

# Frequency of depression among patients with neurocysticercosis

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## ABSTRACT

Neurocysticercosis (NCC) is a common central nervous system infection caused by *Taenia solium* metacestodes. **Objective:** To investigate the occurrence of depression in patients with calcified NCC form. The study group consisted of 114 patients subdivided in four groups: NCC with epilepsy, NCC without epilepsy, epilepsy without NCC and chronic headache. **Method:** Depression was evaluated and quantified by the Hamilton Rating Scale for Depression (HRSD-21). **Results:** Percentage of patients with depression was as follows: group 1 (83%); group 2 (88%); group 3 (92%); group 4 (100%). The majority of patients had moderate depression. **Conclusion:** Incidence of depression in all groups was higher than in the general population. It is possible that, in a general way, patients with chronic diseases would have depression with similar intensity. NCC is associated with the presence of depression.

**Key words:** depression, neurocysticercosis, psychiatric disturbs, infectious diseases, neuroinfection.

## Depressão em pacientes portadores de neurocisticercose

## RESUMO

Neurocisticercose (NCC) é uma infecção do sistema nervoso central comum causada por metacestodes da *Taenia solium*. **Objetivo:** investigar a ocorrência de depressão nos pacientes com NCC forma calcificada. O grupo de estudo é formado por 114 pacientes subdivididos em quatro grupos: NCC com epilepsia, NCC sem epilepsia, epilepsia sem NCC e cefaléia crônica. **Método:** A presença de depressão foi determinada e quantificada pela Escala de Depressão de Hamilton (HRSD-21). **Resultados:** A porcentagem de pacientes com depressão foi: grupo 1 (83%); grupo 2 (88%); grupo 3 (92%); grupo 4 (100%). A maioria dos pacientes apresentou depressão moderada. **Conclusão:** A incidência da depressão em todos os grupos foi mais elevada do que na população geral, contudo não houve diferença entre os grupos estudados. É possível que, de uma maneira geral, os pacientes portadores de doença crônica apresentarem a depressão em intensidade similar. NCC está associada com a presença de depressão.

**Palavras-chave:** depressão, distúrbios psiquiátricos, doenças infecciosas, neurocisticercose, neuroinfecção.

Neurocysticercosis (NCC) is the most common parasitic infection of the human central nervous system (CNS)<sup>1</sup>. It is caused by the larval form of the pork tapeworm *Taenia solium*. It occurs endemically in rural areas of developing countries in Asia, Africa, Latin America and Central Europe where prevalence rates vary from 0.1 to 4.0%. It may also be found in urban ar-

reas of developed countries among specific ethnic subgroups<sup>1,2</sup>. In Brazil, the highest prevalence is in the southeast and south areas. It is more frequent in adults, between the third and fourth decades of life, and there is no predisposition for gender or race<sup>3</sup>.

The clinical picture usually includes seizures and headache. Psychiatric dis-

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turbs are typically present in the course of the disease and were extensively studied by psychiatrists at the beginning of the 20<sup>th</sup> century<sup>4-6</sup>. Psychiatric syndromes that mimic schizophrenia, major affective disorders and dementia have been reported<sup>7</sup>. Few recent studies have tried to describe the psychopathologies associated with NCC using appropriate instruments for psychiatric assessment<sup>8</sup>.

The objective of this study was to evaluate the presence of depression among NCC patients with the calcified chronic form, as well as to correlate the results with clinical aspects and to compare with other chronic diseases such as epilepsy and chronic headache. There is a huge paucity of information in the medical literature on this topic.

## METHOD

This study was approved by the Hospital de Clínicas, Universidade Federal do Paraná (HC-UFPR) IRB. Participants were selected in the neuroinfection, epilepsy and headache outclinics and neurology infirmaries of HC-UFPR. A total of 114 consecutive unselected patients, 62 women and 52 men, were distributed in the following groups:

### Study group

65 patients with NCC, diagnosed according to the criteria of Del Brutto et al.<sup>9</sup>, with positive cerebrospinal fluid (CSF) immunological assays (IFI and ELISA). NCC was classified in inactive forms according with Sotelo et al.<sup>10</sup>. All 65 patients had calcified intraparenchymatous lesions on CT, and were further subdivided in two groups:

**Group 1** – NCC with epilepsy (n=48). All patients have partial complex seizures with secondary generalization, and were under anticonvulsant drug therapy; CSF:

WBCs (mean±SD) 11±32 cells/mm<sup>3</sup>, median 1.5 cells/mm<sup>3</sup>; glucose 62±21 mg/dL, median 59 mg/dL; total protein 52±56 mg/dL, median 35mg/dL.

