

Demographic and clinical phenotypic differences between people with dissociative seizures and those with other psychiatric disorders

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Background

A large amount of literature surrounds the differences between dissociative neurological symptom disorder with non-epileptic seizures (DNSD-S) and epilepsy.

Aims

To explore the research gap on phenotypic differences between DNSD-S and other psychiatric disorders.

Method

We conducted a case–control study of 1860 patients (620 patients with DNSD-S and 1240 controls with other psychiatric disorders) seen at the South London and Maudsley Hospital NHS Trust between 2007 and 2019.

Results

Compared with the controls, the patients with DNSD-S were more likely to be female (76 v. 47%, $P < 0.001$), of White ethnicity (77 v. 60%, $P < 0.001$), married (34 v. 14%, $P < 0.001$) and living in areas of lower socioeconomic status (-3.79 , 95% CI -2.62 to -4.96 , $P < 0.001$). Two peaks for age at diagnosis were observed for DNSD-S: the early 20s and late 40s. After 31 years of age, men's chance of being diagnosed with DNSD-S increased from 19 to 28% ($P = 0.009$). People with DNSD-S presented more commonly with a history of a neurological episodic or paroxysmal disorder (OR = 12, 95% CI 7.82–20.26), another dissociative disorder (OR = 10, 95% CI 1.64–65.95) or unclassified signs or

symptoms (OR = 4, 95% CI 2.61–6.43). Neither anxiety, depression nor other somatoform disorders predicted subsequent diagnosis of DNSD-S, and controls had a larger proportion of preceding psychiatric diagnoses than patients with DNSD-S (65 v. 49%, $P < 0.001$).

Conclusions

This is the first study comparing demographic and phenotypic correlates of patients with DNSD-S against a large cohort of psychiatric patients. These data will inform development and drive service needs in psychiatry for people with DNSD-S.

Keywords

Non-epileptic seizures; dissociative disorders; neuropsychiatry; neuropsychology; psychopathology.

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Dissociative neurological symptom disorder with non-epileptic seizures (DNSD-S) is characterised by seizures or convulsions that are not consistent with a recognised disease of the nervous system, other mental or behavioural disorders or other health condition. Classified within the functional neurological disorders in DSM-5 and dissociative neurological symptom disorder in ICD-11, they are associated with a range of motor, sensory and mental manifestations and impaired self-control. Dissociative disorders have been reported as highly prevalent in psychiatric out-patient samples, and epidemiological studies have shown incidence rates for DNSD-S ranging between 1.5 and 4.9 per 100 000 per year, with prevalence rates ranging between 2 and 33 per 100 000.^{1,2} With one in five referrals to a first seizure neurology clinic due to DNSD-S,³ ultimately both neurologists and psychiatrists will find themselves responsible for explaining the diagnosis to patients. They will need to be equipped with knowledge to explain a referral to psychiatry and how DNSD-S is different from other more well-known conditions in psychiatry, while providing an explanation of the mechanism behind how patients can develop physical symptoms through inorganic means. Clinicians will find it useful to give further reasons using an evidenced-based archetypal presentation, reassuring patients that they are not alone.

Despite increased interest into the aetiology of DNSD-S over the past decade, the bulk of the literature thus far has only focused on factors differentiating DNSD-S from epilepsy.^{4,5} This is valuable at a diagnostic level, as people with DNSD-S are often misdiagnosed with epilepsy and *vice versa*. However, DNSD-S is a psychiatric

