# Stressful life events and maltreatment in conversion (functional neurological) disorder: systematic review and meta-analysis of case-control studies

*Lea Ludwig, Joëlle A Pasman, Timothy Nicholson, Selma Aybek, Anthony S David, Sharon Tuck, Richard A Kanaan, Karin Roelofs, Alan Carson, Jon Stone*

## Summary

**Background** Stressful life events and maltreatment have traditionally been considered crucial in the development of conversion (functional neurological) disorder, but the evidence underpinning this association is not clear. We aimed to assess the association between stressors and functional neurological disorder.

**Methods** We systematically reviewed controlled studies reporting stressors occurring in childhood or adulthood, such as stressful life events and maltreatment (including sexual, physical abuse, and emotional neglect) and functional neurological disorder. We did a meta-analysis, with assessments of methodology, sources of bias, and sensitivity analyses.

**Findings** 34 case-control studies, with 1405 patients, were eligible. Studies were of moderate-to-low quality. The frequency of childhood and adulthood stressors was increased in cases compared with controls. Odds ratios (OR) were higher for emotional neglect in childhood (49% for cases *vs* 20% for controls; OR 5·6, 95% CI 2·4–13·1) compared with sexual abuse (24% *vs* 10%; 3·3, 2·2–4·8) or physical abuse (30% *vs* 12%; 3·9, 2·2–7·2). An association with stressful life events preceding onset (OR 2·8, 95% CI 1·4–6·0) was stronger in studies with better methods (interviews; 4·3, 1·4–13·2). Heterogeneity was significant between studies ($I^2$ 21·1–90·7%). 13 studies that specifically ascertained that the participants had not had either severe life events or any subtype of maltreatment all found a proportion of patients with functional neurological disorder reporting no stressor.

**Interpretation** Stressful life events and maltreatment are substantially more common in people with functional neurological disorder than in healthy controls and patient controls. Emotional neglect had a higher risk than traditionally emphasised sexual and physical abuse, but many cases report no stressors. This outcome supports changes to diagnostic criteria in DSM-5; stressors, although relevant to the cause in many patients, are not a core diagnostic feature. This result has implications for ICD-11.

**Funding** None.

## Introduction

Conversion (functional neurological symptom) disorder (DSM-5) refers to patients who have neurological symptoms in the absence of neurological disease, encompassing symptoms such as limb weakness, seizures, and movement disorders. Such disorders are one of the most common reasons for neurological referral (16% of new referrals)[1] and are as disabling and distressing as neurological counterparts such as multiple sclerosis or epilepsy.[2] Traditionally, the disorder has been diagnosed on both the absence of neurological disease and the "conflicts or other stressors [that] precede the initiation or exacerbation of the symptom or deficit".[3] However, the most recent edition of DSM-5 dropped the association with conflicts or other stressors as an explicit diagnostic criterion and emphasised the need to find positive clinical features such as Hoover's sign in functional leg weakness or a sudden prolonged motionless unresponsive episode with eyes closed in dissociative (non-epileptic) seizure. This change has not been universally welcomed and whether ICD-11 will follow suit is uncertain.

Stressors, either recent life events, maltreatment around the time of symptom onset, or historical stressors, particularly childhood sexual abuse, have been considered key factors for the cause of functional neurological disorder since the time of Briquet's 1859 Clinical and Therapeutic Treatise on Hysteria.[4] In 1895, Breuer and Freud described the processes by which such psychological stress was converted into physical symptoms in their seminal Studies on Hysteria,[5] giving the condition its name—conversion disorder—and a theory for cause that remains the bedrock of practice for most clinicians today.

However, critics of the conversion hypothesis have commented that the empirical evidence to support the hypothesis is poor and that the dominance of the theory distorts clinician's appreciation of the limitations of the available literature and inhibits the development of alternate or expanded models.[6]

Previous reviews summarising studies of stressors, including maltreatment and stressful life events, in functional neurological disorder have either not been systematic,[6] or have only reviewed non-epileptic

**Department of Clinical Psychology and Psychotherapy, Universität Hamburg, Hamburg, Germany** (L Ludwig MSc); **Developmental Psychopathology** (J A Pasman MSc), **Behavioural Science Institute** (K Roelofs PhD), **and Donders Institute for Brain Cognition and Behaviour** (K Roelofs), **Radboud University, Nijmegen, Netherlands; Section of Cognitive Neuropsychiatry, Institute of Psychiatry Psychology & Neuroscience, King's College London, London, UK** (T Nicholson PhD, S Aybek MD, A S David MD); **Laboratory for Behavioral Neurology and Imaging of Cognition, Fundamental Neurosciences Department, Geneva University, Geneva, Switzerland** (S Aybek); **Epidemiology and Statistics Core, Edinburgh Clinical Research Facility, Edinburgh, UK** (S Tuck MSc); **Department of Psychiatry, University of Melbourne, Austin Health, Heidelberg, VIC, Australia** (R A Kanaan PhD); **Florey Institute for Neuroscience and Mental Health, Heidelberg, VIC, Australia** (R A Kanaan); **Department of Clinical Neurosciences** (A Carson MD, J Stone PhD) **and Department of Rehabilitation Medicine** (A Carson), **NHS Lothian, Edinburgh, UK; and Centre for Clinical Brain Sciences, University of Edinburgh, Edinburgh, UK** (A Carson, J Stone, L Ludwig)

Correspondence to:
Dr Alan Carson, Centre for
Clinical Brain Sciences, University
of Edinburgh, C/O Robert
Fergusson Unit, Royal Edinburgh
Hospital, Edinburgh EH10 5HF, UK
**a.carson@ed.ac.uk**

## Research in context

### Evidence before this study

In the past decade, interest in conversion (functional neurological) disorders has upsurged. Largely dismissed during the latter part of the 20th century as a historical entity that was usually the product of misdiagnosis, high-quality evidence now shows that such disorders are common, disabling, and can be diagnosed accurately. The dominant view of cause had been that these symptoms arose as a consequence of the conversion of psychic distress into physical symptoms. With new research came new theories of cause; in particular, increasingly sophisticated models of mechanism based in neurosciences. These theories challenged the dominant view of psychological stressors being converted into physical symptoms. One view is that these new studies were complementary and simply explained the mechanism of conversion. Other clinicians and researchers took the stance that this mechanism was alternate and that conversion disorder could occur in the absence of identifiable exposure to stressors. DSM-5 took the latter view and was explicit that the presence of such stressors was no longer required, although paradoxically went for a compromise name: conversion (functional neurological symptoms) disorder. This opinion was not met with universal approval, and passionate debate still exists, but has often been shaped by individuals citing case examples from their own practice and less attention has been paid to the existing data from case-control studies. As a group of clinical researchers who have been involved in this debate but from opposing perspectives, we sought to systematically review the available literature. We searched PubMed and Science Direct for case-control studies in English from 1965 to Nov 4, 2016, with the search terms ("psychogenic" OR "conversion disorder" OR "non-epileptic") AND ("abuse" OR "life event") AND ("control" OR "controlled" OR

"case-control"). This search was supplemented by reviewing the reference lists of eligible studies and previous reviews. After removing duplicates and ineligible studies, we included 34 studies in our systematic review and meta-analysis.

