay & Léger, 2010).

Neuropsychological predictors and correlates

Neuropsychological predictors and correlates were identified across three neurological disorders: stroke, multiple sclerosis and ALS. Overall, evidence of general intellectual impairments was revealed by several studies whereby emotionalism was correlated with a lower performance and full-scale IQ scores on the WAIS-R (Feinstein et al., 1997). Mild cognitive impairment following a stroke was associated with emotionalism (Wang et al., 2016) and there is an increased risk of moderate cognitive impairment of emotionalism in a sample of participants with multiple sclerosis (Fitzgerald et al., 2018). However, an association between emotionalism and intellectual impairments at 6- and 12-months post-stroke was identified but with no association at one month in participants with crying only episodes of emotionalism (Andersen et al., 1995). This could highlight further questions of whether global impairments reflect the extent of damage in the brain and/or the likely impact on network functioning rather than specific lesion locations for emotionalism.

Investigations of executive functioning were assessed and revealed a negative correlation between DKEFS card sort and card sort description (Hanna et al., 2016). Additionally, individuals with emotionalism generated significantly less words on the COWAT, revealed deficits in verbal fluency, visual memory, slower processing speed (Hanna et al., 2016), took longer to perform the Stroop test and a trend was revealed for patients with emotionalism making more total errors on the WSCT (Feinstein et al., 1999; McCullagh et al., 1999). These studies highlight individuals with emotionalism had impairments in inhibition and strategy generation.

This evidence could highlight the disruptions of the anterior cingulate cortex and prefrontal regions of the brain, which are involved in the executive attention network, which has a key function associated with executive functioning (Posner et al., 2007). Overall the findings of the anatomical studies are consistent with deficits in working memory, inhibitory control and regulating emotions. Although the evidence in this review is correlational, meaning it is difficult to draw definite conclusions due to issues with causality, these studies do

suggest a relationship between certain neuropsychological factors and emotionalism, which should be further investigated.

Psychological predictors and correlates

There were only three studies exploring psychological predictors and correlates of emotionalism in participants following a stroke. Evidence of an association between avoidance and emotionalism was reported in two studies (Eccles et al., 1999; Wei et al., 2016). Previous research has found that emotionalism causes distress, embarrassment and avoidance of social interactions (Wortzel et al., 2008) where this could be viewed as similar to social anxiety-isolation as a consequence to emotionalism. Ideas of reference were associated with emotionalism and embarrassment potentially interacting in this relationship (Calvert et al., 1998). This highlights beliefs of emotionalism held by individuals and the socially disabling effects. In this review, two studies also found an association between low social support and emotionalism. Further research would be beneficial to validate these findings and could be important to explore if associations exist in other neurological disorders.

Research has found individuals with emotionalism have an increased likelihood of developing psychiatric outcomes such as depression (Tang et al., 2004), anxiety (Knapp et al., 2020) and anger (Kneebone & Lincoln, 2012). These outcomes could be hypothesized as developing as a result of the impact of emotionalism. To date there is no psychological theory explaining emotionalism; however, these findings indicate the potential to explore social support, social self-consciousness and related avoidance as possible modifiable psychological treatment targets with individuals with emotionalism.

Future research

Further research is required exploring psychological predictors and correlates such as avoidance and coping styles in individuals following a stroke as only a limited number of studies were identified and no studies explored psychological predictors in other neurological disorders. Future research could help to identify potential reversible psychological/behavioural maintaining factors. This is clinically important as research has indicated how prevalent emotionalism is in neurological disorders, whereby further research could help inform clinical practice and potential psychological treatments. It is important more longitudinal and RCT studies are carried out to explore potential predictors and correlates, which could help to overcome the limitation of causality raised with cross-sectional studies and increase the methodological quality. Further research is also required exploring predictors and correlates in neurological disorders such as vascular dementia as this review highlighted a disproportionate number of studies across neurological disorders.

Specifically, from the findings in this review, future research could investigate the hypothesis relating to genetic vulnerability, serotonergic pathways,

executive inhibitory control, avoidance and social support in the development and longer-term maintenance of emotionalism. Furthermore, there is a need for better measurement of emotionalism as the majority of studies included in this review used either the CNS-LS (Moore et al., 1997) or PLACS (Robinson et al., 1993). Both these measures have limitations and undetermined psychometric characteristics in stroke populations and were not derived from consensus diagnostic criteria.

