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ORIGINAL COMMUNICATION

Neurological diseases and risk of suicide attempt: a case–control study

Astrid Eliasen[1] · Kim Peder Dalhoff[1] · Henrik Horwitz[1,2]

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Abstract

Introduction Neurological diseases have a profound impact on quality of life. We investigated the risk of suicide attempt in ten neurological diseases.

Methods Case–control study. Cases were identified from the Danish Poison Information Centre database in the period 2006–2013. The prevalence of ten neurological diagnoses was compared with the prevalence in a randomly sampled age- and gender-matched control group.

Results We identified 8974 cases of suicidal attempt and 89,740 controls. We found an association between suicide attempt in nine of ten neurological diseases and disease groups, including stroke [odds ratio (OR) 3.1, 95% confidence interval (CI) (2.8–3.6)], Huntington's disease [OR 8.8, 95% CI (3.2–24.1)], amyotrophic lateral sclerosis [OR 5.0, 95% CI (1.7–14.6)], Parkinson's disease [OR 2.9, 95% CI (1.8–4.6)], Alzheimer's disease and other degenerative diseases [OR 4.8, 95% CI (3.1–7.5)], multiple sclerosis [OR 1.5, 95% CI (1.1–2.1)], epilepsy [OR 4.5, 95% CI (4.1–5.0)], hereditary and idiopathic neuropathy [OR 2.2, 95% CI (1.1–4.3)] and myasthenia gravis [OR 4.3, 95% CI (2.0–9.4)].

Conclusion Nine out of ten chronic neurological diseases were associated with an increased risk of suicide attempt. These data must be considered for clinicians treating this vulnerable group of patients.

Keywords Suicide attempt · Self-poisoning · Neurological diseases · Neuropsychiatry

Introduction

Suicidal behavior is an important consideration in patients with neurological diseases, as it can be a desperate last resort to escape from the burdensome chronic symptoms. Compared to the management of physical symptoms, there is less attention on the psychological consequences of living with a neurological disease, and the psychiatric comorbidities are often unrecognized and untreated [1].

Previous research has found an increased risk of suicide in patients with certain neurological diseases, including epilepsy, stroke, multiple sclerosis (MS), Huntington's disease, amyotrophic lateral sclerosis (ALS) and Parkinson's disease [2–8], whereas suicide attempts in patients with neurological diseases are less well-studied. Deliberate self-poisoning is the most common method of suicide attempt [9], but whether there is a positive association with individual neurological diseases has yet to be investigated.

We did a large case–control study of the association between individual neurological diseases and suicide attempt by self-poisoning.

Methods

Data sources

The Danish National Patient Register (DNPR) contains information on all somatic in- and out-patients in Danish hospitals, whereas the Danish Psychiatric Central Research Register (PCRR) register hold data of patients treated at psychiatric departments in Denmark [10]. For each patient contact, one primary and optional secondary

✉ Henrik Horwitz
henrik_horwitz@hotmail.com

Astrid Eliasen
astrid_eliasen@hotmail.com

Kim Peder Dalhoff
kim.peder.dalhoff@regionh.dk

[1] Department of Clinical Pharmacology, Bispebjerg and Frederiksberg Hospital, University of Copenhagen, Bispebjerg Bakke 23, 2400 Copenhagen, NV, Denmark

[2] Frederiksberg, Denmark

diagnoses are recorded according to the International Classification of Diseases, 10th Revision (ICD-10) [11].

The Danish Poison Information Centre (DPIC) opened in 2006 and offers a nationwide 24-h telephone advisory service for healthcare professionals and the public on all toxicological issues.

The Danish "Centrale Person Register" (CPR) includes individual information on the unique personal identification number (CPR number), which is used in national registers. We cross-referenced the CPR numbers from the DPIC database with the DNPR and the PCRR.

Study population

Patients aged 20 or older and recorded in the DPIC database with poisoning with suicidal intent in the period 1 August 2006–31 December 2013, were selected as cases. For each case we randomly draw ten age- and gender-matched controls living in Denmark at the date of poisoning.

Procedures

We extracted data from the DNPR and calculated the prevalence of ten ICD-10-coded neurological diseases and disease groups such as stroke, Huntington's disease, ALS, Parkinson's disease, Alzheimer's disease and other degenerative diseases, MS, epilepsy, hereditary and idiopathic neuropathy, myasthenia gravis and primary disorders of the muscle. Patients were regarded as suffering from these diseases if they had been diagnosed prior to the index date.