### Added value of this study

To our knowledge, this review provides the most comprehensive aggregation of the evidence from case-control studies since 1965. We covered the full phenotype of conversion (functional neurological) disorder, including both seizure disorders and motor or sensory disorders. We examined the frequency of stressful life events and of different types of maltreatment in childhood and adult life in patients with conversion (functional neurological) disorder and in both healthy controls and controls with neurological disease and psychiatric disorders. In addition to a qualitative review of individual studies, we quantitatively evaluated the association between stressors and functional neurological disorder, and did subgroup and sensitivity analyses to investigate sources of bias to understand the limitations to our data.

### Implications of all the available evidence

Our results show that the rate of childhood and adult stressful life events and maltreatment, particularly emotional neglect, is increased in patients with conversion (functional neurological) disorder compared with controls. The association was stronger in cases of childhood onset and when we compared with healthy controls as opposed to disease controls. However, a proportion of cases report no stressors. We concluded that stressors are relevant to the cause and development of conversion (functional neurological) disorder and therefore a potential treatment target, but exposure to such stressors is not an essential diagnostic feature. Our findings support the changes to DSM-5 and have implications for ICD-11.

seizures[7,8] or childhood sexual abuse.[7] These reviews suggested an association of stressors and functional neurological disorder, but were of limited scope. When looking at more broad phenotypes, reviews of somatic symptom disorders have notionally included functional neurological disorder, but either did not identify much of the existing primary literature[9] or were focused on functional somatic syndromes such as irritable bowel syndrome or chronic fatigue, which overlap with, but are different from, functional neurological disorder.[10]

Technically, the study of maltreatment—used here as an umbrella term for sexual and physical abuse as well as emotional neglect—and stressful life events is challenging for many reasons. These challenges include patients' willingness to disclose sensitive information (and possibly even awareness of it or of its potential relevance), recall bias, difficulty determining over what timeframe stressors are relevant, whether those that are present are relevant to cause, and the selection of appropriate controls. The use and selection of control

groups is of particular importance as the rates of recent and historical stressors vary in different clinical (whether psychiatric or neurological) and healthy populations.

Furthermore, the descriptive terminology is at times ill defined and, in doing a systematic review, we are partly dependent on the definitions used in individual studies. Thus, during the process of data amalgamation, it becomes inevitable that compromises are made between the uniqueness of an individual event and its psychological context, and the need to impose a taxonomy to allow quantitative study. We have developed a glossary of terminology that, although imperfect, allows for clarity and reproducibility (appendix).

We aimed to do a systematic review of the association between childhood and adult stressful life events and maltreatment and conversion (functional neurological) disorder by reviewing all quantitative case-control studies since 1965 and comparing frequencies in functional neurological disorder populations with those frequencies in healthy, neurological or psychiatric disorder control

populations. We excluded physical injury, physiological events, or diseases as we have previously described their association to functional neurological disorder in previous systematic reviews and prospective studies.[2,11,12]

While setting our aims we were cognisant of two further arguments. First, we can only measure reported life events and maltreatment. Different techniques can result in better or poorer reporting, but ultimately a distortion might exist between what was reported and what occurred. Second, thinking about stressful life events and maltreatment has been argued to be misleading and it is the patient's inner psychological state that matters, which clinicians and researchers say can only be uncovered by prolonged psychotherapy. This argument is exemplified by one of Freud's original cases of treated hysteria, Fräulein Elisabeth von R.[5] Freud considered the stressor was having romantic feelings for her brother-in-law, which the patient always denied. She also disputed Freud's assertion that she recovered from her functional neurological disorder symptoms. The truth of the matter is unresolved. Our view is a pragmatic one: testing of subjective evaluation of emotions in a quantitative study would be very difficult and, more importantly, no empirical case-control data of this type for functional neurological disorder have been suitable for quantitative meta-analytic evaluation. Our study therefore evaluated the occurrence of reported events.

## Methods

### Search strategy and selection criteria

We searched the databases PubMed and Science Direct and the reference lists of eligible studies and reviews[13,14] from 1965 to Nov 4, 2016. Search terms were ("psychogenic" OR "conversion disorder" OR "non-epileptic") AND ("abuse" OR "life event") AND ("control" OR "controlled" OR "case-control").

Studies were included if (i) they reported on patients with conversion (functional neurological) disorders, described as functional, non-organic, psychogenic, hysterical, or conversion disorder; (ii) they reported data comparing cases with at least one control group on the type, severity, frequency, or temporal association of maltreatment or stressful life events, experienced in childhood or adulthood; and (iii) when the size of each group was at least ten. We included studies in paediatric as well as adult populations. When multiple publications were from the same study, we chose the one with the more complete primary outcomes. Studies were excluded (i) when the data of interest were presented only with p values and with no numerical values in each group; (ii) when the same data have been reported previously; or (iii) when studies were not available in English.

### Data analysis

All primary studies were reviewed by one author (LL). A second author (JAP) checked the data and any discrepancies were arbitrated by two other authors (AC and JS). We collected data regarding (i) the setting of the samples; (ii) the nature of case and control groups; (iii) the sex and age of patients and controls; (iv) the instruments used to measure stressors; (v) the data on stressors; and (vi) the data from those studies that stated explicitly that the person had not had any maltreatment or stressful life event.

We assessed methodological quality of eligible studies using an adaptation of the Newcastle–Ottawa Quality Assessment Scale for case-control studies.[15] The scale was adapted following the recommendations from Paras and colleagues.[9] Individual quality items are listed in the appendix. The quality was assessed twice (by LL and JAP) and any disagreements were resolved by a further author (AC).

We calculated odds ratios (OR) with 95% CI for both dichotomous and continuous data. We used statistical approaches described by Borenstein and colleagues[16] that allow data pooling. Furthermore, we used a proportion meta-analysis summary statistic for dichotomous data. Subgroup and sensitivity analyses were planned for the following grouping variables: study quality (median split of rating on quality scale, high vs low), type of control group (neurological disorder vs psychiatric disorder vs healthy control), age of population studied (children vs adults), type of symptom (non-epileptic seizures vs other symptoms), the time period where stressors occurred, and setting of the study (patients recruited in neurology vs psychiatry settings). We ran fixed-effect and random-effect models using StatsDirect (version 3.1.12). We quantified heterogeneity[17] using a random-effect model, and publication bias using the Egger bias statistic and inspection of funnel plots. When more than one set of data from an individual study could be included in a summary meta-analysis, we used a hierarchy to choose one set to avoid duplication in the summary statistic: stressful life events (data from more recent timepoints first), childhood stressful life events, sexual abuse, physical abuse, emotional neglect, neurological control group, psychiatric control group, and healthy control group.

Finally, we calculated population attribution fractions (PAF) around the main estimates,[18] taking data from a range of differing sources offering estimates based mainly on high-quality systematic reviews and meta-analyses of population prevalence.[19–25] PAF[26] is a measure of the contribution of a risk factor to a disease or a death at a population rather than individual level. It is the proportional reduction in population disease or mortality that would occur if exposure to a risk factor were reduced to an alternative ideal exposure scenario (eg, no tobacco use). PAF gives a measure of the effect of a given causal exposure based on the frequency of its occurrence in the population as a whole and its effect in increasing the relative risk to an individual.