**Group 2** – NCC without epilepsy (n=17); CSF: WBCs (mean±SD) 19±48 cells/mm<sup>3</sup>, median 2.1 cells/mm<sup>3</sup>; glucose 59±6 mg/dL, median 56 mg/dL; total protein 129±274 mg/dL, median 35 mg/dL.

### Control group

49 patients with CT without cysts or calcifications suggestive of NCC were further subdivided in the following two groups:

**Group 3** – Patients with history of epilepsy (temporal lobe epilepsy and cryptogenic epilepsy), under anti-convulsive drug at the time of the study, but not associated with NCC (n=25). Patients were not in the post-seizure period.

**Group 4** – Patients with history of chronic headache (n=24).

### Evaluation of depression

Depression was evaluated by the Portuguese version of the 21 item Hamilton Rating Scale for Depression (HRSD-21)<sup>11</sup>. The scale was applied by the same researcher in a blind way. Scores above 25 points identify severe depression; between 18 and 24 moderate depression; between 7 and 17 mild depression; and 0 to 6 indicate no depression<sup>11</sup>.

Epidemiological characteristics of the participants in each group are shown in Table 1. Comparing the groups with NCC (groups 1+2) with the groups without NCC (groups 3+4) there is no statistic difference between age,

**Table 1.** Epidemiological characteristics of participants in each group.

Group	n	Age (years)	Male		At least eight years of education		Live in rural area	
		(mean±SD)	n	(%)	n	(%)	n	(%)
Group 1	48	38±12	24	50	38	79	10	21
Group 2	17	40±12	7	41	13	76	13	76
Group 3	25	33±13	13	52	20	80	5	20
Group 4	24	46±13	8	33	22	92	2	8

**Table 2.** Gender distribution of depression scores by the HRSD-21.

Score	Male		Female		Total	p
	N	%	N	%	N	
> 25	8	25	24	75	32	0.007*
18-24	12	35	22	65	34	0.007*
7-17	22	61	14	39	36	0.287
< 7	10	83	2	17	12	–

gender and years of education ( $p=0.769$ ;  $0.594$  and  $0.368$  respectively). According with the origin of the patient, patients with NCC have higher proportion of participants that lived in rural area,  $p=0.013$  (Table 1).

### Statistical method

Continuous variables were compared using the Kruskal-Wallis and Mann Whitney non-parametric tests. Chi-square and Fisher's exact test was used for qualitative variables. Results are shown as mean plus standard deviation or frequencies and percentage, and significance level ( $p$ ). A  $p$  value  $\leq 0.05$  was considered significant.

### RESULTS

Patients with NCC (groups 1 and 2) showed a frequency of depression of 85% (55/65), and the frequency of depression among the patients without NCC (groups 3 and 4) was 96% (47/49). There was no difference between the percentage of depression (Fisher's exact test  $p=0.0665$ ; MW  $p=0.1394$ ). There was no difference between the scores of depression in the groups with NCC and without NCC.

Depression was more frequent in women 97% (60/62) than in men 81% (42/52),  $p=0.01$ . Scores indicating severe or moderate depression were more frequent in women, while men tend to have mild depression (Table 2).

Frequencies of depression observed in each groups were: group with NCC and epilepsy 83% (40 patients); group with NCC without epilepsy 88% (15 patients); group with epilepsy not associated with NCC 92% (23 patients); group with chronic headache 100% (24 patients). Scores of depression in the different groups are shown in Fig 1.

Scores (mean $\pm$ SD) of depression by the HRSD-21 in the different groups studied were; group 1,  $19\pm 11\%$ ; group 2,  $17\pm 9\%$ ; group 3,  $19\pm 8\%$ ; group 4,  $21\pm 8\%$ ;  $p=0.268$  (Fig 1).

In group 1, 31% had scores between 18 and 24 (moderate depression); and in group 2, 41.2% had scores between 7 and 17 (mild depression) (Fig 2).

