# Adverse life events and psychosocial stressors in functional neurological disorder: a retrospective cohort and case–control study using a large international electronic health record database

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## Summary

**Background** Adverse life events and other stressors were central to historical 'Freudian' models of functional neurological disorder (FND), which have been increasingly replaced by more nuanced biopsychosocial models. Studies of the aetiological relevance of stressors have been limited by small sample sizes.

**Methods** Retrospective cohort analyses using a large international electronic health records network (TriNetX), including ICD-10 codes, were performed. Between 2015 and 2025, 147,595 individuals were diagnosed with FND. The rates of adverse life events and psychosocial stressors were compared to matched cohorts with migraine and generalised anxiety disorder (GAD) diagnoses. We also investigated associations between FND and the presence of stressors, including the stressor type and whether it occurred in childhood or adulthood.

**Findings** Rates of abuse or neglect (1·33%), assault (2·42%), and psychosocial and socioeconomic difficulties (10·63%) were significantly higher in FND compared to migraine (0·42%/0·93%/3·43%, respectively) and GAD (0·75%/1·29%/7·69%, respectively) ($p < ·0001$ for all comparisons). A history of physical and sexual abuse was more prevalent in FND than in comparison groups. Psychological abuse was more common in FND than in migraine, but not when compared to GAD. FND cases with recorded stressors were younger, more often female, and more frequently diagnosed with functional/dissociative seizures than those without stressors. Further, these stressors were associated with an increased prevalence of psychiatric comorbidities, pain, and fatigue. Different stressor types had distinct influences on clinical presentations. Adult-onset adversity was associated with higher rates of psychiatric comorbidities, pain and fatigue.

**Interpretation** A record of adversities was at least 2·5 times more common in FND than in migraine, and about 1·5 times more common than in GAD, varying by stressor type. Psychosocial stressors were particularly common. The presence of stressors, as well as their type, shapes the presentation of FND. Life history should therefore be considered when assessing individuals with FND.

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**Keywords:** Functional neurological disorder; FND; Conversion Disorder; Trauma; Life events; Stress

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## Research in context

### Evidence before this study

Functional neurological disorder (FND) is increasingly recognised as a common, disabling, and treatable condition. While traditional psychological models, influenced by Freud's theories, have suggested that traumatic experiences are unconsciously repressed and converted into neurological symptoms, the presence of stressors is no longer a requirement for a diagnosis. We searched PubMed on 10 April 2025 without language restrictions using the terms ("functional neurological" OR "psychogenic" OR "conversion disorder" OR "non-epileptic") AND ("life event" OR "abuse" OR "stress") AND ("control" OR "controlled" OR "case-control"). Several smaller studies reported a higher prevalence of various stressors in individuals with FND compared to healthy or clinical controls, and these findings were also reflected in the results of two meta-analyses. Both highlighted substantial variability of findings across studies and noted that many were underpowered to yield conclusive results. Investigating a larger cohort would enable a more fine-grained analysis of the FND phenotype and comorbidities in relation to stressor exposure, as well as allow for assessment of the impact of distinct types of stressors.

### Added value of this study

To our knowledge, this is the largest fully representative clinical cohort study to date examining the relationship between past adverse experiences and neurological or mental health outcomes.

The prevalence of documented stressors in FND was compared to two comparator cohorts: migraine and generalised anxiety disorder, which were well matched for demographic variables. Individuals with FND exhibited higher rates of adulthood and childhood abuse, history of assault, as well as psychosocial and socioeconomic difficulties. Rather than the traditionally recognised adverse events such as physical or sexual abuse, the most pronounced differences were observed for psychosocial and socioeconomic stressors, which were also the most frequently documented. A detailed analysis of the impact of stressors on clinical features of FND revealed demographic and clinical differences in individuals with a history of stressors, along with distinct effects based on the type and timing of stressor exposure.

### Implications of all the available evidence

A history of traumatic experiences is relevant to the development of FND, and the presence and nature of stressors may influence its clinical phenotype. Our findings highlight the importance of a comprehensive life history assessment in diagnosing and managing FND. However, adverse events are not universally present in FND, and they also appear in individuals with other neurological or mental health conditions, as well as in the healthy population. Therefore, they should not form the basis for diagnosing FND, nor should they be sought out excessively when no such history is disclosed. An interplay between past experiences and individual biological vulnerability may contribute to the development of FND. Future research is essential to uncover the mechanisms underlying resilience and susceptibility that contribute to this variability of outcomes. This could also guide the development of more targeted and effective treatments.

## Introduction

Functional neurological disorder (FND) is characterised by neurological symptoms, such as weakness, movement disorders, and seizures, that occur in the absence of structural nervous system pathology. It is a common and disabling condition. A range of terms, including "conversion", "dissociative", and "psychogenic", are commonly used to describe these symptoms, which were formerly referred to as "hysteria". The evolving terminology reflects the shifting perspectives on the condition, alternating between neurological and psychiatric frameworks for over 150 years.[1] Aetiological explanations have historically been dominated by psychological models, particularly those rooted in Freudian theory, proposing that distressing experiences or emotional states are unconsciously repressed and subsequently "converted" into motor or sensory symptoms, serving to alleviate the unbearable emotional conflict.[2]

This model has been increasingly challenged due to inconsistent evidence for the presence of such stressors in all patients, difficulties inferring causality for stressors commonly encountered in the general population, as well as increasing awareness of the circular, and the seemingly impossible to disprove, argument that if a stressor is not found then it must have been repressed.[3,4] This has contributed to changes in diagnostic criteria in both DSM-5 and ICD-11, where the presence of stressors is no longer a requirement for diagnosis. However, while these findings have helped to challenge stereotypical assumptions about FND in the majority of cases, both controlled studies and meta-analyses continue to demonstrate an overall increased prevalence of severe adverse life events among individuals with FND.[5–8] Major stressors may play a significant aetiological or perpetuating role in a subset of FND patients, carrying potential implications for treatment. While much of the existing literature emphasises past traumatic experiences, the role of psychosocial and socioeconomic stressors in FND has received less attention. Further, it remains unclear if adverse life events and psychosocial stressors influence the clinical phenotype of FND.