### Role of the funding source

There was no funding source for this study.

| | Symptoms | Setting | Recruitment sample | Functional neurological disorder (n) | Control (n) | Measurement | Data | Time period | Sexual abuse | Physical abuse | Other |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Akyuz et al (2004)[27] | Non-epileptic seizures | Neuropsychiatry | Consecutive | 33 | 30 with epilepsy | Childhood abuse and neglect questionnaire | Dichotomous | Childhood | 33% vs 7%; p=0·009 | 79% vs 17%; p=0·0001 | 61% vs 13% for emotional abuse; p=0·0001; 42% vs 27% for emotional neglect; p=0·190 |
| Almis et al (2013)[28] | Non-epileptic seizures | Psychiatry | Non-consecutive | 22 | 22 healthy | Not described | Dichotomous | Childhood | 9% vs 5%; p=0·55 | 5% vs 5%; p=1·000 | NR |
| Alper et al (1993)[29] | Non-epileptic seizures | Neurology | Consecutive | 57 | 140 with epilepsy | Structured Clinical Interview for DSM-5 | Dichotomous | Childhood | 24% vs 7%; p<0·001 | 16% vs 3%; p<0·001 | 32% vs 9% for sexual or physical abuse, or both; p<0·0001 |
| Arnold et al (1996)[30] | Non-epileptic seizures | Neurology | Consecutive | 14 | 27 with epilepsy | Investigators' own structured interview | Dichotomous | Lifetime | 0% vs 11% | 43% vs 0% | 86% vs 33% for any trauma; p=0·004; 28% vs 18% for sexual and physical abuse |
| Baker et al (2012)[31] | Functional voice disorder | Neurology | Non-consecutive | 73 | 55 with disease,* 66 healthy* | Life Events and Difficulties Schedule | Dichotomous | Lifetime | 32% vs 18% vs 11%; p=0·008 | 41% vs 29% vs 14% (violence); p=0·025 | 49% vs 33% vs 21% for sexual and physical abuse; p=0·002; 74% vs 22% vs 14% for 1 year before onset (one or more severe life events); p<0·001; 21% vs 11% vs 9% for moderate life event; p=0·112 |
| Bakvis et al (2009)[32] | Non-epileptic seizures | Neurology | Non-consecutive | 19 | 20 healthy | Traumatic Experiences Checklist | Dichotomous | Lifetime | 74% vs 5%; p<0·001 | 63% vs 5%; p<0·001 | 74% vs 10% for emotional neglect; p<0·001; 89% vs 10% for any interpersonal trauma; p<0·001 |
| Barnett et al (1971)[33] | Functional neurological disorder | Psychiatry | Consecutive | 46 | 63 with "psychophysiologic disorders"† | Scoring medical records | Dichotomous | Lifetime | 7% vs 3% (childhood "seduction") | NR | 89% vs 87% for stress present, precipitating stressor |
| Berkhoff et al (1998)[34] | Non-epileptic seizures | Neurology and psychiatry | Non-consecutive | 10 | 10 with epilepsy | Investigators' own unstructured interview | Dichotomous | Lifetime | 20% vs 0%; p=0·179 | 10% vs 0%; p=0·317 (childhood) | NR |
| Betts and Boden (1992)[35] | Non-epileptic seizures | Psychiatry | Consecutive | 96 | 87 psychiatry, 132 with epilepsy | Case note review, only categorised with corroboration | Dichotomous | Lifetime | 54% vs 32% vs 25% | NR | NR |
| Binzer et al (1998)[36] | Functional motor disorder | Neurology | Consecutive | 30 | 30 neurology | Own Memories of Child-Rearing Experiences or Self-report | Dichotomous | Childhood | 3% vs 0% | NR | NR |
| Binzer et al (2004)[37] | Non-epileptic seizures | Neurology | Consecutive | 20 | 20 with epilepsy | Own Memories of Child-Rearing Experiences or Life Events Inventory | Continuous and dichotomous | Childhood and adulthood | 30% vs 5%; p=0·090 (incest) | NR | Number of events 1 year before onset; p<0·001; number of events in 3 months before onset, NS |
| Chabrol et al (1995)[38] | Functional neurological disorder‡ | Neurology | Consecutive | 15 | 40 neurology | Not described | Dichotomous | Adulthood | NR | NR | 66% vs 73% for emotional stress before onset; p=0·17, NS |
| Dikel et al (2003)[39] | Non-epileptic seizures | Neurology | Consecutive | 17 | 34 with epilepsy | Life Events Checklist | Dichotomous | Lifetime | 71% vs 32%; p=0·01 (childhood) | NR | 100% vs 68% for any assault (lifetime); p=0·008 |

(Table 1 continues on next page)

| | Symptoms | Setting | Recruitment sample | Functional neurological disorder (n) | Control (n) | Measurement | Data | Time period | Functional neurological disorder vs controls | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| | | | | | | | | | Sexual abuse | Physical abuse | Other |
| (Continued from previous page) | | | | | | | | | | | |
| House et al (1988)[40] | Functional voice disorder | Neurology | Consecutive | 56 | 382 healthy (Camberwell series) | Life Events and Difficulties Schedule | Dichotomous | Lifetime | NR | NR | 14% vs 8% for severe life event 1 month before onset; 23% vs 25% for 1 year before onset |
| Jawad et al (1995)[41] | Non-epileptic seizures | Psychiatry | Consecutive | 46 | 50 psychiatry | Unstructured psychiatric interview | Dichotomous | Lifetime | 9% vs 8%; p=0.9 | NR | NR |
| Kaplan et al (2013)[42] | Non-epileptic seizures | Neurology | Consecutive | 91 | 81 with epilepsy | Childhood Trauma Questionnaire | Dichotomous | Childhood | 38% vs 25%; p=0.05 | 35% vs 20%; p=0.03 | 44% vs 30% for emotional abuse; p=0.059 |
| Kozlowska et al (2011)[43] | Functional neurological disorder | Paediatric psychiatry | Consecutive | 76 | 76 healthy | School-aged Assessment of Attachment (age 6–13 years) and Transition to Adulthood Attachment Interview | Dichotomous | Childhood | NR | 15% | 13% emotional neglect; 75 vs 12% for unresolved loss and trauma; p<0.0001 |
| Kranick et al (2011)[44] | Functional motor disorder§ | Neurology | Non-consecutive | 64 | 39 neurology, 39 healthy | Childhood Trauma Questionnaire and TLEQ | Continuous | Childhood and lifetime | p=0.7 (childhood) | p=0.01; p=0.09 (childhood)¶ | p<0.0001, p<0.007¶ for emotional abuse; p<0.10 for emotional neglect; p<0.0001, p<0.0001¶ for total trauma, childhood; p=0.03, p=0.3¶ for number of events; p=0.001, p=0.04¶ for number of episodes (TLEQ) |
| Kuyk et al (1999)[45] | Non-epileptic seizures | Neurology | Non-consecutive | 27 | 47 with temporal lobe epilepsy, 25 with non-temporal lobe epilepsy | Trauma Questionnaire | Dichotomous | Lifetime | 33% vs 4% vs 0%; p<0.001 (non-epileptic seizures vs other) | 26% vs 6% vs 16%; p=0.053 (non-epileptic seizures vs other) | 37% vs 23% vs 24% for emotional neglect; NR; 44% vs 26% vs 24% for any abuse, NR |
| Litwin et al (2001)[46] | Non-epileptic seizures | Neurology | Non-consecutive | 10 | 31 with epilepsy | Dissociative Disorders Interview Schedule (with background history questions) | Dichotomous | Lifetime | 60% vs 13%; p<0.005 (one-tailed) | 50% vs 29%; p>0.05; NR | NR |
| McDade and Brown (1992)[47] | Non-epileptic seizures | Neurology | Consecutive | 18 | 18 with epilepsy | Unstructured psychiatric interview | Dichotomous | Childhood | 17% vs 5% | NR | NR |
| Mökleby et al (2002)[48] | Non-epileptic seizures | Neurology | Consecutive | 23 | 23 psychiatry, 23 healthy | Mini International Neuropsychiatric | Dichotomous | Lifetime | NR | NR | 30% vs 17% vs 0% abuse (sexual or physical), NS |

