

SYMPTOM FREQUENCY CHARACTERISTICS OF THE HAMILTON DEPRESSION RATING SCALE OF MAJOR DEPRESSIVE DISORDER IN EPILEPSY

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SUMMARY

Background: Depressive disorders are common among patients with epilepsy (PWE). The aim of this study was to explore symptom frequencies of 17-item Hamilton Depression Rating Scale (HDRS-17) and recognize the clinical characteristics of Major Depressive Disorder in PWE.

Subjects and methods: A sample of 40 adults outpatients with epilepsy and depression was diagnosed using SCID-I for DSM-IV-TR and HDRS-17. The total HDRS-17 score was analysed followed by the exploratory analysis based on the hierarchical model.

Results: The frequencies of HDRS-17 items varied widely in this study. Insomnia related items and general somatic symptoms items as well as insomnia and somatic factors exhibited constant and higher frequency. Feeling guilty, suicide, psychomotor retardation and depressed mood showed relatively lower frequencies. Other symptoms had variable frequencies across the study population.

Conclusions: Depressive disorders are common among PWE. In the study group insomnia and somatic symptoms displayed highest values which could represent atypical clinical features of mood disorders in PWE. There is a need for more studies with a use of standardized approach to the problem.

Key words: major depressive disorder - depressive disorders, - epilepsy – HDRS - factor analysis

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INTRODUCTION

Depression is the most frequently reported psychiatric comorbidity in patients with epilepsy (PWE) with point prevalence reaching up to 62% (Barry 2007, Ettinger 2004, Hermann 2000).

Several studies were performed based solely on screening instruments (Krishnamoorthy 2006) with only a limited number of research using standardized structured psychiatric interview to produce diagnosis. Moreover, the clinical tools being used in general population may not be valid in PWE. Also, various factors associated with epilepsy including anti-epileptic drugs (AEDs) side effects as well as atypical symptomatology could affect the accuracy and clinical presentation of psychiatric diagnosis in PWE (Kanner 2001).

Most common clinical instruments used in PWE are Neurological Disorder Depression Inventory for Epilepsy (NDDIE, Gilliam 2006), Beck Depression Inventory (BDI) and Hospital Anxiety and Depression Scale (HADS) which are self-report screening tools. Hamilton Depression Rating Scale (HDRS) is a rating scale filled out by a qualified clinician and it represents the gold standard for the assessment of severity of depression in a general population (Hamilton 1960). It explores some of the core symptoms of depression such as low mood, insomnia, agitation, anxiety, and weight loss. The aim of the present study was an attempt to examine clinical characteristics of MDD and other depressive disorders based on symptoms frequencies in HDRS-17.

SUBJECTS AND METHODS

Study sample

A group of 40 adult outpatients with epilepsy and co-morbid depressive disorder was explored in the study. All individuals underwent a complete neurological examination on selection. Enrolment criteria were as follows: (1) diagnosis of epilepsy according to the International League Against Epilepsy criteria (ILAE 1989) (2) age of more than 18 years (3) willing to provide a written informed consent to undergo the experimental procedures, (4) absence of severe medical diseases (5) absence of borderline, antisocial personality disorder, drug/alcohol abuse/dependence.

The study was performed in agreement with the Declaration of Helsinki following the approval of the Ethic Research Committee of the Institution. For each study participant, written consent was obtained.

Evaluation

The same psychiatrist assessed all subjects. Psychiatric diagnosis was confirmed using the Structured Clinical Interview (SCID-I) (First et al. 2000) for DSM-IV-TR (4th ed., text rev, American Psychiatric Association (APA) 2000). SCID-I is an internationally validated, structured interview that has been used extensively as a diagnostic tool for DSM-IV-TR psychiatric disorders (First 2000). The severity of depression was evaluated using the 17-item version of Hamilton Rating Scale for Depression (HDRS-17) (Hamilton 1960). Both instru-

ments, the SCID-I and the HDRS-17, were administered in a standardized way and in the same sequence in all patients. The total HDRS-17 score was analysed followed by the exploratory analysis based on the hierarchical model including depression, insomnia, anxiety and somatic symptoms features (Cole 2004, Shafer 2006).

Statistics

Statistical procedures were performed using Statistica 10.0.1011. Frequencies and descriptive statistics were analyzed for each variable. Comparisons between patients with current MDD and patients without MDD were made using Mann-Whitney's U-test for non-normally distributed data. To explore the influence of factors on the occurrence of depression, the stepwise logistic regression model was used. A value of $p < 0.05$ was considered to be statistically significant.