In the present study, we investigated a large electronic health records (EHR) database to examine the

occurrence of documented severe adverse life events preceding a diagnosis of FND, and to explore associations between specific stressors and distinct FND phenotypes. We recognise the inherent limitations of EHR-based research, including the inability to capture individuals' subjective experiences, which are often crucial for understanding future mental health outcomes.[9] Further, life events are under-recorded in EHR.[10] Accordingly, we prioritised comparisons of relative prevalences with matched comparator groups, as absolute rates of recorded adversity are likely to underestimate their true occurrence.

We aimed to: (i) assess the prevalence of documented adverse life events before the diagnosis of FND, compared to two control cohorts—one with a neurological and one with a mental health diagnosis; (ii) compare the clinical features of FND patients with and without documented life events; (iii) explore the clinical phenotypes of FND associated with different types of life stressors; and (iv) evaluate features of FND relative to when in life the stressor occurred. We hypothesised that adverse life events would be more frequently recorded in FND compared to control conditions, and that their presence, type, and timing (occurring in childhood or adulthood) would be associated with variations in the clinical phenotype of FND.

## Methods

### Data and study design

The study used TriNetX, a global federated health research network that compiles de-identified EHR data from over 164 million patients. The database includes structured clinical data, such as demographic information and diagnoses coded using ICD-10. Contributing healthcare organisations continuously update their data. We utilised the Global Collaborative Network, within which the identities of healthcare organisations and their specific contributions remain undisclosed to comply with legal and ethical standards. Cohorts are generated via the TriNetX user interface by applying inclusion and exclusion criteria. They can be matched for confounding factors and compared for outcomes of interest across specified time periods.[11] As site and country information is anonymised within the network, balancing across these variables cannot be implemented. Like other studies utilising the TriNetX network, this retrospective study is exempt from obtaining informed consent, and institutional ethical approval was not required. The data analysed are secondary data, do not involve intervention or interaction with human subjects, and have been de-identified in line with the de-identification standard outlined in Section §164.514(b) (1) of the HIPAA Privacy Rule (http://trinetx.com). The RECORD reporting guidelines were followed.

### Definition of FND and comparison cohorts

The FND cohort comprised patients aged 13 to 80 who received a new diagnosis of FND between 1 January 2015 and 15 April 2025, the date of the main analysis. The diagnosis of FND was defined as any of the following ICD-10 diagnostic categories: Conversion disorder with motor symptom or deficit (F44.4), Conversion disorder with seizures or convulsions (F44.5), Conversion disorder with sensory symptom or deficit (F44.6), Conversion disorder with mixed symptom presentation (F44.7), Other dissociative and conversion disorders (F44.89), Dissociative and conversion disorder, unspecified (F44.9). These ICD-10 categories are most commonly used to code for the typical phenotypes of FND: functional motor disorder, functional/dissociative seizures, functional sensory disorder, FND with mixed symptoms, and other or unspecified FND. Other diagnoses from the F44 diagnostic category, such as dissociative fugue, dissociative amnesia, dissociative stupor, and dissociative identity disorder, were excluded from the FND definition in this study, as these codes are not typically used for the most common FND phenotypes.[12]

Contemporaneous cohorts of patients aged 13–80 years with migraine (G43) and generalised anxiety disorder (GAD) (F41.1) were evaluated. Migraine was selected due to some shared features with FND, including a broad age distribution, female predominance, and a multifactorial aetiology encompassing biological, psychological, and social factors.[13] In addition, stress is the most common precipitating factor for migraine,[14] supporting its relevance for studying life events. Given our interest in the role of psychosocial stressors in FND, GAD was selected as a comparator due to its well-established association with chronic stress. It also shares cognitive-affective features with FND, such as altered interoceptive awareness, while remaining distinct in symptom manifestation.[15]

### Variables of interest

ICD-10 codes related to stressful or traumatic life events were identified. These included confirmed adult or child neglect, physical, sexual or psychological abuse, assault, clinical encounters following alleged rape or physical abuse, and problems related to employment, housing, economic circumstances, social environment, upbringing, and economic circumstances (detailed in Supplementary Methods). All codes that were documented up to and including the date of the index event (i.e. diagnosis of FND or comparator conditions) were included in the analysis.

### The prevalence of stressors in FND compared to control cohorts

The FND cohort was compared to each control cohort: migraine and GAD. To ensure group differences were

not due to differences in demographic variables, the cohorts were matched before comparison for age at diagnosis, gender, race, and ethnicity (detailed in Supplementary Methods). A propensity score-matching algorithm integrated into the TriNetX platform was used. The algorithm employs logistic regression to calculate propensity scores based on user-specified covariates. It then applies a greedy nearest-neighbour matching algorithm with a 1:1 ratio to pair cases and controls.

The prevalence of stressor diagnoses in EHR was compared between matched cohorts of patients with FND and migraine, as well as between matched FND and GAD cohorts using z-tests within the TriNetX platform, which also provides standardised mean differences (SMDs) as a measure of between-group imbalance. Odds ratios (ORs) with 95% confidence intervals (CIs) were subsequently calculated in R (version 4.5.0). Statistical significance was set at $p < 0{\cdot}0025$ (applying Bonferroni correction for comparison of 20 variables in each cohort pair).