(Table 1 continues on next page)

| | Symptoms | Setting | Recruitment sample | Functional neurological disorder (n) | Control (n) | Measurement | Data | Time period | Functional neurological disorder vs controls | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| | | | | | | | | | Sexual abuse | Physical abuse | Other |
| (Continued from previous page) | | | | | | | | | | | |
| Nicholson et al (2016)[49] | Functional motor disorder | Neurology and neuropsychiatry | Consecutive | 43 | 28 psychiatry, 28 healthy | Life Events and Difficulties Schedule | Dichotomous | Lifetime | 42% vs NA vs 14%; p=0.014 | 23% vs NA vs 21%; p=0.86 | 56% vs 21% vs 18% for severe life event 1 month before onset; p=0.001 (CD vs HC); p=0.004 (CD vs DC); 47% vs 11% vs 0% for severe escape event, p=0.001 (CD vs HC); p<0.002 (CD vs DC) |
| Ozcetin et al (2009)[50] | Non-epileptic seizures | Psychiatry | Non-consecutive | 56 | 59 healthy | Childhood Trauma Questionnaire | Continuous | Childhood | p<0.001 | p<0.001 | Emotional neglect; p<0.001 |
| Plioplys et al (2014)[51] | Non-epileptic seizures | Neurology | Non-consecutive | 55 | 35 healthy | Children's Hassle Scale | Dichotomous | Childhood | 15% vs 3%; p=0.2 | 13% vs 6%; p=0.3 | 42% vs 17% for emotional neglect; p=0.01; lifetime adversities; p=0.02, (non-epileptic seizures>control) |
| Proença et al (2011)[52] | Non-epileptic seizures | Neurology | Non-consecutive | 20 | 20 with epilepsy | Childhood Trauma Questionnaire | Continuous | Childhood | p=0.123 | p=0.144 | Emotional neglect; p=0.013; maltreatment total; p=0.014 |
| Reilly et al (1999)[53] | Non-epileptic seizures | Neurology | Consecutive | 40 | 40 with irritable bowel syndrome, 40 with epilepsy | Medical History Questionnaire | Dichotomous | Childhood and adulthood | 30% vs 30%; 15% (adult); 33% vs 30% vs 15%; (childhood) | 18% vs 23% vs 0% (adult); 53% vs 40% vs 13% (childhood); non-epileptic seizures vs other p<0.001 | 45% vs 33% vs 13% for adulthood, emotional neglect; 60% vs 45% vs 23% for childhood, emotional neglect, non-epileptic seizures vs other; p<0.001 |
| Roelofs et al (2002)[54] and Roelofs et al (2005)[55]|| | Functional neurological disorder** | Psychiatry | Non-consecutive | 54 | 50 psychiatry | Structured Trauma Interview or VRMG, Life Events Self-report Questionnaire | Continuous and dichotomous | Childhood and adulthood | 24% vs 14%; p=0.85 | 28% vs 20%; p=0.28 | Recent life events (12 month), NS |
| Salmon et al (2003)[56] | Non-epileptic seizures | Neurology | Consecutive | 81 | 81 with epilepsy | Medical History Questionnaire | Dichotomous | Childhood and adulthood | 32% vs 15% for adult; p<0.001; 31% vs 16% for childhood; p<0.05 | 14% vs 4% adult; p<0.05; 36% vs 21% for childhood; p<0.05 | 31% vs 26%, adult, emotional neglect; NS; 53% vs 32%, for childhood, emotional neglect; p<0.01 |
| Say et al (2014)[57] | Non-epileptic seizures | Paediatric neurology | Consecutive | 34 | 23 with epilepsy, 35 healthy | Investigators' own questionnaire | Dichotomous | Childhood | 12% vs 0% vs 0%; p=0.02 | 27% vs 9% vs 6%; p=0.03 | 53% vs 13% vs 11% for stressful life events; p<0.001 |
| Scévola et al (2013)[58] | Non-epileptic seizures | Neurology | Non-consecutive | 35 | 49 with epilepsy | Structured Clinical Interview for the DSM | Dichotomous | Lifetime | 26% vs 4%; p=0.007 | 14% vs 12%; p=0.41 | 49% vs 25% for emotional neglect; p=0.02 |

(Table 1 continues on next page)

## Results

In total, 34 case-control studies met the inclusion criteria, providing stressful life events data for 1405 patients with functional neurological disorder and 2227 controls, which included healthy participants as well as individuals with neurological disease and psychiatric disorder (table 1; figure 1). In 24 studies,[27–30,32,34,35,37,39,41,42,45–48,50–53,56–58,60,61] data were presented for patients with non-epileptic seizures, five[33,38,43,54,59] reported on general or mixed functional neurological disorder, three[36,44,49] provided data on functional motor disorders, and two[31,40] reported on functional voice disorder (also known as functional dysphonia).

31 studies[27–42,44–50,52–54,56,58–61] included adult participants (mean age 37·1 years [SD 6·7], range 18–77 years), whereas the remaining three studies[43,51,57] came from a paediatric setting (13·7 years [0·9], 9–18 years). Both the cases and controls were mostly female participants (79·7% cases *vs* 72·2% controls). In 25 of the 34 studies[27,29,30,32,34,36–40,42,44–48,51–53,56–61] the patients were recruited from a neurology setting, eight[28,33,35,41,43,49,50,54] were from a psychiatry setting, and one study[31] came from a mixed setting. 18 studies[27,29,30,33,34,36–39,42,45–47,52,53,56,58,61] compared the functional patient group with a neurological disease control group, mainly with epilepsy; seven studies[28,32,40,43,50,51,59] compared with healthy controls, and two studies[41,54] with other psychiatric disorders control groups. In the remaining seven studies,[31,35,44,48,49,57,60] data were presented that derived from a comparison with two control groups concurrently (mostly including a healthy and a neurological control group).

14 studies[30–35,39–41,45,46,48,49,58] reported whether stressors had taken place at any moment in life. Two studies[38,60] specifically reported on stressors in adulthood, and 11 studies[27–29,36,42,43,47,50–52,57] reported on those stressors having occurred during childhood. Seven studies[37,44,53,54,56,59,61] presented separate rates for stressors that occurred during childhood and for those that occurred during lifetime or adulthood. Nine studies[31,33,37–40,49,55,57] specified the temporal associations of life events with symptom onset.

All of the studies assessed stressors retrospectively. Study setting was either a neurology clinic, psychiatry clinic, or other. 20 studies[27,29–31,33,35–43,48,53,56,57,60] recruited a consecutive sample. In 27 studies[27,29–32,36,37,39–49,51–54,56–60] the diagnosis was made by a specialist. 14 adult sample studies[28,32,37,44–48,50,54,57,58,60,61] reported symptom duration (excluding studies using symptom duration as an inclusion or exclusion criterion; mean 77·1 months [SD 58·2]). Of those, eight studies compared symptom duration between cases and controls (three[46,60,61] of them showing a significant difference), but none tried to match controls on the basis of symptom duration.