Conclusions and clinical implications

This was the first systematic review that investigated the predictors and correlates of emotionalism across neurological disorders. The evidence in the review emphasizes the importance of serotonin which highlights any brain area that is relatively more involved in serotonin (production, modulation of function) might show up as more likely damaged across neurological populations. This could suggest there is not a specific anatomical or neuropsychological "signature" because of the widespread presence of serotonin related mechanisms in the brain and beyond. However, findings from the review implicated bulbar and frontal areas as well as white matter tracts involved in connecting frontal, posterior/brain stem/midbrain regions. Potentially a diathesis-stress model of emotionalism could be tentatively proposed whereby if serotonin pathways are disrupted in any specific location this might increase vulnerability to emotional expression in response to a trigger/stressor and in turn facilitating avoidance. However, there are some stronger associations perhaps reflective of areas more heavily implicated in serotoninergic activity. This highlights important factors that could be considered by clinicians and health care policy whereby support is offered to individuals to assist with earlier identification of emotionalism following a diagnosis of a neurological disorder as well as offering treatment or management.

Disclosure statement

No potential conflict of interest was reported by the author(s).

Funding

This systematic review was conducted as part of the first authors Doctorate in Clinical Psychology Training at the University of East Anglia (UEA).

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Appendix. Systematic review search strategy

Table A1. Search terms for PsycINFO, PubMed and CINAHL complete databases.

Participant/population	AND	Outcome
Stroke – "stroke" OR "cerebr* accident" OR "cva" OR "apoplexy" OR (MM "Stroke")	AND	"emotionalism" OR "emotional lability" OR "emotional dysregulation" OR "involuntary emotional expression disorder" OR "involuntary crying" OR "involuntary laughing" OR "lability of mood" OR "pathological laughing" OR "pathological crying" OR "pseudobulbar affect" OR "emotional incontinence" OR "pathological display of affect" OR "inappropriate laughing" OR "inappropriate crying"
Multiple sclerosis – "MS" OR "multiple sclerosis" OR "Sclerosis Disseminated" OR (MM "Multiple Sclerosis")	AND	"emotionalism" OR "emotional lability" OR "emotional dysregulation" OR "involuntary emotional expression disorder" OR "involuntary crying" OR "involuntary laughing" OR "lability of mood" OR "pathological laughing" OR "pathological crying" OR "pseudobulbar affect" OR "emotional incontinence" OR "pathological display of affect" OR "inappropriate laughing" OR "inappropriate crying"
Parkinson's disease – "idiopathic parkinson* disease" OR "paralysis agitans" OR "parkinson* disease idiopathic" OR "parkinson* disease" OR "primary parkinsonism" OR (MM "Parkinsonian Disorders")	AND	"emotionalism" OR "emotional lability" OR "emotional dysregulation" OR "involuntary emotional expression disorder" OR "involuntary crying" OR "involuntary laughing" OR "lability of mood" OR "pathological laughing" OR "pathological crying" OR "pseudobulbar affect" OR "emotional incontinence" OR "pathological display of affect" OR "inappropriate laughing" OR "inappropriate crying"
Traumatic brain injury – "traumatic brain injury" OR "TBI" OR "brain injury" OR "head injury" OR "head trauma" OR "traumatic encephalopathy" OR "acquired brain injur*" OR (MM "Brain Injuries")	AND	"emotionalism" OR "emotional lability" OR "emotional dysregulation" OR "involuntary emotional expression disorder" OR "involuntary crying" OR "involuntary laughing" OR "lability of mood" OR "pathological laughing" OR "pathological crying" OR "pseudobulbar affect" OR "emotional incontinence" OR "pathological display of affect" OR "inappropriate laughing" OR "inappropriate crying"
Alzheimer's disease – "alzheimer* disease" OR "dementia" OR (MM "Alzheimer Disease")	AND	"emotionalism" OR "emotional lability" OR "emotional dysregulation" OR "involuntary emotional expression disorder" OR "involuntary crying" OR "involuntary laughing" OR "lability of mood" OR "pathological laughing" OR "pathological crying" OR "pseudobulbar affect" OR "emotional incontinence" OR "pathological display of affect" OR "inappropriate laughing" OR "inappropriate crying"
Vascular dementia – "vascular dementia" OR "VaD" OR (MM "Dementia, Vascular")	AND	"emotionalism" OR "emotional lability" OR "emotional dysregulation" OR "involuntary emotional expression disorder" OR "involuntary crying" OR "involuntary laughing" OR "lability of mood" OR "pathological laughing" OR "pathological crying" OR "pseudobulbar affect" OR "emotional incontinence" OR "pathological display of affect" OR "inappropriate laughing" OR "inappropriate crying"
Amyotrophic lateral sclerosis – "ALS" OR "amyotrophic lateral sclerosis" OR "Lou Gehrig* disease" OR "motor neurone disease" OR "MND" OR (MM "Amyotrophic Lateral Sclerosis")	AND	"emotionalism" OR "emotional lability" OR "emotional dysregulation" OR "involuntary emotional expression disorder" OR "involuntary crying" OR "involuntary laughing" OR "lability of mood" OR "pathological laughing" OR "pathological crying" OR "pseudobulbar affect" OR "emotional incontinence" OR "pathological display of affect" OR "inappropriate laughing" OR "inappropriate crying"