As a part of our sensitivity analysis, we also investigated whether patients were diagnosed with a somatoform disorder, e.g. psychogenic movement disorders or psychogenic seizures (ICD-10 F44 and F45).

We also examined whether our results were confounded by other chronic disorders displayed in Table 3. We did not adjust for disorders, which was mediated by the neurological disease, e.g. organic psychosis, depression or anxiety [12, 13].

Statistical analysis

We used ordinary Chi-square tests and the *T* test when applicable. We compared age differences between cases and controls within certain neurological diseases, and employed an ANOVA model, which accounted for gender differences (Table 1).

The association between ten neurological diseases/disease groups and suicide attempt by self-poisoning was analyzed using conditional logistic regression [14]. This analysis yielded the age- and gender-adjusted odds ratio (OR) (Table 2). The OR approaches the relative risk, due to the rare disease assumption.

Furthermore, we investigated if there was a disease–gender interaction, by running the same analysis including an interaction term (Table 2) [15].

Finally, we used the conditional logistic regression model to explore if our results were confounded by somatic or psychiatric comorbidity (Table 3).

Ethics

This study was approved by the Danish Data Protection Agency (BBH-2013-039/02514). Anonymized, retrospective register studies do not require ethical approval or written informed consent according to the Danish Act on Processing of Personal Data.

Results

Patient characteristics

During the 7-year study period (1 August 2006–31 December 2013), we identified 8974 cases of suicide attempt by self-poisoning in adults aged 20 years or older. These cases were matched with 89,740 controls with similar demographic features. Table 1 displays the demographic characteristics of cases and controls.

Neurological diseases and risk of suicide attempt

In Table 1, we present the demographic characteristics of cases and controls with a neurological diagnosis. Out of 8974 patients who attempted suicide, we found 938 (11%) suffering from a neurological disease, distributed among 1030 different diagnoses. In the control group, only 3% ($n = 2890$) had a neurological disease. Thus, living with a chronic neurological disease was strongly associated with the risk of a suicide attempt. This effect was more pronounced in males [OR 4.2, 95% confidence interval (CI) (3.7–4.7)], than in females [OR 3.3, 95% CI (3.0–3.6)] (p value for disease–gender interaction = 0.0026).

Patients newly diagnosed (within 3 months) with a neurological disease had an even higher risk of attempting suicide [OR 7.9, 95% CI (5.6–11.4)], with no sign of gender difference (p value for disease–gender interaction = 0.35).

Specific disorders

In Table 2, the association between neurological diseases and suicide attempt by self-poisoning is presented. The strongest association with suicide attempt was seen for patients with Huntington's disease. A two- to fivefold increased risk was seen for stroke, ALS, Parkinson's disease,

Table 1 Patient characteristics

	Cases ($n=8974$)	Controls ($n=89.740$)	p
Demographics overall			
Male [n (%)]	3348 (37)	33,480 (37)	1.0
Female [n (%)]	5626 (63)	56,260 (63)	
Mean age in years (SD)	41.5 (15.6)	41.5 (15.6)	0.98
	Cases ($n=938$)	Controls ($n=2890$)	p
Demographics of the neurological patients			
Male [n (%)]	407 (43)	1122 (39)	0.013
Female [n (%)]	531 (57)	1768 (61)	
Mean age in years (SD)	47.1 (17.0)	50.5 (19.1)	<0.0001
Study diseases and disease groups (ICD-10)	Cases Mean age in years (SD)	Controls Mean age in years (SD)	p
Age of the neurological patients			
Stroke (I60–64)	57.1 (15.2)	61.9 (16.3)	<0.0001
Huntington's disease (G10)	52.0 (12.4)	46.8 (12.1)	0.44
Motor neuron disease (ALS) (G12.2)	57.4 (14.1)	55.9 (17.4)	0.84
Parkinson's disease (G20)	66.1 (11.7)	69.1 (13.4)	0.34
Alzheimer's disease and other degenerative diseases (G30–32)	58.7 (16.0)	70.2 (16.4)	0.0025
Multiple sclerosis (G35)	47.9 (13.3)	47.0 (12.6)	0.64
Epilepsy (G40)	39.8 (13.9)	40.3 (16.5)	0.54
Hereditary and idiopathic neuropathy (G60)	51.8 (17.0)	46.6 (17.7)	0.39
Myasthenia gravis (G70.0)	58.1 (18.5)	44.9 (15.7)	0.048
Primary disorders of the muscle (G71)	33.7 (6.8)	40.6 (13.1)	0.31

p p value, SD standard deviation, *ICD-10* international classification of diseases, 10th revision