We performed a sensitivity analysis to account for any possible systematic difference in recorded stressor rates due to the possibility of a more thorough life history assessment in cases of FND. In this analysis, we included only records of life events and psychosocial stressors that were recorded up to 1 day before the diagnosis of FND or control conditions, in this way ensuring that records of stressors and diagnoses of FND, migraine, and GAD were coded during distinct healthcare encounters. In a second sensitivity analysis, we restricted the time window for recorded events to between 3 years and 1 day prior to the diagnosis of FND or control conditions, aiming to increase the likelihood that these records were causally relevant to the development of FND (Supplementary Methods).

### Features of FND with and without documented stressors

Individuals with FND and a documented history of stressors were compared to those without documented stressors of confirmed abuse, neglect or abandonment, encounters for examination or observation following alleged rape or physical abuse, and problems related to family or socioeconomic circumstances. In addition, cases with diagnoses of suspected abuse, neglect or abandonment were also excluded from this comparator cohort.

Age, gender, FND type and psychiatric comorbidities were compared between the two groups. Additional pain and fatigue diagnoses were compared as common comorbidities in FND with implications for prognosis (detailed in Supplementary Methods). All diagnoses in the EHR were considered, without application of temporal filters. Within the TriNetX platform, patient characteristics were compared with the z-test for categorical variables (diagnostic categories) and the Student's t-test for continuous variables (age). ORs with 95% CIs were also calculated. Statistical significance was set at $p < 0{\cdot}0025$ (applying Bonferroni correction for comparison of 20 variables).

### Features of FND associated with different stressors

Age at diagnosis, FND subtype, psychiatric comorbidities, and diagnostic categories related to pain and fatigue (assessed without temporal restrictions) were compared across cohort pairs to examine the influence of the type of life events. Comparisons (z-tests for proportions) among patients with FND were made between individuals with no documented stressors and: (i) those with a history of neglect or abandonment, physical, sexual or psychological abuse, or medical encounters following alleged abuse; and (ii) those with documented problems related to employment, housing, economic circumstances, or the social environment. Only stressors documented on or before the first FND diagnosis were included, as the focus was on potential contributors to the development of FND. Because multiple stressors may co-occur in an individual, making it difficult to disentangle the impact of a single factor, analyses were limited to cohorts with only one type of stressor. To assess the effect of (i) neglect, physical, sexual or psychological abuse, cases with codes indexing economic or social adversity were excluded. Conversely, to evaluate the role of (ii) economic and social adversity, individuals with any record of neglect or abuse were excluded.

### Features of FND associated with adverse events in childhood and adulthood

To assess the influence of the timing of adversity onset across the lifespan, we compared the features specified above in individuals with FND exposed to adverse events (neglect or abandonment, physical, sexual or psychological abuse, or examination following alleged rape or physical abuse) during childhood versus adulthood. Baseline characteristics were compared using z-tests for categorical variables and t-test for age, and ORs with 95% CIs were calculated. Statistical significance was set at $p < 0{\cdot}0025$ (applying Bonferroni correction for the analysis of 20 variables of interest).

### Role of the funding source

There was no funding source for this study.

## Results

### The prevalence of stressors in FND compared to control cohorts

147,595 individuals with FND were included (41·6% with a diagnosis of functional/dissociative seizures, 28·9% with functional motor disorder, 13·3% with functional sensory disorder, 5·6% with FND with mixed symptom presentation, 9·6% with other specified FND,

and 19·1% with unspecified FND). As comparator cohorts, 2,887,473 individuals with migraine and 2,480,459 with GAD satisfied the inclusion criteria. After matching for demographic variables, 147,595 remained in each group for the comparison with FND (Supplementary Tables S1 and S2).

In individuals with FND, a documented diagnosis related to adverse life events—abuse, neglect or other maltreatment (1·3%), assault (2·4%), and difficulties related to socioeconomic or psychosocial circumstances (10·6%)—was more common than in those with migraine (0·4%, 0·9%, and 3·4%, respectively) or GAD (0·7%, 1·3%, and 7·7%, respectively) (Table 1). ORs for abuse and psychosocial stressors were broadly comparable in both cohort comparisons. However, among the categories examined, socioeconomic and psychosocial