condition and the mainstay of treatment is psychiatric and psychological.⁶ For all these reasons, it is astonishing the limited amount of data about phenotypic differences between DNSD-S and other mental disorders. These data are of great relevance for care provision, planning and outcome studies. In addition, the majority of available studies are affected by a number of methodological limitations, including small samples and retrospective design,^{6,7} with only one study so far conducted at a population level.⁸ Goldstein and colleagues have taken the first step to characterising the typical presentation of people with DNSD-S.⁸ However, more data are needed to validate the preceding and predictive factors of DNSD-S in comparison with other psychiatric conditions. Findings suggest that comorbid neurological diseases occur in 10% of people with functional neurological disorders² and comorbid epilepsy in 10–30% of people with DNSD-S.⁹ Research suggests that affective disorders can appear in 42%¹⁰ and functional somatic symptoms in 66–70%^{11,12} of people with DNSD-S, with personality disorders also being common.¹³ Data on medical and psychiatric history research are available from several studies, yet all previous studies were conducted with small samples, or lacked a psychiatric control group or used people with epilepsy. In addition to this, most studies used a top-down design to probe for diseases, with researchers using self-report or relying on experience to ask for the presence of specific conditions. It would be more robust to collect diagnostic data directly from clinical notes. This is a case–control study investigating the clinical characteristics of individuals with DNSD-S at diagnosis, in a large cohort of people with other mental disorders.

Method

Design, setting and data source

Medical records of patients seen at the South London and Maudsley NHS Foundation Trust (SLaM) between 1 January 2007 and 6 November 2019 were analysed. SLaM is a National Health Service mental health trust that provides mental healthcare to a population of roughly 1.3 million residents in London, UK, as well as a national referral service. In 2007, the National Institute for Health Research (NIHR) Biomedical Research Centre at SLaM and King's College London developed the Clinical Record Interactive Search (CRIS) system. CRIS provides researchers with regulated access to anonymised information contained in SLaM's medical records, including over 250 000 patients.^{14,15}

CRIS was approved as a secondary data resource by the National Research Ethics Committee South Central Oxford C (ref: 18/SC/0372). The CRIS Research Oversight Committee granted our project access in March 2018 (project number 18-033).

Participant selection

Patients with DNSD-S were identified using CRIS by searching for the ICD-10 code F44.5 (Dissociative seizures) as a diagnosis. Patients for whom the code F44.5 was not the primary psychiatric diagnosis were excluded because a secondary diagnosis is not considered the main condition in a phenotype, nor as driving the major effect on the patient's life. Furthermore, we wanted to focus on DNSD-S as the primary problem from a psychopathological point of view, rather than conditions where DNSD-S could be considered the consequence of other major psychiatric conditions, thus masking the specific contribution of DNSD-S compared with a general sample of patients with psychiatric disorders. Inclusion of DNSD-S as a secondary diagnosis would have potentially biased the sample, especially because it is compared with a general sample of patients with psychiatric diagnoses. Cases and controls with missing demographic data were excluded. All patients with DNSD-S referred to SLaM already have a documented diagnosis of DNSD-S according to International League Against Epilepsy (ILAE) criteria¹¹ made in an epilepsy centre.

For every DNSD-S 'case' we selected the two closest patients in time who were diagnosed in SLaM with a different primary psychiatric diagnosis (F code in ICD-10) on the day the 'case' received theirs. Controls were excluded if they had any history of 'dissociative seizures' and each control could only be used as a match once.

Outcome variables

We gathered demographic data regarding participant's gender, age, ethnicity, marital status, socioeconomic score and age at diagnosis. These variables were generally taken straight from CRIS. For temporal variables such as marital status, the most recent information at or before diagnosis was taken. For socioeconomic status, the active address on the 6 November 2019 or the most recent preceding address was used. Addresses were allocated to area scores according to the English Index of Multiple Deprivation (2015)¹⁶, giving a score of 1 (most deprived) to 32 844 (least deprived). Data on specific past psychiatric conditions were pulled from the CRIS database because we assumed that diagnoses delivered in a mental health service would be more accurate than diagnoses made in primary care. Data on past medical diagnoses were gathered by incorporating data from the Hospital Episode Statistics (HES) database (National Health Service, 2017). The HES database is linked with the CRIS database via a third-party clinical linkage data service using deterministic or probabilistic matching if/as required.¹⁵ This database contains details of all diagnoses, admissions and out-

patient appointments at NHS hospitals across England. Owing to the vast number of conditions within medicine, we initially grouped medical diagnoses using the main chapters of ICD-10 to highlight any significantly associated medical categories. Given that past research has highlighted epilepsy in patients with dissociative seizures, we also broke down the G (neurology) ICD category to assess the predictivity of all neurological conditions.