Table A2. Search terms for Embase database.

1. stroke.mp.
2. (cerebr* adj3 accident).mp.
3. cva.mp.
4. apoplexy.mp.
5. cerebrovascular accident/
6. MS.mp.
7. (multiple adj3 sclerosis).mp.
8. (sclerosis adj3 disseminated).mp.
9. multiple sclerosis/
10. (idiopathic adj3 parkinson* adj3 disease).mp.
11. (paralysis adj3 agitans).mp.
12. (parkinson* adj3 disease adj3 idiopathic).mp.
13. (parkinson* adj3 disease).mp.
14. (primary adj3 parkinsonism).mp.
15. Parkinson disease/
16. (traumatic adj3 brain adj3 injury).mp.
17. TBI.mp.
18. (brain adj3 injury).mp.
19. (head adj3 injury).mp.
20. (head adj3 trauma).mp.
21. (traumatic adj3 encephalopathy).mp.
22. (acquired adj3 brain adj3 injur*).mp.
23. traumatic brain injury/
24. (alzheimer* adj3 disease).mp.
25. dementia.mp.
26. Alzheimer disease/
27. (vascular adj3 dementia).mp.
28. VaD.mp.
29. multiinfarct dementia/
30. ALS.mp.'
31. (amyotrophic adj3 lateral adj3 sclerosis).mp.
32. (Lou adj3 Gehrig* adj3 disease).mp.
33. (motor adj3 neurone adj3 disease).mp.
34. MND.mp.
35. amyotrophic lateral sclerosis/
36. emotionalism.mp.
37. (emotional adj3 lability).mp.
38. (emotional adj3 dysregulation).mp.
39. (involuntary adj3 emotional adj3 expression adj3 disorder).mp.
40. (involuntary adj3 crying).mp.
41. (involuntary adj3 laughing).mp.
42. (lability adj3 of adj3 mood).mp.
43. (pathological adj3 laughing).mp.
44. (pathological adj3 crying).mp.
45. (pseudobulbar adj3 affect).mp.
46. (emotional adj3 incontinence).mp.
47. (pathological adj3 display adj3 of adj3 affect).mp.
48. (inappropriate adj3 laughing).mp.
49. (inappropriate adj3 crying).mp.

*[mp = title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word].

Stroke: 1 or 2 or 3 or 4 or 5 and 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49.

Multiple sclerosis: 6 or 7 or 8 or 9 and 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49.

Parkinson's disease: 10 or 11 or 12 or 13 or 14 or 15 and 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49.

Traumatic Brain Injury: 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 and 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49.

Alzheimer's disease: 24 or 25 or 26 and 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49.

Vascular Dementia: 27 or 28 or 29 and 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49.

Amyotrophic lateral sclerosis: 30 or 31 or 32 or 33 or 34 or 35 and 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49.