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Misdiagnosis of an underlying medical condition as Conversion Disorder/Functional Neurological Disorders (CD/FND) still occurs

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Running title: Predictors of misdiagnosis in CD/FND

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994 words
2 Tables

1. Introduction

Undetected medical conditions can be misdiagnosed as Conversion Disorder/Functional Neurological Disorder(CD/FND). Although misdiagnosis is considered a rare occurrence since the introduction of improved diagnostic imaging procedures,(1-3) there is no recent estimate of this. We therefore conducted a study to explore how often a medical condition was misdiagnosed as CD/FND in a sample of consecutive outpatients referred for treatment to the Clinical Centre of Excellence for Body Mind and Health (CLGG); a tertiary mental health centre for Somatic Symptom Disorders and Related Disorders (SSRD). Patients had been diagnosed with CD/FND elsewhere. We systematically explored the type and duration of CD/FND, psychiatric and somatic comorbidity, early childhood trauma, childhood sexual abuse, stressful life events, use of medication, family history of CD/FND and demographic factors in all patients. We evaluated which of these predictors were associated with misdiagnosis.

2. Methods

The current study used a cross-sectional observational design with inclusion between February 1st 2010 and December 31st 2017. The research protocol was approved by the IRB of GGz Breburg (2017–03/ 2019-01).

2.1 Description of setting and sampling technique

CLGG provides expert diagnosis, treatment and second opinions for the 5% of the most complex patients with SSRD in the Netherlands. It was awarded for its rigorous standards in research, diagnostic evaluations and treatment provision in 2014 and 2019. CLGG is nationally one of the last resorts for treatment resistant cases, and patients at intake on average received treatment for 5 years elsewhere.(4)

The standard intake procedure at the CLGG includes assessment of psychological symptoms, adverse childhood events and stressful life events by questionnaires; semi structured psychiatric evaluation(PSE) and psycho-diagnostic assessment complemented by MINI interview;(5) assessment of somatic symptoms by a questionnaire measuring physical symptoms, medical history and a physical examination including a neurological component. The patient's existing somatic history and diagnostic assessments that led to the diagnosis of CD/FND are then reviewed, compared with the findings at intake, and discussed in a multidisciplinary team meeting which includes medical doctors, psychiatrists, (neuro)psychologists, and a nurse specialised in trauma treatment. After this multidisciplinary review, any diagnostic considerations are revisited with the referring clinician and DSM-IV(6) and DSM-5(7) classification as CD/FND or as misdiagnosis is established.

2.2 Statistical analysis

Chi-squared analyses and independent samples t-tests explored differences in demographic, clinical or other predictive characteristics between confirmed CD/FND cases versus misdiagnosed cases.

3. Results

Based upon this systematic re-evaluation of cases, it became apparent that nine(12%) patients had an underlying medical condition explaining their initial and current somatic symptoms. The diagnosis and medical disciplines involved in the original CD/FND diagnosis are listed in Table 1. - Insert Table 1 -
No significant differences were observed in the presence of predictors between the confirmed CD/FND cases and the misdiagnosed cases, as shown in Table 2. This would suggest that, although comorbidity, trauma and current stressors are often present in CD/FND, exploring such patient factors cannot contribute to establishing the diagnosis CD/FND. – Insert Table 2. –

4. Discussion

Several serious chronic medical conditions came to light, which had remained hidden and had been left untreated for long periods of time. We consider this finding of high clinical relevance, as, given existing neurological literature, we would expect a much smaller percentage of misdiagnosed cases.(8) Furthermore, primary care studies found that repeated diagnostic assessments conducted after well-performed initial diagnostic procedures, identified no or only 0.5% underlying medical conditions in patients with medically unexplained symptoms(MUS)(9). Based on that research, Dutch guidelines recommend to abstain from repeat diagnostic procedures in MUS(10, 11) and the multidisciplinary treatment guideline for CD/FND omits the possibility of misdiagnosis completely.(12) However, while such recommendations may apply to a broad range of MUS in the primary care setting, in addition to CD/FND in neurology settings, they may not necessarily apply to cases of CD/FND receiving years of unsuccessful treatment after initial diagnostic assessment.
The misclassification of unrecognised underlying somatic conditions as CD/FND may occur more often in severe and chronic cases, such as underlying neurological conditions with slow, insidious onset, including progressive supranuclear palsy,(13) MSA, and hypertensive leukoencephalopathy. Rare conditions such as epileptic transient global amnesia may go unrecognized. Conditions such as Morbus Hashimoto have a higher chance to be missed due to their variable prevalence in different populations, as well as an often undetected (depending on diagnostic tests used) preclinical stage.(14) Diseases which present in more severe forms than a priori expected can go undetected in conditions such as Ehlers Danlos Syndrome or endometriosis. This may especially occur in patients who have