Statistical analysis

All variables were analysed using IBM SPSS Statistics software, version 25 for Windows. Chi-square tests were used to compare gender, ethnicity, marital status and all medical and psychiatric history. *T*-tests were used to compare means of age at diagnosis and deprivation score. Exploratory analyses included chi-square comparisons within the DNSD-S group and between-group comparisons of age at diagnosis, split by the median. Binary logistic regression was used to further assess all significant variables from previous analyses to produce odds ratios.

Results

A total of 930 patients were identified to have a diagnosis of DNSD-S. Of these, 104 had DNSD-S as a secondary diagnosis and were therefore removed, leaving 826 in the final DNSD-S group. Statistical comparisons between the secondary diagnosis group and the final DNSD-S group showed no significant differences on all demographic variables apart from gender, where those with primary DNSD-S showed a greater proportion of females (76 v. 62%, $\chi^2 = 8.207$, d.f. = 1, $P = 0.004$). Finally, cases or controls missing any demographic data were removed to leave a clean data-set of 620 cases with 1240 matched controls. The primary diagnoses of the cohort are shown in Table 1. Demographic frequencies, averages and between-group comparisons statistics are displayed in Table 2.

On average, those in the DNSD-S group were younger than the controls (33.4 v. 44.6 years). Age-at-diagnosis distributions are shown in Figs 1 and 2. The DNSD-S group distribution shows two peak ages at which patients generally received their diagnosis: one in their early 20s and one in their early 40s. Exploring this further, we split the DNSD-S group by median (31 years) and re-ran chi-square comparisons. Ethnicity showed no group differences above or below age 31 years. For gender, those in the DNSD-S group were overall still more likely to be female, but the proportion of males who received a diagnosis of DNSD-S significantly increased after 31 years of age, from 19.4 to 28.3% ($\chi^2 = 6.794$, d.f. = 1, $P = 0.009$, $\phi = 0.009$). We did not compare temporal variables because these will be age dependent.

Historic mental and neurological conditions both showed significant differences between our groups, which confirmed the decision to further break down these two categories from the CRIS and HES databases. All prior diagnoses that reached significance were input into a logistic analysis alongside demographic variables. The results, including odds ratios, are displayed in Table 3. Individuals with DNSD-S were identified by this model with a sensitivity of 84.4%, and controls were correctly discriminated with a specificity of 92.6% (overall correct classification: 89.8%).

Discussion

This is the first study investigating demographic phenotypic differences between individuals with DNSD-S and those with other psychiatric diagnoses. Those with DNSD-S were more likely to be female (76 v. 47%), of White ethnicity (77 v. 60%), married or

Table 1 Primary diagnoses for the cohort

	Frequency, <i>n</i>	% ^a
DNSD-S group		
Dissociative seizures	620	100
Control group		
Psychosis	381	30.7
Depressive/mood disorder	185	14.9
Mental and behavioural disorders due to use of alcohol and drugs	173	14.0
Anxiety disorder (phobic/general/OCD/PTSD)	107	8.6
Mania/bipolar disorder	106	8.5
Dementia	57	4.6
Hyperkinetic/conduct/unspecified childhood-onset disorder	57	4.6
Personality disorders	65	5.2
Other organic mental disorder/condition (e.g. delirium/unspecified)	32	2.6
Developmental disorders	17	1.4
Eating disorder	13	1.0
Delirium	7	0.6
Dissociative other/motor	6	0.5
Other somatoform disorders (neurasthenia or depersonalisation)	6	0.5
Unspecified mental disorder with physiological dysfunction	<5 ^b	<4 ^b

DNSD-S, dissociative neurological symptom disorder with non-epileptic seizures; OCD, obsessive-compulsive disorder; PTSD, post-traumatic stress disorder.
a. Percentages (%) are of the total cohort or control group.
b. To maintain confidentiality, frequency values considered 'small' (*n* < 5) were not shown individually.

cohabitating (34 *v.* 14%) and to live in areas of lower socioeconomic status (25.7 *v.* 29.5%).