RESULTS

A group of 40 PWE with diagnosis of any depressive disorder according to DSM-IV-TR was selected for symptoms and factors analysis. A diagnosis of Major Depression (current episode) was established in 21 (22%) patients. The severity of depression was measured with HDRS-17 in the group of patients with MDD (n=21) and other depressive disorders group (n=19). The mean HDRS-17 total in depressed patients are shown in Table 1. In the subgroup with current MDD the severity of depressive symptoms with HAMD-17 was mild in 5 patients, moderate in 6 patients, severe in 5 patients and the most severe in 5 patients. The subgroup with other depressive disorders (n=19) was characterized in majority by mild severity of symptoms (n=11). Only in one case moderate severity of depression was observed with the remaining 7 severity did not exceed 6 points threshold for depression in HDRS-17 (Figure 1).

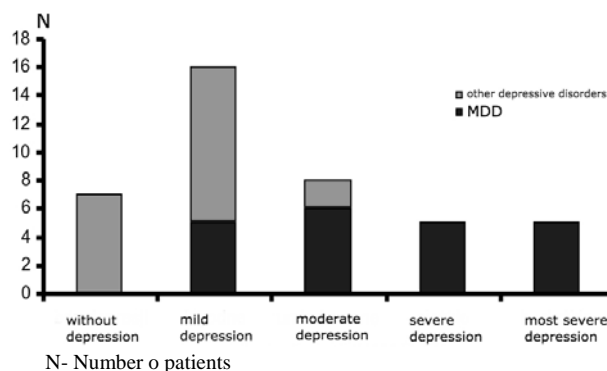


Figure 1. Mean HDRS-17 scores of patients with depressive disorders (n=40)

The relative frequencies of each symptom/item of the HDRS-17 in the subgroup of patients with MDD was also examined. The relative severity of every symptom/item, was calculated for each patient using formula:

$$\frac{13 \times n}{\sum_{i=1}^{17} n_i} \text{ for items, with maximum value reaching 4 points}$$

or

$$\frac{26 \times n}{\sum_{i=1}^{17} n_i} \text{ for items, with maximum value 2 points}$$

$\times n$ - severity of specific item,

$\sum_{i=1}^{17} n_i$ - total score for severity of depressive symptoms/items in HDRS-17

In the study subgroup of patients with MDD highest scores were obtained for all three of insomnia related items (H4, H5 and H6). Higher scores were also found for somatic symptoms general (H13) and genital symptoms (H14). In the study group low scores were obtained for the following items: feelings of guilt (H2), suicide (H3), psychomotor retardation (H8), agitation (H9), hypochondriasis (H15), reduced insight (H17) (Figure 2).

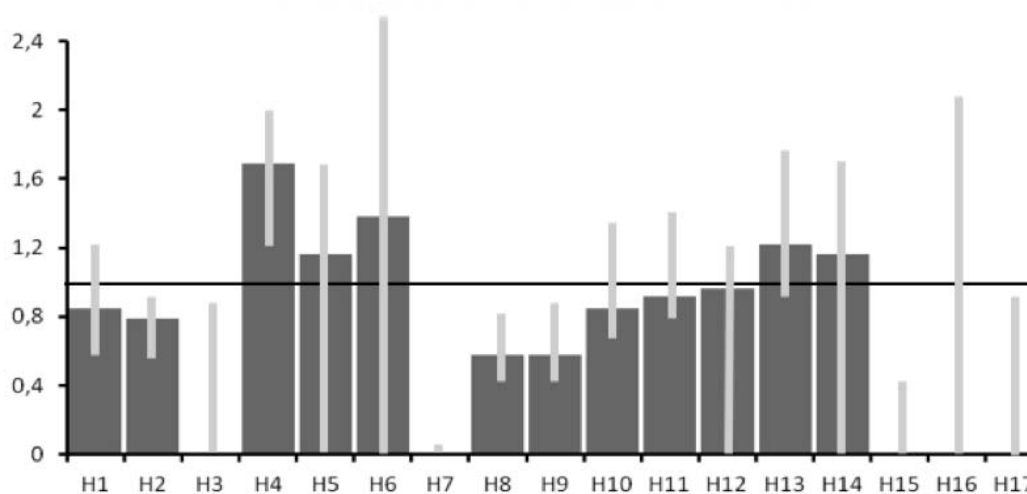


Figure 2. The relative severity of symptoms/items of HAM-D-17 in the subgroup of patients with MDD according to DSM-IV-TR (median values and interquartile range shown)