In nine studies[27,30,34,39,42,46,49,54,57] the interviewer (for outcome) was masked to the diagnosis. The Life Events and Difficulties Schedule (LEDS)[62] is often regarded as the gold standard for such assessments in this field because it comprises of a detailed interview designed to detect a wide

| Symptoms | Setting | Recruitment sample | Functional neurological disorder (n) | Control (n) | Measurement | Data | Time period | Functional neurological disorder vs controls | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | Sexual abuse | Physical abuse | Other |
| (Continued from previous page) | | | | | | | | | | |
| Functional neurological symptoms (excluding non-epileptic seizures)†† | Neurology | Non-consecutive | 45 | 45 healthy | Early Trauma Inventory Life Events Questionnaire | Continuous | Child and adulthood | NR | NR | Emotional neglect; p<0·001; negative life events (12 month); p<0·001 |
| Non-epileptic seizures | Neurology | Consecutive | 40 | 20 with epilepsy, 40 healthy | Life Event Scale (from Psychiatric Epidemiology Research Interview) | Continuous | Adulthood | NR | NR | Negative stressful life events at 5 years before; p=0·55; negative stressful life events at 12 months before; p=0·06; distress negative life event; p=0·009; non-epileptic seizures>healthy control |
| Non-epileptic seizures | Neurology | Non-consecutive | 25 | 33 with epilepsy | Life Events Checklist | Continuous and dichotomous | Childhood and lifetime | p=0·10; adulthood | p=0·03; adulthood; p=0·35; childhood | 44% vs 33%, abuse (physical or sexual); number of events; p=0·03; total stress score; p=0·004 |

Steffen et al (2015)[59]

Testa et al (2012)[60]

Tojek et al (2000)[61]

NR=not reported. NS=not significant. TLEQ=Trauma Life Events Questionnaire. CD=cases (conversion disorder). HC=healthy controls. DC=depression controls. VRMG=Vragenlijst Recent Meegemaakte Gebeurtenissen. *Disease control was organic voice disorder. †Including peptic ulcer, enteritis, ulcerative colitis, asthma, angina, hypertension, and migraine. ‡47% motor symptom, 13% sensory symptom, 20% seizures, and 20% mixed presentation (according to DSM-IV). §Tremor 62%, dystonia 17%, myoclonus 12%, gait or balance 29%, weakness 15%, and speech 12%. ¶Covared for depression. ‖Same patient sample but offered different analyses. **28 motor disorder (51·9%), four non-epileptic seizures (7·4%), three sensory (5·6%), and 19 mixed symptoms (35·2%). ††Negative somatoform dissociative symptoms; 15 dissociative motor disorder or dissociative movement disorder or dissociative anesthesia and sensory loss or dissociative sensitivity disorder; 30 multiple dissociative movement and sensitivity disorders.

*Table 1*: Studies of conversion (functional neurological) disorder included in meta-analysis
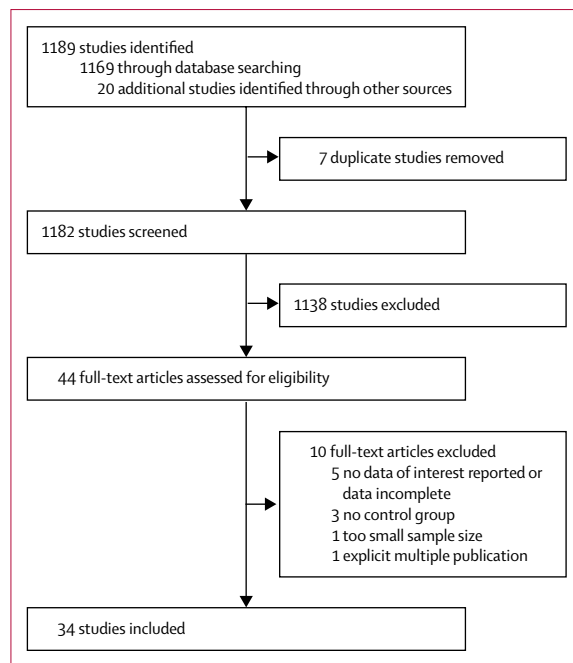
1189 studies identified
  1169 through database searching
  20 additional studies identified through other sources

7 duplicate studies removed

1182 studies screened

1138 studies excluded

44 full-text articles assessed for eligibility

10 full-text articles excluded
  5 no data of interest reported or
    data incomplete
  3 no control group
  1 too small sample size
  1 explicit multiple publication

34 studies included

*Figure 1:* **Study selection**

array of events, but these are then rated blind and contextualised to participants' life and circumstances to measure potential impact. Only three studies[31,40,49] used the LEDS interview. Most studies used standardised, structured questionnaires[27,32,36,37,39,42,44,45,50–53,56,59–61] or standardised interviews[29,33,43,46,48,55,58] to assess stressors. Four studies[30,34,41,47] used investigator-designed interviews, one[57] an investigator-designed questionnaire, and two[33,35] used case record data. Two studies[28,38] did not report how stressors were assessed.

The overall quality varied considerably among studies, ranging from 2–8 (with a possible maximum score of 11) on our modified Newcastle—Ottawa scale (appendix). The median score was 5 (IQR 4–6).

With regards to the association of reported stressors and the occurrence of functional neurological disorder, in the meta-analysis, we assessed the data (both continuous and dichotomous) in the form of ORs according to type of stressor and other study characteristics (figure 2). Heterogeneity was high for nearly all analyses, so random-effect analyses are presented throughout and data for sensitivity analyses are presented together (figure 2, table 2). When available, we have given summary statistics for the dichotomous data (table 2). In summary, we found higher rates of reported stressors, both recent and from childhood, in patients with functional neurological disorder compared with controls (figure 2, table 2). The risk was higher for childhood-onset symptoms than in adult life (figure 2, table 2). The OR was higher for emotional neglect (49% for cases *vs* 20% for controls; OR 5·6, 95% CI 2·4–13·1) than for either physical abuse (30% *vs* 12%; 3·9, 2·2–7·2)

or sexual abuse (24% *vs* 10%; 3·3, 2·2–4·8; figure 2, table 2).

Calculation of the proportion of cases of functional neurological disorder that had not experienced stressors was less straightforward. Most studies only reported the rates of individual stressors found, but obviously if it is reported that, say, 34% of subjects were sexually abused, one cannot impute that 66% suffered from no other form of stressor. Only 13 studies[29,30,31,39,40,43,45,48,49,53,54,58,61] presenting dichotomous data reported that they had systematically ascertained that the participants had not had either severe life events, assessed by the LEDS, or any subtype of maltreatment (table 3, figure 3). However, it was clear that the rigour underpinning the assessment of no stressor, or what was meant by no stressor, was variable and we divided these 13 studies according to the method used (figure 3). Three studies used the LEDS: one[49] examined patients with functional motor disorder, with 16% reporting no severe events, and two[31,40] examined patients with functional dysphonia, finding conflicting results of 26% and 77% reporting no severe life events (figure 3). Five studies[30,43,53,54,58] examined a wide range of stressors but used a clinical interview rather than a structured inquiry about the experience of stressors (no stressful life events or maltreatment were reported as 14%, 15%, 25%, 51%, and 68%; figure 3). Two studies[45,48] looked at all forms of maltreatment, including sexual abuse, physical abuse, and emotional neglect, but not stressful life events, reporting no exposure as 56% and 70%, and three studies[29,39,61] reported data only for those participants who had not been physically or sexually abused, with rates of 0%, 56%, and 68% (figure 3).