Table 2 Association between neurological diseases and suicide attempt by self-poisoning

Study diseases and disease groups	Cases [n (%)]	Controls [n (%)]	Odds ratio (95% CI)	p	p_{int}	Odds ratio* (95% CI)
Stroke	342 (3.8)	1181 (1.3)	3.1 (2.8–3.6)	<0.0001	0.058	3.0 (2.6–3.4)
Huntington's disease	7 (0.08)	8 (0.01)	8.8 (3.2–24.1)	<0.0001	0.21	8.8 (3.2–24.1)
Motor neuron disease (ALS)	5 (0.06)	10 (0.01)	5.0 (1.7–14.6)	0.0033	0.68	5.6 (1.9–16.6)
Parkinson's disease	23 (0.26)	82 (0.09)	2.9 (1.8–4.6)	<0.0001	0.39	2.9 (1.8–4.6)
Alzheimer's disease and other degenerative diseases	29 (0.32)	61 (0.07)	4.8 (3.1–7.5)	<0.0001	0.43	4.1 (2.6–6.6)
Multiple sclerosis	48 (0.53)	314 (0.35)	1.5 (1.1–2.1)	0.0060	0.18	1.5 (1.1–2.1)
Epilepsy	553 (6.2)	1292 (1.4)	4.5 (4.1–5.0)	<0.0001	0.33	4.0 (3.6–4.4)
Hereditary and idiopathic neuropathy	10 (0.11)	46 (0.05)	2.2 (1.1–4.3)	0.026	0.66	2.2 (1.1–4.3)
Myasthenia gravis	9 (0.10)	21 (0.02)	4.3 (2.0–9.4)	0.0003	0.028	4.5 (2.0–9.9)
Primary disorders of the muscle	4 (0.04)	36 (0.04)	1.1 (0.4–3.1)	0.84	0.67	0.6 (0.1–2.3)

Odds ratio: the age- and gender-adjusted odds ratio for the association between neurological diseases and suicide attempt by self-poisoning

P: the p value for the corresponding odds ratio

P_{int}: the p value for gender and disease interaction on risk of suicide attempt. Only statistical significant for patients with myasthenia gravis, meaning that males with this disease had a significantly higher risk of attempting suicide

Odds ratio*: patients diagnosed with somatoform diagnoses (ICD-10 F44–45) classified as healthy

CI confidence interval, *p p* value, *ALS* amyotrophic lateral sclerosis

Table 3 Association between neurological diseases and suicide attempt by self-poisoning adjusted for other chronic comorbidities

	Study diseases and disease groups	Stroke	Huntington's disease	Motor neuron disease (ALS)	Parkinson's disease	Alzheimer's disease and other degenerative diseases	Multiple sclerosis	Epilepsy	Hereditary and idiopathic neuropathy	Myasthenia gravis	Primary disorders of the muscle
Comorbidities (ICD-10)	Odds ratio (95% CI)	3.1 (2.8–3.6)	8.8 (3.2–24.1)	5.0 (1.7–14.6)	2.9 (1.8–4.6)	4.8 (3.1–7.5)	1.5 (1.1–2.1)	4.5 (4.1–5.0)	2.2 (1.1–4.3)	4.3 (2.0–9.4)	1.1 (0.4–3.1)
Schizophrenia (F20)	19.4 (17.4–21.6)	3.1 (2.7–3.6)	9.3 (3.4–25.9)	5.3 (1.8–15.6)	2.6 (1.6–4.2)	4.8 (3.0–7.5)	1.6 (1.1–2.1)	3.9 (3.5–4.4)	2.1 (1.0–4.3)	3.7 (1.6–8.5)	1.3 (0.5–3.6)
Bipolar affective disorder (F31)	22.8 (19.6–26.4)	3.2 (2.8–3.6)	7.6 (2.7–21.8)	6.0 (2.0–18.0)	2.3 (1.4–3.9)	4.2 (2.6–6.7)	1.5 (1.1–2.1)	4.4 (4.0–4.9)	2.2 (1.1–4.4)	3.8 (1.6–8.8)	1.1 (0.4–3.2)
Psychoactive substance use (F10–F19)	34.8 (32.1–37.7)	2.3 (2.0–2.7)	6.5 (1.8–23.3)	5.1 (1.6–16.6)	2.7 (1.6–4.6)	2.7 (1.5–4.6)	1.5 (1.1–2.1)	3.3 (2.9–3.7)	2.1 (0.9–4.5)	4.8 (2.1–11.3)	0.7 (0.2–2.6)
Heart failure (I50)	2.1 (1.7–2.6)	3.1 (2.7–3.5)	8.8 (3.2–24.3)	4.9 (1.7–14.4)	2.8 (1.8–4.5)	4.8 (3.1–7.5)	1.5 (1.1–2.1)	4.5 (4.1–5.0)	2.2 (1.1–4.3)	4.0 (1.8–8.7)	1.1 (0.4–3.0)
COPD and asthma (J40–J47)	2.7 (2.5–2.9)	2.9 (2.6–3.3)	8.7 (3.1–24.2)	4.5 (1.5–13.5)	2.9 (1.8–4.6)	4.5 (2.9–7.1)	1.5 (1.1–2.0)	4.3 (3.9–4.8)	2.0 (1.0–4.0)	4.1 (1.9–9.1)	1.1 (0.4–3.1)