| | | FND (N = 147,595) | Migraine in matched cohort (N = 147,595) | | | | GAD in matched cohort (N = 147,595) | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | N (%) | N (%) | OR (95% CI) | SMD | p | N (%) | OR (95% CI) | SMD | p |
| Adult and child abuse, neglect and other maltreatment | | 1967 (1·33) | 624 (0·42) | 3·18 (2·91–3·48) | 0·098 | <0·0001 | 1103 (0·75) | 1·79 (1·67–1·93) | 0·058 | <0·0001 |
| Neglect or abandonment | Adult | 29 (0·02) | ≤10 (0·01) | 2·90 (1·41–5·95) | 0·011 | **0·0023** | ≤10 (0·01) | 2·90 (1·41–5·95) | 0·011 | **0·0023** |
| | Child | 44 (0·03) | 12 (0·01) | 3·67 (1·94–6·94) | 0·016 | **<0·0001** | 41 (0·03) | 1·07 (0·70–1·64) | 0·001 | 0·7448 |
| Physical abuse | Adult | 284 (0·19) | 80 (0·05) | 3·55 (2·77–4·55) | 0·039 | **<0·0001** | 153 (0·10) | 1·86 (1·53–2·26) | 0·023 | **<0·0001** |
| | Child | 133 (0·09) | 56 (0·04) | 2·38 (1·74–3·25) | 0·021 | **<0·0001** | 74 (0·05) | 1·80 (1·35–2·39) | 0·015 | **<0·0001** |
| Sexual abuse | Adult | 685 (0·46) | 144 (0·10) | 4·77 (3·99–5·72) | 0·069 | **<0·0001** | 263 (0·18) | 2·61 (2·27–3·01) | 0·051 | **<0·0001** |
| | Child | 412 (0·28) | 145 (0·10) | 2·85 (2·35–3·44) | 0·042 | **<0·0001** | 205 (0·14) | 2·01 (1·70–2·38) | 0·031 | **<0·0001** |
| Psychological abuse | Adult | 54 (0·04) | 13 (0·01) | 4·16 (2·27–7·61) | 0·018 | **<0·0001** | 41 (0·03) | 1·31 (0·88–1·98) | 0·005 | 0·1822 |
| | Child | 156 (0·11) | 59 (0·04) | 2·65 (1·96–3·57) | 0·024 | **<0·0001** | 132 (0·09) | 1·18 (0·94–1·49) | 0·005 | 0·1571 |
| Encounter for examination and observation | | | | | | | | | | |
| Following alleged rape | Adult | 258 (0·17) | 68 (0·05) | 3·80 (2·91–4·96) | 0·039 | **<0·0001** | 91 (0·06) | 2·84 (2·23–3·60) | 0·033 | **<0·0001** |
| | Child | 38 (0·03) | 14 (0·01) | 2·71 (1·47–5·01) | 0·012 | **0·0009** | 22 (0·01) | 1·73 (1·02–2·92) | 0·008 | 0·008 |
| Following alleged physical abuse | Adult | 150 (0·10) | 69 (0·05) | 2·18 (1·63–2·89) | 0·020 | **<0·0001** | 82 (0·06) | 1·83 (1·40–2·40) | 0·016 | **<0·0001** |
| | Child | 141 (0·10) | 64 (0·04) | 2·20 (1·64–2·96) | 0·020 | **<0·0001** | 81 (0·05) | 1·74 (1·32–2·29) | 0·015 | **<0·0001** |
| Assault | | 3571 (2·42) | 1370 (0·93) | 2·65 (2·49–2·82) | 0·116 | **<0·0001** | 1906 (1·29) | 1·90 (1·79–2·00) | 0·084 | **<0·0001** |
| Potential hazards related to socioeconomic and psychosocial circumstances | | 15,682 (10·63) | 5065 (3·43) | 3·35 (3·24–3·46) | 0·284 | **<0·0001** | 11354 (7·69) | 1·43 (1·39–1·46) | 0·102 | **<0·0001** |
| Problems related to employment and unemployment | | 1950 (1·32) | 584 (0·40) | 3·37 (3·07–3·70) | 0·100 | **<0·0001** | 1448 (0·98) | 1·35 (1·26–1·45) | 0·032 | **<0·0001** |
| Problems related to housing and economic circumstances | | 4803 (3·25) | 1240 (0·84) | 3·97 (3·74–4·23) | 0·171 | **<0·0001** | 2622 (1·78) | 1·86 (1·77–1·95) | 0·094 | **<0·0001** |
| Problems related to social environment | | 1729 (1·17) | 537 (0·36) | 3·25 (2·95–3·58) | 0·093 | **<0·0001** | 1207 (0·82) | 1·44 (1·34–1·55) | 0·036 | **<0·0001** |
| Problems related to upbringing | | 3693 (2·50) | 675 (0·46) | 5·59 (5·14–6·07) | 0·170 | **<0·0001** | 2282 (1·55) | 1·63 (1·55–1·72) | 0·068 | **<0·0001** |
| Other problems related to primary support group, including family circumstances | | 4393 (2·98) | 1453 (0·98) | 3·09 (2·91–3·28) | 0·143 | **<0·0001** | 3714 (2·52) | 1·19 (1·14–1·24) | 0·028 | **<0·0001** |

Case numbers are provided with percentages in parentheses. Odds ratios (OR) with 95% confidence intervals (CI), standardised mean differences (SMD), and p values (highlighted in bold if significant after Bonferroni correction for 20 variables examined in each cohort comparison, p < 0·0025) for the group comparisons are provided. Counts between 1 and 10 are reported as ≤10 (for statistical analyses within TriNetX, these are treated as 10). Counts are reported as 0 when no cases meet the inclusion criteria.

***Table 1:*** **Life events in functional neurological disorder (FND) compared to migraine and generalised anxiety disorder (GAD).**

stressors were most commonly present, resulting in larger absolute differences between cohorts, as evidenced by higher SMD values, both when evaluated as a group and across individual stressor types.

Compared to socioeconomic and psychosocial stressors, abuse and neglect were less common across all cohorts. History of physical or sexual abuse was more frequent in FND compared to migraine or GAD. Effect sizes for both cohort comparisons were larger for adulthood physical and sexual abuse than for the corresponding childhood abuse codes. Psychological abuse was more frequent in FND than in migraine, but there were no differences between FND and GAD.

In the sensitivity analysis excluding records of adversity from the same day as the first diagnosis of FND or control conditions, the qualitative pattern of differences between FND and control conditions for all examined stressors remained unchanged, apart from the rates of adult neglect or abandonment being no longer significantly more common in FND compared to migraine and GAD (Supplementary Table S3).

In the sensitivity analysis limited to events recorded between 3 years and 1 day before diagnosis, the overall pattern remained similar, with group differences in all examined socioeconomic and psychosocial stressors remaining significant. However, differences between FND and migraine were reduced for neglect and encounters following alleged childhood rape or physical abuse. Reduced group differences were also seen between FND and GAD for adult neglect, child physical abuse, and encounters for examination following alleged physical abuse (Supplementary Table S6).

### Features of FND with and without documented stressors

13,479 individuals with FND and any recorded life stressor were compared to 123,594 individuals without documented stressors (Table 2). Patients with stressors were, on average, younger and more frequently female. FND in these patients was more often classified as functional/dissociative seizures or unspecified FND, while functional motor disorder, functional sensory disorder, and FND with mixed symptoms were less common. Further, mental health disorders, along with pain and fatigue, were more prevalent in FND patients with documented stressors (Table 2).