Our study identified two peak ages at diagnosis. The first peak, during the patients' early 20s, has been previously documented by a number of studies.¹ The second peak, in their late 40s, is of particular interest. Differences between early- and late-onset DNSD-S have been explored in a cohort of 241 patients, which showed that individuals with late-onset DNSD-S were more likely to be male and have severe physical health problems.¹⁷ Our results confirm that, although women are overall four times more likely to have DNSD-S than men, significantly more men were diagnosed with DNSD-S over the median age of 31 years (61%) compared with

women (49%). In this regard, it must be emphasised that our study reported age at diagnosis rather than age at symptom onset and for this reason the two peaks do not necessarily reflect a different underlying aetiology or syndromic differences. However, Goldstein and colleagues⁸ found a similar trend in terms of age at onset, supporting the intriguing possibility of genuine aetiological differences.

In terms of medical history and comorbidities, compared with psychiatric controls, people with DNSD-S were 12 times more likely to have a previous diagnosis of a paroxysmal neurological condition such as epilepsy, and 10 times more likely to have had a diagnosis of a dissociative disorder, including dissociative amnesia, motor and anaesthesia symptoms. This may reflect a previous misdiagnosis of epilepsy⁴ but also the close relationship between DNSD-S and other dissociative disorders.

The rate of concomitant psychiatric diagnoses is another important finding of our study. Historically, people with DNSD-S have been considered 'complex' because of the high rates of concomitant psychiatric problems.¹⁸ Our study found that one in two in the DNSD-S group had a concomitant psychiatric problem but this is not statistically different from our psychiatric control group, pointing out that individuals with DNSD-S do not present a more complex psychiatric comorbidity pattern compared with those with other psychiatric disorders. More specifically, previous research has shown anxiety disorders (such as post-traumatic stress disorder, PTSD), depression and personality disorder to be common in people with DNSD-S.^{10,13} Our results suggest that they are common but they are not specific to patients with DNSD-S compared with those with other psychiatric conditions, as a personality disorder predictor remained non-significant, and both anxiety disorder and depression showed significant predictors, but odds ratios were minimal (<1). Previous findings reflect the nature of the comparison, which most of the time was with epilepsy.

Finally, our study contributes to the debate about the role of somatisation and dissociation in people with DNSD-S. Previous authors have pointed out this role.¹⁹ However, our study found a low prevalence rate for somatisation in the DNSD-S group that is not statistically different from the rate in the psychiatric controls. Although it may be the case that somatisation symptoms are common,¹⁹ our results show, clinically, that they may be underdiagnosed and that dissociation symptoms, episodic paroxysmal disorders, and symptoms, signs and abnormal clinical and laboratory

Table 2 Demographic frequencies, averages and comparison statistics of the DNSD-S group and controls