difficulty expressing themselves,(15) for example because of language, cultural background, education level, age, or feelings of shame. Treatment settings may also be a relevant factor as they may lack appropriate expertise or infrastructure to explore these conditions as possible options. For example, specialty mental health settings often lack integrated somatic services, especially if they are based outside the general hospital setting. Whilst avoiding unnecessary tests and iatrogenic harm remains of paramount importance,(16) clinicians should be aware that a substantial percentage of chronic CD/FND patients may have an underlying disease.

5. Limitations

Although the study size is larger than in most other studies, and similar to the 1998 landmark study on CD,(1) the sample size can be considered a limitation.

6. Conclusions

Our findings show that misdiagnosis of an underlying medical condition as CD/FND still occurs in chronic cases within the specialist mental health setting. Large scale interdisciplinary research studies with collaborating psychiatrists and neurologists are required to confirm these findings and to contribute to the re-evaluation of guidelines for assessment of CD/FND. Also, these findings warrant the serious consideration of diagnostic re-evaluations in chronic cases. There is a clear call for structurally embedding somatic re-examination and re-evaluation in specialist mental health settings, by consultation liaison and integrated care models which involve psychiatrists, referring neurologists and primary care physicians. Such a provision, that has shown to be beneficial at case level,(13) is unfortunately not currently widely available. Policymakers should support the development of such sustainable somatic evaluation facilities and services.

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Table 1. Characteristics of misdiagnosed cases (N=9)

Age	Gender	Duration of treatment elsewhere	Referred to CLGG by	Initial CD/FND diagnosis confirmed by	Main presenting symptom	ACE	Somatic diagnosis	Confirmed by
63	Female	48 months	Psychiatrist	Neurologist	Falling	Yes, childhood sexual abuse	Progressive Supranuclear Palsy	Neurologist* after consultation by multidisciplinary team CLGG; MRI
21	Female	96 months	Psychiatrist, general practitioner (GP)	Neurologist, orthopedist, revalidation clinic	Weakness	No	Ehlers Danlos Syndrome	Multidisciplinary team CLGG in consultation with referring clinicians
68	Female	24 months	Psychiatrist	Internal medicine	Tremor	No	M. Parkinson, later Multiple System Atrophy (MSA)	Neurologist, and second opinion neurologist
39	Female	60 months	Psychiatrist	Neurologist	Pressure head, fatigue	No, but sexual abuse at 19 years	Myopia	Multidisciplinary team CLGG in consultation with referring clinicians
49	Male	36 months	Neurologist, GP	Neurologist	Non-epileptic seizures of dissociative nature	No	Epileptic Transient Global Amnesia	Neurologist, Epilepsy clinic
45	Male	16 months	Psychiatrist	Neurologist, internal medicine, cardiologist	Motor symptoms, cognitive symptoms	No	Treatment resistant hypertension and leukoencephalopathy	Multidisciplinary team CLGG in consultation with referring clinicians
30	Female	36 months	Revalidation doctor, GP	Revalidation doctor	Muscle twitching, paresthesia	No	M. Hashimoto, treatment resistant	Multidisciplinary team CLGG in consultation with referring clinicians
36	Female	24 months	Psychiatrist, GP	Revalidation doctor	Pain, paresthesia, weakness leg	Yes, childhood sexual abuse	Pseudoradicular syndrome	Multidisciplinary team CLGG in consultation with referring clinicians
21	Female	108 months	Psychiatrist	Neurologist	Pain, falling	No	Endometriosis with vasovagal collapses	Multidisciplinary team CLGG in consultation with gynecologist