### Features of FND associated with distinct life stressors

1473 individuals with FND and documented neglect or abuse and 6673 individuals with FND and records of socioeconomic difficulties were included in this analysis. Compared to those without documented stressors (123,594 cases), individuals with documented neglect or abuse were, on average, younger and more frequently female (Table 2). Diagnoses of functional/dissociative seizures and unspecified FND were more common in this group, whereas functional motor disorder and other specified FND were less common. Psychiatric comorbidities, pain, and fatigue were also more frequent.

In contrast, patients with recorded social and economic adversities (problems related to employment and unemployment, housing and economic circumstances, and social environment) were less often female and did not differ significantly in age compared to those without documented stressors (Table 2). The presentations of functional/dissociative seizures, other specified or unspecified FND were more common in this group, while other subtypes were diagnosed less frequently. Mental health disorders, pain, and fatigue were also more common in this group.

### Features of FND associated with adverse events in childhood and adulthood

Clinical features were compared between 714 individuals who experienced abuse, neglect or other maltreatment as children and 1292 individuals with adult exposure to these adverse events. Individuals with childhood exposure were younger than those exposed to such events in adulthood. No gender differences were observed between the two groups (Table 3).

Post-traumatic stress disorder was present in over half of all cases and was more common among individuals with adulthood-onset stressors. In addition, psychoactive substance use disorders and schizophrenia were more prevalent in this group. There was no significant difference in the prevalence of depression or anxiety. Pain and fatigue were more common in individuals exposed to abuse in adulthood.

## Discussion

Adverse life events, including abuse, assault, and socioeconomic adversities, were recorded more than 2·5 times as often in individuals with FND than in those with migraine, and about 1·5 times as often as in those with GAD. Both childhood and adulthood stressors were more prevalent in FND. A history of physical and sexual abuse was more common in FND than in either comparison group. Conversely, psychological abuse was more frequent in FND than in migraine, but not when compared to GAD. The imbalance between cohorts was largest for socioeconomic and psychosocial stressors. People with FND and a history of adverse life events were younger and more frequently female than those without such stressors, although this pattern varied depending on the type of life event. The presence of life events also influenced the phenotype: functional/dissociative seizures, psychiatric comorbidities, pain and fatigue were consistently more common in those with a history of adverse life events.

While life events of any type were more frequently recorded in FND compared to the control cohorts, there

| | No adverse event (N = 123,594) | Any adverse event (N = 13,479) | | | Neglect or abuse (N = 1473) | | | Social or economic circumstances (N = 6673) | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | OR (95% CI) | p | | OR (95% CI) | p | | OR (95% CI) | p |
| Demographics | | | | | | | | | | |
| Age: mean (SD) | 46·8 (19·4) | 43·2 (18·0) | SMD = 0·190 | **<0·0001** | 34·0 (15·1) | SMD = 0·738 | **<0·0001** | 47·3 (16·9) | SMD = 0·031 | 0·0209 |
| Female gender | 85,350 (69) | 9661 (72) | 1·13 (1·09–1·18) | **<0·0001** | 1313 (89) | 3·68 (3·12–4·33) | **<0·0001** | 4139 (62) | 0·73 (0·70–0·77) | **<0·0001** |
| FND subtype | | | | | | | | | | |
| Functional motor disorder | 40,348 (33) | 3533 (26) | 0·73 (0·70–0·76) | **<0·0001** | 400 (27) | 0·77 (0·69–0·86) | **<0·0001** | 1718 (26) | 0·72 (0·68–0·76) | **<0·0001** |
| Functional/dissociative seizures | 53,594 (43) | 6666 (49) | 1·28 (1·23–1·32) | **<0·0001** | 867 (59) | 1·87 (1·68–2·07) | **<0·0001** | 3083 (46) | 1·12 (1·07–1·18) | **<0·0001** |
| Functional sensory disorder | 18,681 (15) | 1571 (12) | 0·74 (0·70–0·78) | **<0·0001** | 249 (17) | 1·14 (1·00–1·31) | 0·0568 | 650 (10) | 0·61 (0·56–0·66) | **<0·0001** |
| Functional disorder with mixed symptoms | 9443 (8) | 904 (7) | 0·87 (0·81–0·93) | **<0·0001** | 97 (7) | 0·85 (0·69–1·05) | 0·1294 | 373 (6) | 0·72 (0·64–0·80) | **<0·0001** |
| Other specified FND | 12,085 (10) | 1334 (10) | 1·01 (0·95–1·08) | 0·659 | 82 (6) | 0·54 (0·44–0·68) | **<0·0001** | 810 (12) | 1·27 (1·18–1·38) | **<0·0001** |
| Unspecified FND | 26,285 (21) | 3707 (28) | 1·40 (1·35–1·46) | **<0·0001** | 384 (26) | 1·31 (1·16–1·47) | **<0·0001** | 1701 (25) | 1·27 (1·20–1·34) | **<0·0001** |
| Psychiatric comorbidities | | | | | | | | | | |
| Generalised anxiety disorder | 22,217 (18) | 4951 (37) | 2·65 (2·55–2·75) | **<0·0001** | 549 (37) | 2·71 (2·44–3·02) | **<0·0001** | 2238 (34) | 2·30 (2·18–2·43) | **<0·0001** |
| Panic disorder | 11,189 (9) | 2780 (21) | 2·61 (2·49–2·73) | **<0·0001** | 352 (24) | 3·15 (2·79–3·56) | **<0·0001** | 1234 (18) | 2·28 (2·14–2·43) | **<0·0001** |
| Post-traumatic stress disorder | 18,055 (15) | 5571 (41) | 4·12 (3·97–4·28) | **<0·0001** | 757 (51) | 6·18 (5·57–6·85) | **<0·0001** | 2392 (36) | 3·27 (3·10–3·33) | **<0·0001** |
| Recurrent depressive disorder | 18,572 (15) | 5002 (37) | 3·37 (3·21–3·47) | **<0·0001** | 524 (36) | 3·12 (2·80–3·48) | **<0·0001** | 2335 (35) | 3·04 (2·89–3·21) | **<0·0001** |
| Mental disorders due to psychoactive substance use | 36,701 (30) | 7822 (58) | 3·27 (3·16–3·39) | **<0·0001** | 778 (53) | 2·65 (2·39–2·94) | **<0·0001** | 4332 (65) | 4·38 (4·16–4·61) | **<0·0001** |
| Schizophrenia | 4585 (3) | 1595 (11) | 3·48 (3·28–3·70) | **<0·0001** | 111 (8) | 2·11 (1·74–2·46) | **<0·0001** | 998 (15) | 4·56 (4·24–4·91) | **<0·0001** |
| Specific personality disorders | 6682 (5) | 2948 (22) | 4·90 (4·67–5·14) | **<0·0001** | 305 (21) | 4·57 (4·02–5·20) | **<0·0001** | 1509 (23) | 5·11 (4·80–5·44) | **<0·0001** |
| Other comorbidities | | | | | | | | | | |
| Unspecified pain | 17,298 (14) | 3234 (24) | 1·94 (1·86–2·02) | **<0·0001** | 394 (27) | 2·24 (2·00–2·52) | **<0·0001** | 1678 (25) | 2·06 (1·95–2·19) | **<0·0001** |
| Headache | 43,647 (35) | 7352 (55) | 2·20 (2·12–2·28) | **<0·0001** | 965 (66) | 3·48 (3·12–3·88) | **<0·0001** | 3514 (53) | 2·04 (1·94–2·14) | **<0·0001** |
| Low back pain | 31,182 (35) | 5460 (41) | 2·02 (1·95–2·09) | **<0·0001** | 632 (43) | 2·23 (2·01–2·47) | **<0·0001** | 2832 (42) | 2·19 (2·08–2·30) | **<0·0001** |
| Malaise and fatigue | 42,392 (34) | 7407 (55) | 2·34 (2·25–2·42) | **<0·0001** | 766 (52) | 2·08 (1·87–2·30) | **<0·0001** | 3880 (58) | 2·66 (2·53–2·80) | **<0·0001** |
| Postviral and related fatigue syndromes | 11,412 (9) | 1873 (14) | 1·59 (1·50–1·67) | **<0·0001** | 251 (17) | 2·02 (1·76–2·32) | **<0·0001** | 954 (14) | 1·64 (1·53–1·76) | **<0·0001** |