When we calculated the PAF, we found that physical abuse had a greater effect on the cause and development of functional neurological disorder (table 2). The PAF for physical abuse was 16·9% if it occurred in childhood and 14·6% in adulthood, assuming a causal association, which was higher than for sexual abuse (8·7% in childhood and 4·8% in adulthood), and to a lesser extent emotional neglect (15·1% in childhood and 11·0% in adulthood), because physical abuse is more prevalent in the population in general (table 2).

For the sensitivity analysis, we hypothesised that various methodological issues related to the nature of the symptom, population recruited, choice of control group, the assessed time period, and the quality of the studies could affect the reported differences in frequency of stressors. We assumed that patients referred to psychiatry would have higher rates of stressors than those patients referred to neurology. In fact, the difference was much less than expected (figure 2).

The most important factor for the interpretation of results, of those we examined, was the choice of comparator group. Results differed when the comparator groups were healthy controls (OR 8·6) compared with any form of disease control (figure 2). Surprisingly,
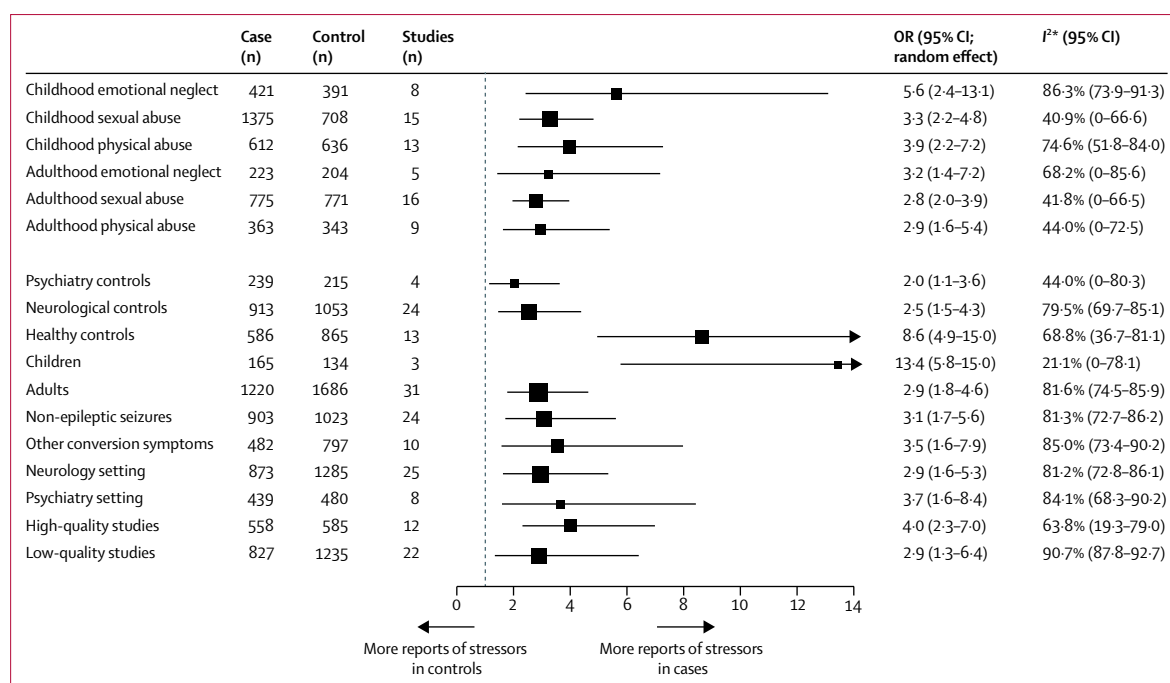
**Figure 2: Summary of meta-analysis of stressors in childhood and adulthood in conversion (functional neurological) disorder including subgroup analyses**
In case of multiple data from one individual study, a hierarchy was used to avoid duplication in the summary statistic: stressful life events (data from more recent timepoints first), childhood stressful life events, sexual abuse, physical abuse, emotional neglect, neurological control group, psychiatric control group, and healthy control group. *25% is low heterogeneity, 50% is moderate, and 75% is high.

| | All studies | | | | PAF | All studies with dichotomous data | | | Only healthy control studies with dichotomous data | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | Studies (n) | Odds ratio (95% CI) | p value | $I^2$ (95% CI)* | | Studies (n) | Cases (%; min–max) | Controls (%; min–max) | Studies (n) | Cases (%; min–max) | Healthy controls (%; min–max) |
| **Childhood** | | | | | | | | | | | |
| Sexual abuse | 15 | 3·3 (2·2–4·8) | <0·0001 | 41% (0–66) | 8·7% | 13 | 24% (3–71) | 10% (0–32) | 2 | 12% (9–15) | 4% (3–5) |
| Physical abuse | 13 | 3·9 (2·2–7·2) | <0·0001 | 75% (52–84) | 16·9% | 10 | 30% (5–79) | 12% (0–21) | 2 | 9% (5–13) | 5% (5–6) |
| Emotional neglect | 8 | 5·6 (2·4–13·1) | <0·0001 | 86% (74–91) | 15·1% | 5 | 49% (30–61) | 20% (13–32) | 1 | 42% | 17% |
| **Adulthood** | | | | | | | | | | | |
| Sexual abuse | 16 | 2·8 (2·0–4·0) | <0·0001 | 42% (0–67) | 4·8% | 14 | 35% (0–74) | 12% (9–19) | 3 | 49% (32–74) | 10% (5–14) |
| Physical abuse | 9 | 2·9 (1·6–5·4) | 0·0004 | 44% (0–73) | 14·6% | 8 | 33% (14–63) | 13% (5–22) | 2 | 43% (23–63) | 13% (5–21) |
| Emotional neglect | 5 | 3·2 (1·4–7·2) | 0·0045 | 68% (0–86) | 11·0% | 4 | 47% (29–61) | 20% (10–26) | 1 | 74% | 10% |

PAF=population attribution fraction. *25% is low heterogeneity, 50% is moderate, and 75% is high. Min=minimum. Max=maximum.

**Table 2: Summary meta-analysis data for studies of maltreatment in conversion (functional neurological) disorder and associated PAFs**

however, the disease comparator choice had little effect and the strength of association was similar irrespective of whether the comparator was neurological (2·5) or psychiatric controls (2·0; figure 2).

When we assessed studies with a high-quality rating compared with those studies with a low rating, we found no difference for study quality (figure 2). Regarding the method used, we compared data from only those studies[31,40,49] that used the well validated LEDS interview (OR 4·3, 95% CI 1·4–13·2; figure 4). Not surprisingly, this outcome showed that the LEDS led to

more reports of stressors than other less rigorous methods, such as questionnaires (figure 4).

When assessing whether the association differed between children and adults, we found that the strength of the association in children for stressors was much stronger than in adults (figure 2). However, numbers of participants in the paediatric studies were low (figure 2).