	DNSD-S group, <i>n</i> = 620		Controls, <i>n</i> = 1240		Test, significance (<i>P</i>), effect size (ϕ , Cramer's <i>V</i> or Cohen's <i>d</i>)
	Frequency, <i>n</i>	%	Frequency, <i>n</i>	%	
Male*	149	24.0	657	53.0	$\chi^2 = 141.09$, d.f. = 1, <i>P</i> < 0.001, $\phi = 0.275$
Female*	471	76.0	583	47.0	
White*	479	77.3	746	60.2	$\chi^2 = 139.88$, d.f. = 5, <i>P</i> < 0.001, <i>V</i> = 0.274
Black*	59	9.5	344	27.7	
Mixed	13	2.1	39	3.1	
Other ethnic group	26	4.2	43	3.5	
Asian*	18	2.9	68	5.5	$\chi^2 = 139.88$, d.f. = 5, <i>P</i> < 0.001, <i>V</i> = 0.274
Chose not to disclose*	25	4.0	0	0.0	
Single*	348	56.1	836	67.4	$\chi^2 = 128.87$, d.f. = 5, <i>P</i> < 0.001, <i>V</i> = 0.263
Married/cohabitating*	213	34.4	173	14.0	
Divorced*	26	4.2	104	8.4	
Widowed*	6	1.0	47	3.8	
Separated*	12	1.9	66	5.3	
Chose not to disclose*	15	2.4	14	1.1	
	Mean	s.d.	Mean	s.d.	
Age at diagnosis, years*	33.4	13.8	44.6	17.5	<i>t</i> = 13.93, d.f. = 1858, <i>P</i> < 0.001, <i>d</i> = 0.71 (m.d. = 11.19, 95% CI 9.62–12.77)
Socioeconomic status* (IMD score)	25.7	14.1	29.5	11.1	<i>t</i> = 6.34, d.f. = 1858, <i>P</i> < 0.001, <i>d</i> = 0.29 (m.d. = 3.79, 95% CI 2.62–4.96)

DNSD-S, dissociative neurological symptom disorder with non-epileptic seizures; m.d., mean difference; IMD, index of multiple deprivation.
* Indicates a significant difference (*P* < 0.05).

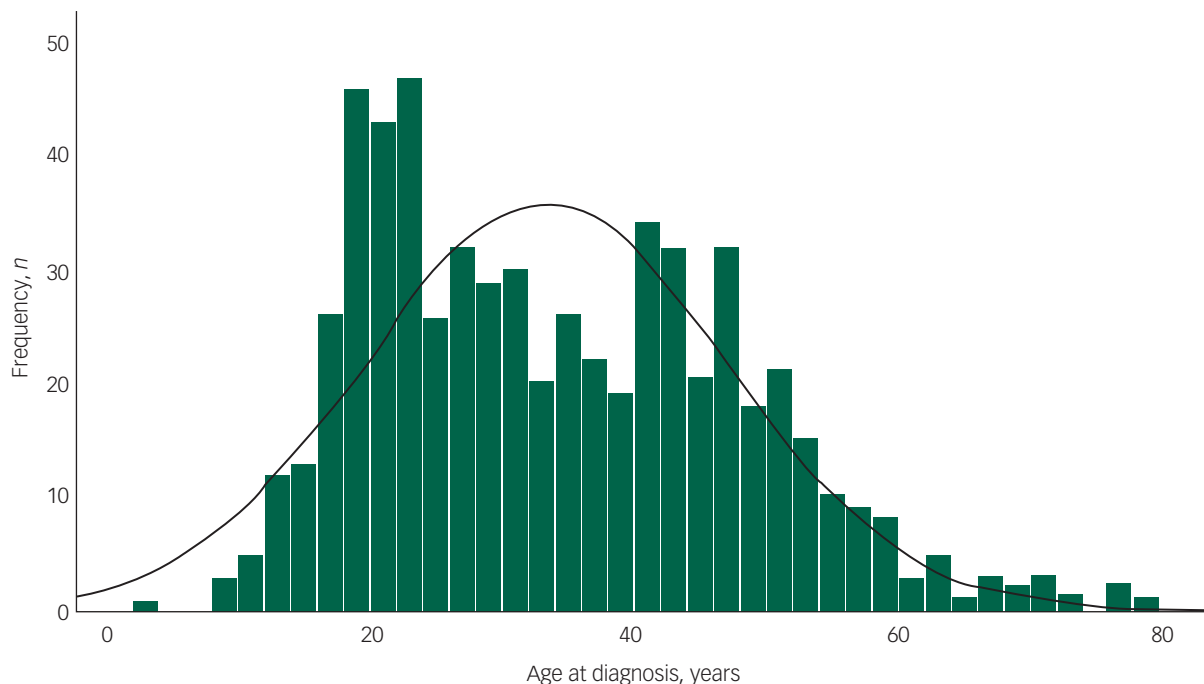


Fig. 1 Age at diagnosis of dissociative neurological symptom disorder with non-epileptic seizures (DNSD-S) in the cases group.