Table 1. Relative frequencies of four factors of HRDS

Study group	N	Depression Median (IQR)	Anxiety Median (IQR)	Insomnia Median (IQR)	Somatic symptoms Median (IQR)
Depressive Disorders DSM-IV-TR	40	0.70 (0.59 to 0.86)	0.73 (0.52 to 0.95)	1.19 (0.33 to 1.83)	1.10 (0.85 to 1.50)
MDD	21	0.69 (0.58 to 0.79)	0.76 (0.54 to 0.90)	1.22 (1.04 to 1.91)	1.15 (0.92 to 1.27)
Other Depressive Disorders	19	0.73 (0.60 to 1.02)	0.70 (0.41 to 1.05)	0.67 (0.00 to 1.83)	1.10 (0.50 to 1.57)
	p*	0.27	0.77	0.14	0.94

* MDD vs. other depressive disorders (Mann-Whitney U-test)

In order to further describe the structure of depressive disorders in PWE symptoms clusters from HDRS were analysed. In the analysis of the HDRS four factors were identified: depression (Items 1, 2, 3, 7, 8), anxiety (Items 9, 10, 11, 15, 17), insomnia (Items 4, 5, 6), somatic symptoms (Items 12, 13, 14, 16) (Cole et al. 2004, Shafer 2006).

The relative frequencies for each factor in the studied groups were examined: MDD and other depressive disorders, using an analogous method as for the evaluation of each of item of the HDRS-17 (see previous section). For each patient the ratios were calculated: frequency of individual factors the to its maximum possible score and the total score to its maximum possible value. The relative score of the individual/specific factors for each patient was measured by the ratio of first one to the other. Results are shown in Tables 1.

Higher score in the group of patients with MDD was found for two factors: insomnia, and somatic symptoms. Insomnia was found to be less severe in other depressive disorders. Differences between groups were not statistically significant.

DISCUSSION

Most studies suggest that depression is the most common psychiatric comorbidity in epilepsy. Depressive disorders in epilepsy usually meet the diagnostic criteria for DSM-IV-TR. Still, some studies suggest that the clinical presentation often deviates from typical presentation in PWE. There is discussion whether and to what extent depression in epilepsy should be treated as different diagnostic category from that observed in the general population.

In this study we attempted to determine the clinical characteristics of depressive disorders in PWE by assessing the severity and frequency of symptoms/items and HRDS symptom clusters analysis. Specific depression factors have implications for both assessment of depression and its treatment (Shafer 2006). The HDRS contains a relatively large number of somatic symptoms and relatively few cognitive or affective symptoms. Hamilton (1960) identified three factors in the HDRS. This study applied the four-component solution: depression, anxiety, insomnia, somatic symptoms which were proposed in numerous studies on the subject (Shafer 2006).

Determining the relative severity of individual HRDS factors in the study group we found significant higher score for insomnia, and somatic symptoms. Insomnia proved to be relatively less pronounced in other depressive disorders. When analysing the frequency of individual depressive symptoms/items included in the HRDS-17 in the subgroup of patients with MDD we found increased scores of all three insomnia related items, especially falling asleep and increased scores of general somatic symptoms. Surprisingly we found relatively low scores for some of "axial" symptoms of depression like feeling guilty, suicide, psychomotor retardation and depressed mood.

There is only limited data on symptomatology of depression assessed with standardized measures in PWE. Mendez et al. (1986) in a seminal study on the subject used DSM-III criteria to analyse and compare depressive symptoms in PWE and in control group. He found that depression in epilepsy was characterised by "the following endogenous depressive traits like neurovegetative signs, psychomotor retardation and prior suicide attempt" (Mendez 1986). In contrast symptoms such as somatization, feelings of guilt, hopelessness/ helplessness were significantly less prominent. It is interesting that in our study some of the core symptoms of depression like feeling guilty, suicide, psychomotor retardation and depressed mood were not prominent which could suggest that standard clinical instruments for depression DSM based do not adequately measure depression in PWE. One of the explanations could be a small study group size and specific population from outpatients clinic that is a referential epilepsy Centre in the Pomeranian area and therefore might not represent the general population of PWE. On the other hand we observed that insomnia and somatic factors displayed highest values which could represent atypical clinical features of mood disorders in PWE like Interictal dysphoric disorder (IDD) Blumer 2004, Amiri 2015) that is characterized by dysphoria, comorbid anxiety, somatic symptoms and sleep problems. Our observations are in the line with recent study by Mula et al. (2014) who validated usage of HDRS in PWE. HDRS showed a high sensitivity and specificity but lower positive predictive in PWE. Also in their study the factor "anxiety/somatic" was displaying the highest AUC value after "psychomotor retardation" which also could suggest the existence of a atypical mood syndrome different from those captured by major categorical systems (Mula 2014).