Studies that examined the occurrence of stressful life events that occurred immediately preceding symptom onset found an increased risk when comparing cases with controls (OR 2·8, 95% CI 1·4–6·0), but when we

| | Cases | Healthy controls | Neurological disorder or psychiatric disorder controls |
|---|---|---|---|
| **No severe life event (assessed by LEDS)** | | | |
| Baker and colleagues (2012)[39] | 26% | 86% | 78% |
| House and colleagues (1988)[40] | 77% | 75% | .. |
| Nicholson and colleagues (2016)[49] | 16% | 36% | 25% |
| **No stressful life events or maltreatment (assessed by clinical interview)** | | | |
| Arnold and colleagues (1996)[30] | 14% | .. | 67% |
| Kozlowska and colleagues (2011)[43] | 25% | 88% | .. |
| Scévola and colleagues (2013)[58]* | 51% | 75% | .. |
| **No stressful life events or maltreatment (rate of no exposure described only in cases)** | | | |
| Reilly and colleagues (1999)[53] | 68% | .. | .. |
| Roelofs and colleagues (2002)[54] | 15% | .. | .. |
| **No exposure to maltreatment (including emotional neglect)** | | | |
| Kuyk and colleagues (1999)[45] | 56% | .. | 75% |
| Mökleby and colleagues (2002)[48] | 70% | .. | 83% |
| **No exposure to physical or sexual abuse** | | | |
| Alper and colleagues (1993)[29] | 68% | 91% | .. |
| Dikel and colleagues (2003)[39] | 0% | .. | 50% |
| Tojek and colleagues (2000)[61] | 56% | .. | 67% |

LEDS=Life Events and Difficulties Schedule. *No report of emotional neglect.

*Table 3:* **Proportion of cases with no exposure to specific stressors when compared with controls**
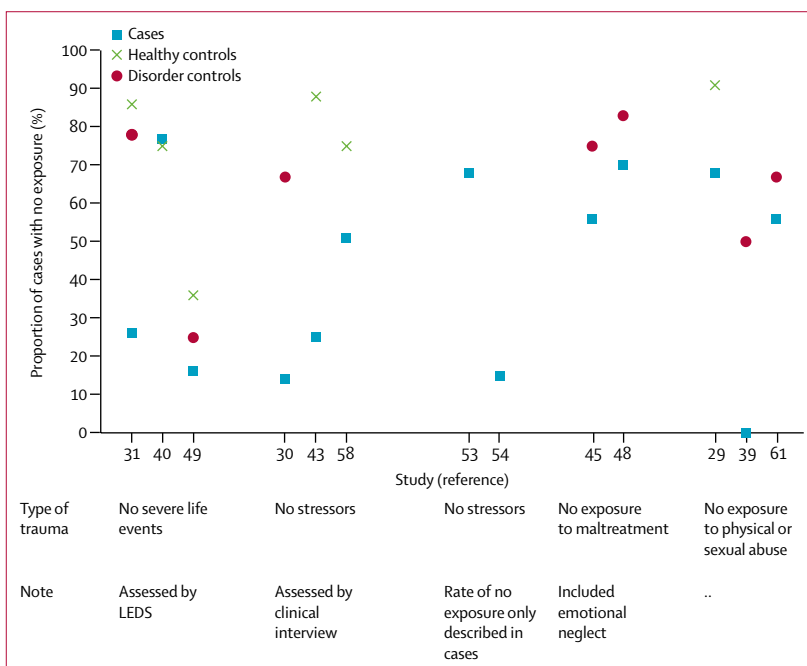


*Figure 3:* **Proportion of cases with no exposure to stressors compared with controls**

looked at studies examining the occurrence of life events throughout adult life the results were equivocal (figure 4). The broad confidence intervals might reflect the high frequency of stressful life events as a normal occurrence in adult life.

Analysis of the time period in which stressful life events occurred (without specification of the association with symptom onset) did not affect the results, with studies assessing events of recent time periods (≤3 months before assessment) showing a similar strength of association to those studies assessing events over a longer time period of 12 months before assessment (figure 4). However, we would caution that there was considerable heterogeneity within studies assessing life events over 12 months (figure 4) and one[49] of the highest quality studies that looked at multiple timepoints leading up to symptom onset found an increasing rate of severe events with increasing proximity to symptom onset.

Regarding publication bias, we produced funnel plots that we visually inspected for all our analyses (appendix). Overall, publication bias was not evident and Egger's bias statistics were non-significant for all summary statistics.

## Discussion

We found that the frequency of childhood and adult stressful life events and maltreatment were increased in patients with functional neurological disorder compared with controls. The strength of the association was higher when the comparison was with healthy controls (OR 8·6) compared with neurological (2·5) or psychiatric (2·0) control groups. A variable, but in some studies substantial, proportion of patients were found to have not reported an identifiable stressor.

ORs can be difficult to interpret because they refer to the probability of two events being associated as opposed to the actual increased risk of that event. As an approximate guide for the reader, most ORs quoted in our study (ie, between 2 and 4) would be seen as a small-to-medium effect. The OR seen in relation to emotional neglect, or the effect of stressors on presentations of functional neurological disorder in children, would be regarded as large effects.[63]

Emotional neglect had a stronger association with the development of functional neurological disorder, whether the neglect occurred in childhood or adult life, than the more traditionally described physical or sexual abuse. Higher-quality studies tended to find a slightly stronger association, but the quality of study and setting did not have the effect we might have expected.

However, emotional neglect is believed to be less prevalent in the population in general than some of the other risk factors studied.[19–25] When assessed as PAFs, which account for the population prevalence of the risk factor and the relative risk increase in the individual, we found that physical abuse in both childhood (16·9%) and adulthood (14·6%) might have the largest PAF, whereas emotional neglect had an attributable risk of 15·1% in
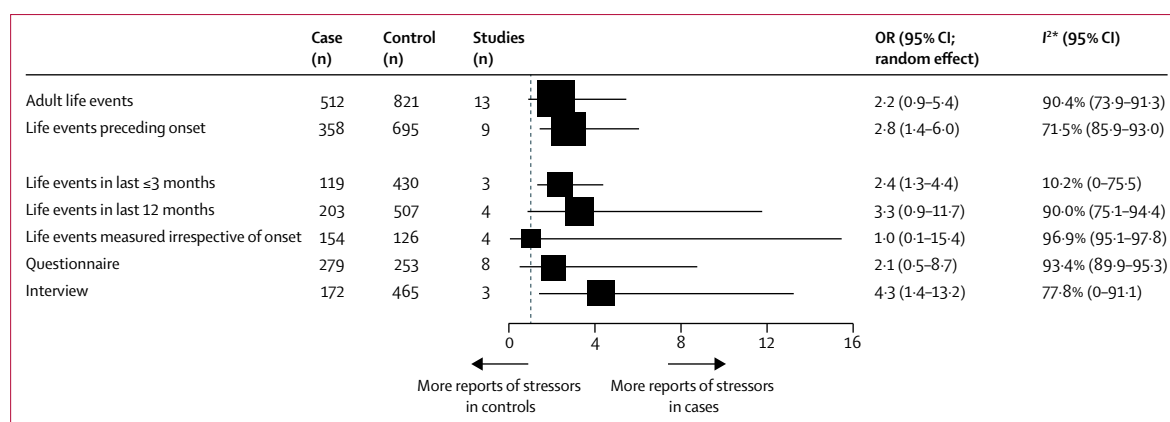
| | Case (n) | Control (n) | Studies (n) | | OR (95% CI; random effect) | $I^{2*}$ (95% CI) |
|---|---|---|---|---|---|---|
| Adult life events | 512 | 821 | 13 | | 2·2 (0·9–5·4) | 90·4% (73·9–91·3) |
| Life events preceding onset | 358 | 695 | 9 | | 2·8 (1·4–6·0) | 71·5% (85·9–93·0) |
| Life events in last ≤3 months | 119 | 430 | 3 | | 2·4 (1·3–4·4) | 10·2% (0–75·5) |
| Life events in last 12 months | 203 | 507 | 4 | | 3·3 (0·9–11·7) | 90·0% (75·1–94·4) |
| Life events measured irrespective of onset | 154 | 126 | 4 | | 1·0 (0·1–15·4) | 96·9% (95·1–97·8) |
| Questionnaire | 279 | 253 | 8 | | 2·1 (0·5–8·7) | 93·4% (89·9–95·3) |
| Interview | 172 | 465 | 3 | | 4·3 (1·4–13·2) | 77·8% (0–91·1) |

More reports of stressors in controls ← → More reports of stressors in cases

*Figure 4:* Summary of meta-analysis of adult stressful life events in conversion (functional neurological) disorder including sensitivity analysis by nature and duration of life event period assessed

In case of multiple data from one individual study, a hierarchy was used to avoid duplication in the summary statistic: stressful life events (data from more recent timepoints first), childhood stressful life events, sexual abuse, physical abuse, emotional neglect, neurological control group, psychiatric control group, and healthy control group. *25% is low heterogeneity, 50% is moderate, and 75% is high.

childhood and 11·0% in adult life. The PAF for childhood sexual abuse (8·7%) was higher than for sexual abuse in adult life (4·8%), suggesting the former might be more relevant, but both had a smaller contribution than physical abuse and emotional neglect.