findings ‘not elsewhere classified’ may be just as, if not, more important. However, we should add the caveat that our sample potentially missed patients who had received an ICD diagnosis code of ‘mixed dissociative disorder’ that included dissociative seizures and who could have potentially showed greater somatisation. Regardless, this is an interesting finding, given the high associations between dissociative mechanisms and adverse events and trauma – both prevalent in the DNSD-S population.²⁰

Limitations

We should bear in mind that our findings will be somewhat influenced by the data’s source; for example, hospital primary care data will not capture lesser medical conditions that do not require hospital attendance. Ideally, we would have analysed the incidence of medical conditions rather than dichotomously recording whether a condition had occurred in the past. However, we did not want to run the risk of being too reductionist when dealing with complex

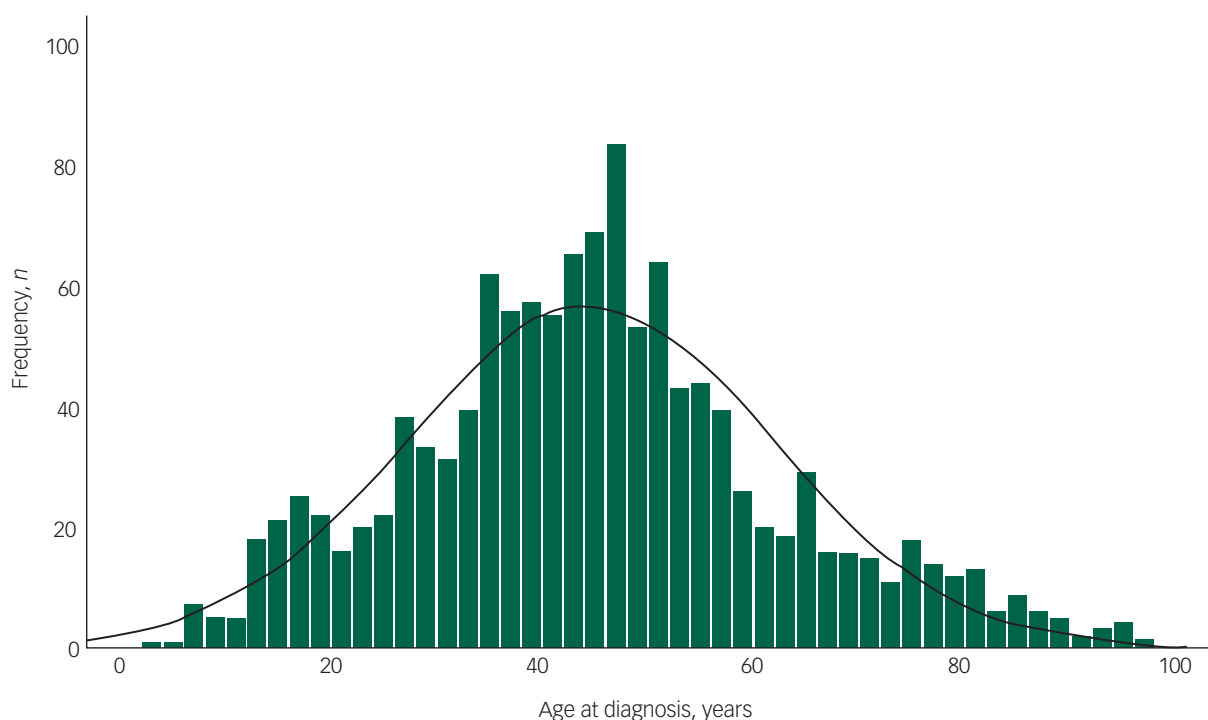


Fig. 2 Age at diagnosis of psychiatric disorders in the control group.