Cell entries represent case numbers with percentages in parentheses, unless specified otherwise. Odds ratios (OR) with 95% confidence intervals (CI) are reported for group comparisons, unless specified otherwise as standardised mean differences (SMD), and p values (highlighted in bold if significant after Bonferroni correction for 20 variables examined in each cohort comparison, p < 0.0025) are provided.

***Table 2:*** **Clinical features of cohorts of patients with functional neurological disorder (FND) and with any adverse life event, documented abuse, or problems related to socioeconomic circumstances, to the cohort without an identified adverse life event.**

| | Childhood exposure (N = 714) | Adulthood exposure (N = 1292) | OR (95% CI) | p |
|---|---|---|---|---|
| Demographics | | | | |
| Age: mean (SD) | 24·9 (11·7) | 39·3 (14·4) | SMD = 1·093 | **<0·0001** |
| Female gender | 619 (87) | 1156 (89) | 1·30 (0·99–1·73) | 0·0619 |
| FND subtype | | | | |
| Functional motor disorder | 193 (27) | 349 (27) | 1·00 (0·81–1·23) | 0·9929 |
| Functional/dissociative seizures | 422 (59) | 780 (60) | 1·05 (0·88–1·27) | 0·5790 |
| Functional sensory disorder | 100 (14) | 231 (18) | 1·34 (1·04–1·72) | 0·0252 |
| Functional disorder with mixed symptoms | 62 (9) | 69 (5) | 0·59 (0·42–0·85) | 0·0037 |
| Other specified FND | 37 (5) | 86 (7) | 1·30 (0·88–1·94) | 0·1876 |
| Unspecified FND | 196 (27) | 321 (25) | 0·87 (0·71–1·07) | 0·2014 |
| Psychiatric comorbidities | | | | |
| Generalised anxiety disorder | 255 (36) | 533 (41) | 1·26 (1·05–1·53) | 0·0150 |
| Panic disorder | 157 (22) | 340 (26) | 1·27 (1·02–1·57) | 0·0316 |
| Post-traumatic stress disorder | 357 (50) | 745 (58) | 1·36 (1·13–1·64) | **0·0010** |
| Recurrent depressive disorder | 264 (37) | 511 (40) | 1·12 (0·92–1·35) | 0·2565 |
| Mental disorders due to psychoactive substance use | 262 (37) | 878 (68) | 3·66 (3·02–4·43) | **<0·0001** |
| Schizophrenia | 37 (5) | 191 (14) | 3·17 (2·20–4·57) | **<0·0001** |
| Specific personality disorders | 122 (17) | 378 (29) | 2·01 (1·60–2·52) | **<0·0001** |
| Other comorbidities | | | | |
| Unspecified pain | 134 (19) | 435 (34) | 2·20 (1·76–2·74) | **<0·0001** |
| Headache | 423 (59) | 940 (73) | 1·84 (1·51–2·23) | **<0·0001** |
| Low back pain | 274 (38) | 803 (62) | 2·64 (1·51–2·23) | **<0·0001** |
| Malaise and fatigue | 301 (42) | 801 (62) | 2·24 (1·86–2·70) | **<0·0001** |
| Postviral and related fatigue syndromes | 75 (11) | 270 (21) | 2·25 (1·71–2·96) | **<0·0001** |

Cell entries represent case numbers with percentages in parentheses, unless specified otherwise. Odds ratios (OR) with 95% confidence intervals (CI) are reported for group comparisons, unless specified otherwise as standardised mean differences (SMD), and *p* values (highlighted in bold if significant after Bonferroni correction for 20 variables examined, $p < 0·0025$) are provided.