- Case described in (34)

Table 2 Demographic and clinical characteristics of confirmed CD/FND (N=64) and misdiagnosed patients (N=9)

	Confirmed CD/FND (n=64)		*Misdiagnosed (n=9)*		X^2	*p*
	n	%	n	%		
Sex						
Male	13	20.3	2	22.2	0.018	.894
Female	51	79.5	7	77.8		
Age	M= 43.14	SD= 11.58	M= 41.33	SD= 16.74	t = 0.414	.680
Relationship status						
Single	21	32.8	3	33.3	4.306	.230
Cohabiting	14	21.9	0	0		
Married	24	37.5	6	66.7		
Long-distance	5	7.8	0	0		
Family status						
Single no children	20	31.3	3	33.3	1.214	.750
Single with children	7	10.9	0	0		
Partner no children	10	15.6	2	22.2		
Partner with children	27	42.2	4	44.4		
Social Network						
Good	27	42.2	4	44.4	0.782	.676
Mediocre	31	48.4	5	55.6		
Bad	5	7.8	0	0		
Education						
Very low	8	12.5	1	11.1	0.338	.987
Low	20	31.3	3	33.3		
Middle	23	35.9	4	44.4		
High	9	14.1	1	11.1		
Very High	1	1.6	0	0		
Work status						
Working	13	20.3	2	22.2	3.089	.686
Sickness Benefits	15	23.4	2	22.2		
Unemployment benefits	4	6.3	0	0		
Social assistance benefit	7	10.9	0	0		
Disabled	18	28.1	2	22.2		
Retired	2	3.1	1	11.1		
Family member with CD/FND	0	0	0	0	-	-
Family member with other psychiatric disorder	24	37.5	3	33.3	0.503	.478
Type of Conversion disorder						
With sensoric symptoms	5	7.8	0	0	3.058	.548
With motor symptoms	25	39.1	5	55.6		
With non-epileptic seizures	9	14.1	1	11.1		
With mixed symptoms	17	26.6	1	11.1		
Other	6	9.4	0	0		
Time between symptom onset to start of treatment						
<3 months	5	7.8	1	11.1	1.143	.767
3 – 6 months	6	9.4	0	0		
6 – 12 months	10	15.6	2	22.2		
>12 months	42	65.6	6	66.7		

Onset						
Acute	27	42.2	3	33.3	0.256	.613
Gradually	37	57.8	6	66.7		
Time from symptom onset to start of treatment in CCLG (months)	M = 61.11	SD= 70.49	M= 46.22	SD= 33.05	t = 0.621	.536
Comorbid disorders						
Personality disorder	26	40.6	3	33.3	5.416	.067
Anxiety disorder	31	48.4	3	33.3	0.723	.395
Depressive disorder	27	42.2	3	33.3	0.256	.613
Psychotic disorder	2	3.1	0	0	0.289	.591
Developmental disorder	11	17.2	0	0	1.821	.177
Addiction	3	4.7	1	11.1	0.629	.428
Thyroid disorder	7	10.9	2	22.2	0.930	.335
Adrenal disorder	0	0	0	0	-	-
Other somatic disorder	17	26.6	1	11.1	1.014	.314
Stroke	7	10.9	0	0	1.089	.297
Epilepsy	2	3.1	0	0	0.289	.591
Other neuro condition	6	9.4	1	11.1	0.027	.868
Other somatic condition	40	62.5	8	88.9	2.440	.118
Use of Medication						
Antidepressants	29	45.3	4	44.4	0.002	.961
Benzodiazepines	17	26.6	1	11.1	1.014	.314
Anti-psychotics	5	7.8	1	11.1	0.114	.736
Pain medication	24	37.5	1	11.1	2.440	.118
Opiates	12	18.8	2	22.2	0.061	.804
Childhood trauma	45	70.3	5	55.6	0.935	.334
Recent life event	41	64.1	6	66.7	0.001	.975
Sexual abuse in childhood	17	26.6	2	22.2	0.077	.781
Death of a loved one	3	4.7	1	11.1	0.629	.428

*p<0.05; **p<0.01 X^2=chi squared, M= mean, SD= standard deviation.