Table 3 Logistic regression results for relative predictors of a diagnosis of DNSD-S^a

	B	s.e.	Wald	d.f.	P	OR ^{b,c,d}	95% CI for Exp(B)	
							Lower	Upper
Age at diagnosis, years*	-0.056	0.007	61.918	1	0.000	0.945	0.932	0.959
IMD score*	-0.015	0.007	5.368	1	0.021	0.985	0.972	0.998
Female*	1.082	0.188	32.957	1	0.000	2.951	2.039	4.269
Ethnicity			7.116	5	0.212			
White	-0.343	0.247	1.938	1	0.164	0.709	0.437	1.150
Black	-0.189	0.463	0.167	1	0.683	0.828	0.334	2.051
Mixed	0.174	0.414	0.176	1	0.675	1.190	0.528	2.680
Other*	-1.013	0.439	5.331	1	0.021	0.363	0.154	0.858
Asian	20.399	7060.346	0.000	1	0.998	722 942 556.108	0.000	
Marital status*			42.050	5	0.000			
Single*	1.374	0.231	35.413	1	0.000	3.953	2.514	6.215
Married/cohabitating	-0.060	0.382	0.025	1	0.874	0.941	0.445	1.991
Divorced	-0.121	0.544	0.049	1	0.824	0.886	0.305	2.574
Separated	0.013	0.764	0.000	1	0.987	1.013	0.227	4.529
Widowed	-0.352	0.586	0.360	1	0.548	0.703	0.223	2.218
Diseases of the eye and adnexa	0.637	0.338	3.553	1	0.059	1.892	0.975	3.670
Diseases of the ear and mastoid process	0.893	0.579	2.382	1	0.123	2.443	0.786	7.592
Respiratory disease	-0.068	0.229	0.087	1	0.768	0.934	0.596	1.465
Diseases of the digestive system	-0.068	0.214	0.101	1	0.751	0.934	0.614	1.421
Diseases of the musculoskeletal system and connective tissue	0.087	0.240	0.132	1	0.716	1.091	0.682	1.745
Diseases of the genitourinary system	0.080	0.228	0.122	1	0.727	1.083	0.692	1.694
Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified*	1.410	0.230	37.500	1	0.000	4.095	2.608	6.430
Factors influencing health status and contact with health services	-0.294	0.216	1.843	1	0.175	0.745	0.488	1.139
Other degenerative diseases of the nervous system	-0.948	1.012	0.878	1	0.349	0.388	0.053	2.814
Episodic and paroxysmal disorders*	2.533	0.243	108.916	1	0.000	12.590	7.824	20.260
Nerve, nerve root and plexus disorders	0.743	0.506	2.157	1	0.142	2.102	0.780	5.668
Diseases of myoneural junction and muscle	0.118	1.235	0.009	1	0.924	1.125	0.100	12.665
Cerebral palsy and other paralytic syndromes	-0.121	0.591	0.042	1	0.838	0.886	0.278	2.824
Other disorders of the nervous system	0.157	0.438	0.129	1	0.719	1.170	0.496	2.760
Dementia	-20.169	4861.184	0.000	1	0.997	0.000	0.000	
Mental and behavioural disorders due to use of alcohol and drugs*	-3.080	0.467	43.530	1	0.000	0.046	0.018	0.115
Psychosis*	-3.477	0.479	52.683	1	0.000	0.031	0.012	0.079
Mania/bipolar disorder	-20.633	2745.750	0.000	1	0.994	0.000	0.000	
Depressive/mood disorder*	-2.323	0.302	59.332	1	0.000	0.098	0.054	0.177
Anxiety disorder (phobic/general/OCD/PTSD) *	-1.499	0.317	22.418	1	0.000	0.223	0.120	0.415
Dissociative other/motor*	2.342	0.942	6.182	1	0.013	10.407	1.642	65.952
Personality disorders	-0.337	0.490	0.473	1	0.492	0.714	0.273	1.865
Mental retardation*	-2.101	0.924	5.174	1	0.023	0.122	0.020	0.748
Developmental disorders	-0.834	0.564	2.188	1	0.139	0.434	0.144	1.311
Hyperkinetic/conduct/unspecified child-onset disorder*	-1.503	0.516	8.491	1	0.004	0.223	0.081	0.611
Unspecified*	-0.572	0.275	4.335	1	0.037	0.565	0.330	0.967
Constant	0.864	0.329	6.904	1	0.009	2.373		