All data presented are odds ratios followed by 95% confidence intervals in brackets. In the first row, the odds ratios represent the age- and gender-adjusted odds ratios for the association between neurological diseases and suicide attempt by self-poisoning, as are also presented in Table 2. In the subsequently rows, the odds ratios represent the age- and gender-adjusted odds ratios for the association between neurological diseases and suicide attempt by self-poisoning adjusted for other chronic comorbidities. The odds ratios in the first column represent the age- and gender-adjusted odds ratios for the association between five different somatic and psychiatric comorbidities and suicide attempt by self-poisoning

ALS amyotrophic lateral sclerosis, *ICD-10* international classification of diseases 10th revision, *CI* confidence interval, *COPD* chronic obstructive pulmonary disorder

Alzheimer's disease, epilepsy and myasthenia gravis. For MS and hereditary and idiopathic neuropathy, the associations were weaker, and patients with primary disorders of the muscle had a risk of suicidal behavior comparable with that in the background population.

Cases with neurological diseases were in general younger than controls with the same diseases (Table 1). Of particular interest, we observed 29 cases with Alzheimer's disease with a mean age of 58.7 years (SD 16.0). Given the age and gender distribution we would only have expected six cases with a mean age of 70.2 years (SD 16.4). This may indicate that these patients attempt suicide early in their course of illness.

The *p* values for gender and disease interaction on risk of suicide attempt in the different neurological conditions are presented in Table 2. With regard to patients with myasthenia gravis, the risk of attempting suicide was higher for men [OR 16.7, 95% CI (4.0–70.7)], than for women [OR 2.2, 95% CI (0.8–6.7)] ($p = 0.028$). A borderline significant effect of disease–gender interaction was seen for patients with stroke, in which men had an OR of attempting suicide of 3.6 [95% CI (3.0–4.3)] and women an OR of 2.8 [95% CI (2.4–3.3)].

In our sensitivity analysis, we investigated the potential impact of misdiagnoses. Somatoform disorders were relatively common in patients diagnosed with epilepsy; thus 14% of the patients with epilepsy in the case group were known to have somatoform diagnoses, as opposed to 3% of the patients with epilepsy in the control group. However, if these patients were reclassified as non-epileptics, it resulted only in marginal effects on the odds ratio. In general, accounting for somatoform disorders did not influence our estimates (Table 2 last column).

We analyzed whether chronic psychiatric and somatic comorbidities were confounders for the association between neurological diseases and suicidal behavior. For epilepsy and Alzheimer's disease, the association could partly be explained by the abuse of alcohol and other psychoactive substances. For further results please see Table 3.

Discussion

This is the first study to investigate the risk of deliberate self-poisoning in patients with chronic neurological diseases. Joshi et al. recently found that 73% of patients attempting suicide had low quality of life, and that patients with low quality of life had a four times increased risk of attempting suicide with reference to patients with high quality of life [16]. Therefore, the results presented in this paper may serve as an indirect comparison of disease severity of psychological health in different neurological diseases. Nine of the ten chronic neurological diseases were associated with a significantly increased risk of suicide attempt by self-poisoning.

In our study, 63% of the cases of suicide attempts were female. This is in concordance with previous research [9]. Interestingly, we found that males with neurological diseases had a higher risk of attempting suicide than their female counterparts, and this may be of some importance for clinicians treating these patients.