***Table 3:*** **A comparison of clinical features of patients with functional neurological disorder (FND) who experienced abuse, neglect or other maltreatment as adults compared to children.**

were notable differences between the two comparisons, particularly regarding abuse. Specifically, emotional abuse as well as childhood neglect or abandonment was more common in FND compared to migraine, but no such differences were observed compared to GAD. In contrast, documented physical and sexual abuse was more prevalent in FND than in both control conditions. Childhood adversities, including physical, sexual, and emotional abuse, have been linked to increased prevalence of anxiety disorders.[16] However, our findings suggest that in addition to this risk, physical or sexual abuse is associated with an additionally increased risk of developing functional neurological symptoms. This is in contrast to findings from a large meta-analysis of traumatic events preceding the onset of FND, where emotional neglect in childhood had a greater effect size than physical or sexual abuse.[6] Importantly, documented adult and child abuse was recorded in only a small proportion of FND cases, though it is likely underreported in EHR.[10] However, the rates of adulthood or childhood neglect, abuse or other maltreatment were around three times more common in FND than in migraine and less than two times more common than in GAD. While the increased rates of this type of severe trauma highlight its relevance to FND, the fact that these rates are on a scale comparable to those observed in control conditions suggests that such events are not universally present among individuals with FND. Additionally, psychosocial and socioeconomic stressors were more frequently documented in FND than in either control cohort, suggesting that different forms of adversity can contribute to the risk of developing FND. The largest effect sizes observed for this group of stressors are consistent with previous findings highlighting the aetiological importance of events related to family, work, and relationships, which were previously identified as the most common category of stressors preceding FND onset.[7]

Demographic differences emerged when comparing FND patients with and without documented stressors. People with exposure to neglect or abuse in childhood had a younger onset of FND than those with exposure in adulthood. In contrast, there was no age difference between individuals with psychosocial or socioeconomic adversities and those without documented adverse events, possibly reflecting differences in the timing of exposure of different types of life events, or suggesting that psychosocial and socioeconomic stressors share additional similarities with the nature and/or timing of undocumented events that could have triggered or precipitated FND in the control cohort.

The presence and type of life events also influenced gender differences. FND patients with any documented adverse event were more frequently female (72%) compared to those without such documented events (69%). 89% of individuals with FND and a history of abuse or neglect were female. Conversely, among those with psychosocial and socioeconomic adversities, the proportion of females was lower, though still constituting a majority (62%). These findings align with previous reports. For example, Nicholson et al.[5] identified that, among females, key life events were most commonly related to abuse, while work-related events and accidents were more common among males.

Functional/dissociative seizures were more common in people with FND with adverse life events, irrespective of the nature of the stressor. This finding supports previous research linking adverse experiences with this specific clinical presentation of FND.[17] The presence of life events influenced the FND phenotype further. First, all evaluated mental health disorders were more commonly present in patients with recorded stressors. This included GAD, panic disorders, post-traumatic stress disorder, depression, mental disorders due to psychoactive substance use, and schizophrenia. The exact nature of the relationship between the stressors and some of these conditions remains difficult to clarify from our data. Previous research has

demonstrated associations between past adverse experiences in childhood and a range of health outcomes, including mental health disorders and health-risk behaviours.[18–20] However, individuals with severe mental illnesses are also at an increased risk of being subjected to violence or abuse.[21,22] In our study, the higher rates of schizophrenia and substance use-related mental disorders among FND patients with a history of abuse in adulthood, compared to those with abuse in childhood, may therefore reflect the increased risk of such adverse experiences in individuals with these mental health conditions.

Individuals with past adverse events exhibited higher rates of comorbid pain (including headache, back pain, or unspecified pain) and fatigue, which may represent correlates of the neurobiological stress response.[23] These symptoms significantly impair quality of life and negatively impact the prognosis of patients with FND.[24–27] Our findings align with previous reports indicating that somatic symptoms are more prevalent in individuals with a history of adverse experiences, even in the absence of FND.[28,29] Taken together, our results support the idea that trauma can modulate the phenotype of FND.[30]

A key strength of our study is its large sample size, with the number of included FND patients exceeding that of the largest previously published work on this topic (a meta-analysis of 51 studies including 4247 patients)[7] by more than 30-fold. Most previous studies were limited by small sample sizes and high heterogeneity of findings, reducing the ability to draw firm conclusions.[6,7] In contrast, our substantial cohort enabled a more fine-grained analysis of FND phenotypes and comorbidities associated with any life events, as well as with specific types of stressors. Comparing life events in FND to two matched control groups, one with a neurological and another with a psychiatric diagnosis, further strengthens the robustness of our findings and allows for a more nuanced interpretation.

The study's limitations arise from its retrospective design and limited information available in the EHR.[10] The rates of documented life events in our FND and control cohorts are substantially lower than reported in previous controlled studies,[6,7] likely due to patients not being asked about or wanting to disclose such events, and even when disclosed, they might not be documented in the notes or subsequently coded.[9,10] It is possible that FND patients are asked more about stressors, given the historical models and past diagnostic criteria requiring their identification. However, the differences in recorded rates of encounters following alleged abuse (Table 1) are less likely to be influenced by this bias, as their presence typically reflects a formal response to a reported or suspected event rather than background psychosocial enquiry. In addition, a similar pattern of results in the sensitivity analysis, excluding records of adversities made on the same day as the diagnosis of FND or control conditions, suggests that group differences are not only a consequence of a more thorough assessment of stressors in individuals with FND.