DNSD-S, dissociative neurological symptom disorder with non-epileptic seizures; IMD, index of multiple deprivation; OCD, obsessive-compulsive disorder; PTSD, post-traumatic stress disorder.

a. Diagnostic categories for mental and neurological conditions are from ICD-10.

b. Odds ratios indicate the predictiveness of developing DNSD-S given the presence of a variable characteristic.

c. $\chi^2 = 1460.728$, d.f. = 39, $P < 0.001$ – model coefficients.

d. $\chi^2 = 9.030$, d.f. = 8, $P = 0.340$ – Hosmer–Lemeshow goodness-of-fit test.

* Indicates a significant contribution to the model.



groups. Plus, this approach would have been more susceptible to reporter bias. Ideally, structured interviews would have been administered to glean these data, minimising reporter bias and allowing accurate diagnosis-frequency calculations. This is especially important in this area, given that there are generally issues with the reporting of complex disorders such as somatisation in routine clinical practice in general. However, owing to the retrospective nature and large numbers, this was not possible for the current study. The data were cross-sectional, and we therefore had to interpret temporal variables such as marital status with caution as they might change. We were unable to record the age at onset of a condition, only the age at which a patient was diagnosed. Next, although in our sample electroencephalogram (EEG) was the gold standard for diagnosis of DNSD-S, we did not check individual EEG results. Some individuals may have diagnoses based on experts' clinical judgement, which, naturally, increases risk of misdiagnoses. We should also bear in mind that patients with DNSD-S classified as a secondary diagnosis were removed

from our sample. As a consequence, our results may not be valid in this population of patients. However, the numbers were small, and the purpose of this study was to focus on patients with DNSD-S as a primary diagnosis. Finally, we should reiterate that we used the ICD codes to group individuals with DNSD-S, which means that we will have missed patients with DNSD-S who also had other dissociative symptoms and were given the diagnosis 'F44.7 Mixed dissociative [conversion] disorders'.

Implications

Our findings aid other studies in clarifying the clinical and demographic characteristics of the DNSD-S patient population relative to the population with other psychiatric conditions. Clinicians should be aware of the increased incidence of DNSD-S diagnoses around the age of 40, rather than simply in the early 20s. The presence of prior paroxysmal symptoms, both neurological and dissociative, are more valid characteristics of DNSD-S than mood

and anxiety conditions. Other pathological conditions may be important when identifying DNSD-S in neurological clinics, but this may not be so important when it comes to pathological aetiology and psychological treatment. Perhaps we place too great an emphasis and assume high psychiatric comorbidity in patients with DNSD-S because of past comparison with patients with epilepsy. The high predictivity of other neurological, functional and dissociative symptoms could suggest a common behavioural aetiology in these patients. It would be helpful for future studies to compare the behaviours and cognitions among DNSD-S patients to establish phenotypes. Any differences would be important to inform therapists of potential areas to target during treatment.

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Data availability

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available owing to patient confidentiality restrictions.

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Author contributions

A.S. and J.S.B. conceived and designed the analysis; A.S., J.S.B. and M.P. collected the data and contributed data and analysis tools; A.S. performed the analysis; A.S., J.S.B. and M.M. wrote the paper.

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Declaration of interest

None.

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