We believe our meta-analysis was strong in terms of identification of appropriate papers, but the meta-analytical method we used has some limitations. We used a rationally derived hierarchy to choose one pair of data to avoid duplicate data appearing in the summary statistic. This technique has clear benefits in providing an objective and replicable way to deal with multiple datapoints. The sensitivity analysis should detect and account for any differences in the choice of datapoints, but our choices were selective and might have affected the results. The quality of the underlying literature also had limitations. Generally, the quality of studies in this field was only fair, with a median quality rating of 5 of 11 on our modified Newcastle–Ottawa scale; although some exceptions were notable. Most individual studies were too small to find conclusive results and heterogeneity was high. However, our meta-analyses and sensitivity analyses had relatively consistent results given the diverse range of settings and methods, suggesting reliable conclusions.

Most studies used self-report questionnaires, which, although quicker and cheaper to use, are generally less sensitive than interviews. Conversely, enquiries into a wide range of possible stressors and gaining extensive details of the context of the participants' lives, as done in a gold standard interview method, such as the LEDS,[62] did lead to higher rates of reporting of stressors. Whichever method was used, a proportion of patients with functional neurological disorder reported no stressors.

The study of stressors has been largely one of retrospective assessment. For childhood stressors, problems with recall bias which can lead to either over-reporting or under-reporting have been well documented,[64,65] but, for stressors occurring in adulthood, some retrospective methods have been validated with independent verification of remembered events[66,67]—eg, up to 5 years with the LEDS (panel).[62]

We do not claim that our study is definitive on the topic of stressors and functional neurological disorder; the evidence has limitations. However, it should be noted that to our knowledge, our study incorporates the full extent of the case-control evidence linking stressors to functional neurological disorder. The extent, and the limitations, of the evidence for such a well engrained theory might come as a surprise to many clinicians.

The clinical and research implications from our findings are important. For the clinician faced with an individual patient, stressful life events and maltreatment should still be considered as a potential factor in the cause and development of functional neurological disorder and, when present, a potential treatment target. However, a proportion of patients do not report any such stressors, and such exposures are common in the general population; therefore, although potentially relevant to the cause, these exposures cannot be regarded as necessary to reach a diagnosis. Furthermore, clinicians should not assume the patient is consciously or unconsciously not reporting stressors if none are forthcoming after thorough questioning. Similar to most clinicians practicing in this specialty, we have had the experience of patients denying exposure to maltreatment only to disclose it later on, but perhaps less memorable are the patients who go through treatment, often recovering, and in whom no such history is ever disclosed. Our results suggest that a proportion of patients report no such stressors, and our experience suggests excessive zeal in searching out maltreatment can be just as harmful as a complete lack of interest. Of note, emotional neglect is associated with a higher individual

**Case finding and recruitment**
- Diagnostic suspicion bias: some patients might have been given the diagnosis because they had experienced stressors, when other patients without stressors might have just been left as "blackouts ?cause".
- Misdiagnosis: suggested to be rare by published studies.
- Recruitment bias: those patients seen in psychiatric clinics might have had more stressors and might present with psychiatric comorbidity.
- DSM definition: patients with functional neurological disorder as defined strictly by DSM-IV or earlier would by definition have to have a "conflict" or "other stressors". In fact, few studies appeared to adhere to DSM.
- Diagnosis: diagnosing functional neurological disorder might alter patients' reviews of their life history and cause an erroneous reassessment of humdrum events as substantial stressors.

**Sample sizes**
Small sample sizes are unlikely to find a significant result even if the effect is present (type II error).

**Blinding**
Only nine studies measured outcome masked to the diagnosis.

**Confounding with comorbidities**
Possibly the case for depression and anxiety. Could also be true for personality disorder and other variables only partially dependent on functional neurological disorder.

**Interviewer factors**
A patient might not trust the interviewer or feel ready to disclose events to them. It is argued that stressors will only be disclosed following prolonged clinical engagement and build up of trust. However, against this argument it should be noted that our results found that those studies which assessed reported stressors solely on the basis of clinical contact had the lowest rates of detection and those which used a very comprehensive structured measure, such as the Life Events and Difficulties Schedule (LEDS), had the highest. What was less clear was the nature of the clinical contact and whether that included patients who had had prolonged psychotherapy.

**Multiple different measures of stressors**

**Difficulties of stressful life event studies in general**
- Recall bias can occur in both directions: patients might overly recall negative versus positive events, other patients might have experienced terrible maltreatment but deny it in interviews and questionnaires.
- Contextualising events: stressful life events take on meaning because of the context in which they occur. Only contextualised methods, such as the LEDS, assess events in this way. Even when they do it is very hard to mask them in studies.
- Timeframe: some studies were not specific regarding the timeframe of stressors and appear to have included also those stressors after symptom onset.
- Symptom-specific events: eg, conflict over speaking out in dysphonia study might be prevalent but hidden in general questionnaires assessing stressors.

**Exposure not usually corroborated with external records**

**Heterogeneity**
If high then considerable caution is warranted when interpreting results of meta-analysis.

**Publication bias**
Negative studies not published.

risk than physical or sexual abuse. Finally, our results clearly indicate that more detailed assessment of stressors results in a higher disclosure rate; it is not a task that should be rushed. Given the absence of diagnostic weight attached to these variables, this part of the assessment might often be better left to future appointments but will vary depending on circumstances.[68]

This systematic review supports the decision to remove the need for a recent stressor from the diagnostic criteria for functional neurological disorder in DSM-5 and suggests that ICD-11 would benefit from following this approach. The diagnosis should be made on the basis of the history plus inconsistent and incongruent neurological signs. However, the review confirms the importance of stressors as risk factors for cause. The implications are that neurologists and psychiatrists (as well as psychologists and psychotherapists) will continue to be essential for this specialty. In terms of ICD-11, it is therefore imperative that the condition is coded in both F and G codes—although we long for the day when we drop this dualistic approach and bring ICD into the 21st century with a unitary code for clinical brain sciences disorders. Work on the association between stressful life events and maltreatment and illness behaviour, as well as altered brain functioning in patients with functional neurological disorder, will move our understanding forward regarding potential mechanisms.[69,70]

In summary, this review has aggregated data from 34 studies with 1405 patients and is consistent in the findings that exposure to stressful life events and maltreatment in childhood and adult life is associated with an increase in the risk of functional neurological disorder, but not all patients with functional neurological disorder have identifiable stressors.

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