Previous research has revealed that certain chronic neurological diseases are associated with an increased risk of suicide [2–8], and our findings are in concordance with this. Bronnum-Hansen et al. found that the risk of suicide in MS was almost twice as high as in the Danish background population, and three times elevated the first year after diagnosis [3]. Stenager et al. investigated suicidal behavior in MS on the Danish island of Funen, and they were not able to find an increased risk of suicide attempt in these patients [17]. In contrast, we found that patients with MS have a 1.5 times increased risk of attempting suicide, compared to the general population.

Suicidal behavior is common in Huntington's disease, and in Farrer's study of 831 patients with this disease, 28% had attempted suicide at least once [6]. The tendency to suicidality in other rare neurological conditions, such as hereditary neuropathy and myasthenia gravis, is unknown, and our results contribute to a better understanding of the severity of these diseases.

Parkinson's disease is a degenerative condition with debilitating symptoms. Lee et al. found that the risk of suicide in patients with Parkinson's disease was approximately two times higher than in the general population [5], which is consistent with the result in our study.

Interestingly, we found a nearly fivefold increased risk of suicide attempts among patients with Alzheimer's disease and other degenerative diseases. Draper did a systematic review of suicidal behavior and assisted suicide in patients with dementia [18], and found no overall risk. However, an intensified focus on dementia has led to earlier diagnosis, which makes the patients more insightful at the time of diagnosis, and facing a grave prognosis probably increase the risk of a suicide attempt [18]. Indeed, this study revealed that cases of suicide attempt with Alzheimer's disease were younger than expected (Table 1).

Suicide in epilepsy has received great attention. Bell et al. conducted a meta-analysis on the topic, and found the risk of suicide 3.3 higher than in the background population [8]. Altura et al. reported that the 2-week prevalence of suicidal ideation in patients with epilepsy was 12.7% [19]. Only few papers have assessed the frequency of suicide attempts in patients with epilepsy, but the results of the available studies are consistent with the data presented in this paper [7].

Strengths and limitations

The large number of patients included and the national collection of data in the study make the results reliable. Danish patients can be identified by their CPR number, enabling bridging of data between the DNPR, the PCRR and the DPIC database. Data of the toxicological enquiries to the DPIC are systematically and prospectively collected. The DNPR and PCRR are cornerstones in Danish epidemiological research, as they provide information on all hospital contacts. However, the validity of the diagnoses in the registries has rarely been examined. Mason et al. recently analyzed the quality of the DNPR with regard to MS, and found that the registry had a completeness/sensitivity of 87% and that the diagnosis was valid in 96% of the cases [20].

We deliberately excluded migraine and other headache disorders, as most of these patients are treated in general practice, and rarely require hospital contact. Therefore, the sensitivity of the DNPR in these conditions is low, and the estimates would be biased by severity.

Psychogenic or functional disorders are common in neurology, and the unskilled neurologist might have a tendency to overdiagnose these patients [21]. Especially our results on rare diseases, such as myasthenia gravis and Huntington's disease, could be biased by such effects. Therefore, we also tested whether the patients were diagnosed with somatoform disorders, and this did not change the conclusions of our study.

The increased risk of suicide attempt in neurological diseases could not be explained by chronic somatic or psychiatric comorbidities (Table 3). However, our study does not provide information of more personal issues, such as reaction to diagnosis, treatment failure, or the effects of behavioral and cognitive abnormalities, which might be considered as primary causes of suicide attempt. This clarification might be useful for clinicians to intervene more efficiently with psychological or additional medical support.

Not all cases of deliberate self-poisoning or suicide attempts are reported to the DPIC. Therefore, the present study only provides relative risks of deliberate self-poisoning in patients with chronic neurological diseases, whereas the relative risk of suicide attempt by other methods than self-poisoning or the absolute numbers remains unknown.

We believe our results are associated with a high internal validity. However, our study was only performed in Denmark, and as suicidal behavior is influenced by cultural and religious factors [22, 23] this limits the external validity.

Conclusion

Living with a chronic neurological disease affects patients' psychological health and impairs health-related quality of life. Our results suggest the importance of assessing the risk of suicide in patients with chronic neurological diseases.

Future research is needed to develop a guideline for the active assessment and intervention of suicidal behavior in neurological patients.

Compliance with ethical standards

Conflicts of interest The authors have nothing to disclose.

Ethical standard This study was approved by the Danish Data Protection Agency (BBH-2013-039 / 02514).

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