Furthermore, previous research has indicated that most key life events of aetiological relevance to FND are not documented.[5] While this represents a limitation in capturing the full scope of life event exposure, it likely affects all study groups. As a result, non-coding is more likely to attenuate effect sizes and group differences, rather than increasing the risk of false positive findings.

Another limitation of non-coding, however, is that likely only the most severe or clinically notable instances were documented. Moreover, the relative prevalences of distinct life events examined may not accurately represent their real-life occurrence. Certain events are more likely to be documented than others, depending on clinical judgement and coding practices. For instance, emotional or psychological abuse, previously reported to be strongly associated with the development of FND,[6] may be documented less consistently than other types of abuse. Similarly, there may be a systematic difference in the recording of childhood versus adulthood events within the available EHR data, with the possibility that (more distant) childhood events are less likely to be documented than adulthood ones. While this does not affect the comparison between clinical conditions, it needs to be considered when gauging the relative prevalence of childhood and adulthood adversity. Taking this reservation into account, the larger effect sizes observed for group comparisons of the rates of adulthood versus childhood adversity contrast much of the existing literature. This finding raises the possibility that adult adversity may be under-recognised and underexplored in clinical and research settings.

Unlike EHR data, self-report questionnaires and, in particular, structured interviews allow for a more comprehensive assessment of life events, capturing the full extent of relevant contextual details, including the timing of events relative to symptom onset, the number of events and their perceived severity, emotional impact, and potential event reactivation near FND symptom onset. EHR also lack the depth needed to investigate escape events, i.e. occurrences where symptoms might provide a solution to the stressors. These aspects are essential for a more in-depth understanding of the underlying mechanisms.[5] Further, environmental influences likely interact with individual biological susceptibility in the pathogenesis of FND.[23] Moreover, non-coding is frequent also in FND, which may limit the generalisability of these cases.[12]

To examine associations between specific adversities and clinical phenotype, we identified subgroups with only one recorded stressor category. While this does not reflect real-world settings, where multiple stressors often co-occur, under-recording in EHR likely means

these groups were more heterogeneous than they appear. This reduces the risk of bias from excluding co-occurring stressors. Future work using multivariate models that account for multiple exposures and incorporate information on their severity, timing, and duration may help further clarify these relationships. Further, while we adopted a broad temporal window to capture a range of relevant events, we recognise that some of the recorded events may not be temporally or causally relevant to the development of FND. However, group differences in psychosocial stressors remained significant even when the time window was restricted to 3 years preceding diagnosis.

Our study evaluated the presence of life events, but could not establish direct causality between a specific event and subsequent FND diagnosis. Detailed, individualised assessments are required to identify a psychological formulation. Just as we caution against hastily constructed formulations in clinical practice, our findings offer support for the contention that there are several aetiological routes to the development of FND.

In summary, a history of life adversities is more prevalent in individuals with FND than in comparison conditions. Our results highlight the phenotypic complexity of FND and suggest that stressors may influence its clinical presentation. They also reinforce the importance of a biopsychosocial formulation in informing an individualised approach to management and may pave the way for future research into the neurobiological links between life adversities and FND.

#### Contributors

RB and MJE designed the study, defined cohort inclusion and exclusion criteria, outcome criteria and analytical approaches. RB performed data analyses. RB and MJE interpreted the data, with contributions from TRN, LA, BS and TAP. RB and LA accessed and verified the underlying study data. RB wrote the original draft. TRN, LA, BS, TAP and MJE reviewed and edited the manuscript. MJE supervised the project. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

#### Data sharing statement

TriNetX returned cohort characteristics as csv files, which we archived. They are available to share upon request. The inclusion criteria used, as specified in Methods and Supplementary Methods, would allow other researchers to identify similar cohorts. However, TriNetX is a dynamic platform with continuously updated data. Therefore, exact case counts may vary over time.

#### Declaration of interests

RB has received honoraria for lectures from AbbVie and support for attending meetings and travel from Medtronic. TRN does medical expert reporting in personal injury and clinical negligence cases, including in cases of FND. He has received financial support for lectures from the FND Society (FNDS). He receives royalties from CRC Press for The Pocket Prescriber textbook series. He also has received grant funding, including for studies related to FND, from the UK National Institute for Health and Care Research (NIHR) and the Medical Research Council (MRC). He is co-chair of the FNDS patient liaison committee and on the medical advisory boards of the charities FND Hope UK and FND Action and a trustee of FND Action. LA prepares medico-legal patient reports as part of official duties at the Department of Neurology in Essen and is a core group member of the Young Neurology Group of the German Society of Neurology (DGN). BS does medical expert reporting in personal injury and clinical negligence cases, including in cases with FND. She is on the medical advisory board of FND Hope (UK) and is a trustee of the Association of British Neurologists. TAP does medical expert reporting in personal injury and clinical negligence cases, including in cases of FND. He has received consultancy fees from Arialys Therapeutics. MJE does medical expert reporting in personal injury and clinical negligence cases, including in cases of FND; has shares in Brain & Mind, which provides neuropsychiatric and neurological rehabilitation in the independent medical sector, including in people with FND; has received financial support for lectures from the International Parkinson's and Movement Disorders Society and the FNDS; receives royalties from Oxford University Press for his book The Oxford Specialist Handbook of Parkinson's Disease and Other Movement Disorder; has received honoraria for medical advice to Teva Pharmaceuticals; receives grant funding, including for studies related to functional neurological disorder, from the National Institute for Health and Care Research and the Medical Research Council; is deputy editor of the European Journal of Neurology; and is on the medical advisory boards of the charities functional neurological disorder (FND) Hope UK and Dystonia UK.

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#### Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.eclinm.2025.103687

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