On the other hand it is important, while reviewing studies on mood disorders in epilepsy, to keep in that in some cases clinical presentation described as "atypical" could be the result from psychiatric expression of seizure activity itself or could be related to the peri-ictal period. Additionally, the psychotropic effects of certain anti-epileptic drugs especially in high doses or poly-pharmacotherapy may mimic some symptoms (e.g. psychomotor retardation or concentration/memory deficits) of depression. Also high comorbidity of anxiety disorders and depression in PWE (Balibey 2015) could adversely "blur" clinical presentation of depression in PWE leading to overrepresentation of atypical depressive syndromes in PWE.

CONCLUSIONS

Depressive disorders represent an important complication of epilepsy affecting quality of life and mortality. Although standard psychiatric tools can be used for diagnosing depression in PWE it often presents some unique features that might require specific diagnostic instruments to be developed. In the study group insomnia and somatic symptoms displayed highest values which could represent atypical clinical features of mood disorders in PWE. There is a need for more studies with a use of standardized approach to the problem.

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Conflict of interest: None to declare.

References

1. American Psychiatric Association: *Diagnostic and statistical manual of mental disorders (4th ed., text rev.)*. Washington, DC, 2000.
2. Amiri M, Hansen CP: *The interictal dysphoric disorder in patients with epilepsy: A doubtful disorder lacking diag tools*. *Seizure* 2015; 24:70-76.
3. Balibey H, Yaşar H, Tekeli H, Bayar N: *Frequency of anxiety and depression in epileptic patients*. *Bulletin of Clinical Psychopharmacology* 2015; 25:136-41.
4. Barry JJ, Lembke A: *Affective Disorders in Epilepsy*. In: Ettinger AB, Kanner AM (eds). *Psychiatric Issues in Epilepsy. A Practical Guide to Diagnosis and Treatment*. Philadelphia, Lippincott Williams & Wilkins, 2-nd edition, 2007, 203-47.
5. Blumer D, Montouris G, Davies K: *The interictal dysphoric disorder: recognition, pathogenesis, and treatment of the major psychiatric disorder of epilepsy*. *Epilepsy Behav* 2004; 5:826-40.
6. Cole JC, Motivala SJ, Dang J, Lucko A, Lang N, Levin MJ et al.: *Structural Validation of the Hamilton Depression Rating Scale*. *J Psychopathol Behav* 2004; 26:241-54.
7. Commission on Classification and Terminology of the International League Against Epilepsy. *Proposal for revised classification of epilepsies and epileptic syndromes*. *Epilepsia* 1989; 30:389-99.
8. Ettinger A, Reed M, Cramer J: *Epilepsy Impact Project Group. Depression and comorbidity in community-based patients with epilepsy or asthma*. *Neurology* 2004; 63:1008-14.
9. First MB, Spitzer RL, Gibbon M, Williams JBW: *Structured Clinical Interview for DSM-IV-TR Axis I Disorders, Research Version, Patient Edition. (SCID-I/P)* New York: Biometrics Research, New York State Psychiatric Institute, 2000.
10. Gilliam FG, Barry JJ, Hermann BP, Meador KJ, Vahle V, Kanner AM: *Rapid detection of major depression in epilepsy: a multicentre study*. *Lancet Neurol* 2006; 5:399-405.
11. Hamilton M: *A rating scale for depression*. *J Neurol Neurosurg Psychiatry* 1960; 23:56-62.
12. Hermann BP, Seidenberg M, Bell B: *Psychiatric comorbidity in chronic epilepsy: identification, consequences, and treatment of major depression*. *Epilepsia* 2000; 41:31-41.
13. Kanner AM, Barry JJ: *Is the Psychopathology of Epilepsy Different from That of Nonepileptic Patients?* *Epilepsy Behav* 2001; 2:170-86.
14. Krishnamoorthy ES: *The evaluation of behavioral disturbances in epilepsy*. *Epilepsia* 2006; 47(Suppl 2):3-8.
15. Mendez MF, Cummings JL, Benson DF: *Depression in epilepsy. Significance and phenomenology*. *Arch Neurol* 1986; 43:766-70.
16. Mula M, Ludice A, La Neve A, Mazza M, Mazza S, Cantello R et al.: *Validation of the Hamilton Rating Scale for Depression in adults with epilepsy*. *Epilepsy Behav* 2014; 41:122-5.
17. Shafer AB: *Meta-analysis of the factor structures of four depression questionnaires: Beck, CES-D, Hamilton, and Zung*. *J Clin Psychol* 2006; 62:123-46.

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