### DISCUSSION

Studies evaluating depression in NCC patients are scarce. In this study, we observed a frequency of depression in groups with NCC of 83% and 88%. There was no statistical difference in the frequency of depression between NCC patients and patients of other chronic neurological diseases prevalent in the general population, such as epilepsy and headache.

Very few publications have considered the psychiatric manifestations of NCC, most of them consisting of case reports of neurological studies with detailed clinical and pathological descriptions. Some studies on NCC published in the beginning of 20<sup>th</sup> century were performed with inpatients from psychiatric hospitals<sup>4-6</sup>.

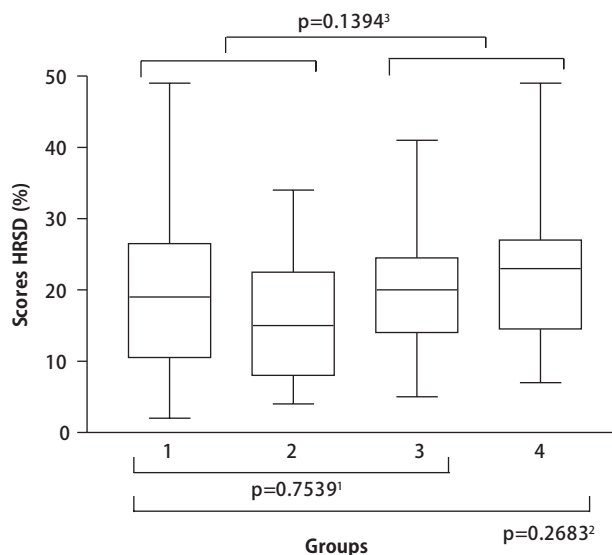


Fig 1. Scores of depression by the HRSD-21 in the different groups. (1) Group 1 compared with group 3; (2) All four groups compared; (3) Groups 1 and 2 compared with groups 3 and 4.

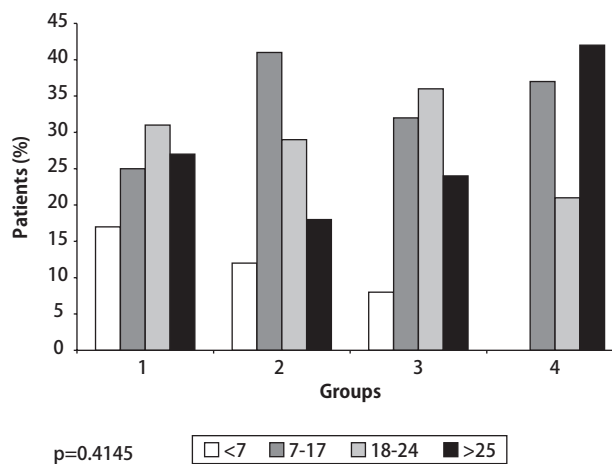


Fig 2. Distribution of scores of depression by the HRSD-21 in the different groups.

The incidence of depression in all groups studied was higher than in the general population. In Brazil, the annual prevalence of depression is not well known, but it is considered to be between 3% and 11% in the general population<sup>12,13</sup>, and about 10% among patients of primary health care<sup>14</sup>. Among inpatients with any physical illness depression prevalence was found to be between 22% and 33%<sup>15</sup>. Approximately 80% of patients that received treatment for a depressive episode will have a second episode throughout their lives<sup>16</sup>.

In this study depression was three times more frequent in women; this is in agreement with previous studies<sup>15</sup>.

In a previous study with NCC patients, depression was the most frequent psychiatric diagnosis in 53%<sup>8</sup>. Psy-

chiatric diagnoses were made by the Present State Examination and the Schedule for Affective Disorders and Schizophrenia. Active disease and intracranial hypertension were associated with higher psychiatric morbidity, and previous history of mood disorders was strongly related to current depression<sup>8</sup>. However, this study did not have a control group. The incidence of depression found in our study is higher probably due to the small size of the groups, although we cannot rule out population characteristics or differences in the psychiatric instrument used for the evaluation.

NCC is a common disease all around the world, and is considered endemic in Brazil<sup>17</sup>. It is common in both genders, in all ethnic groups and all ages, but with predominance between 11 and 35 years<sup>1,17</sup>.

The most frequent clinical manifestations of NCC are seizures (62%), intracranial hypertension syndrome (38%), and meningitis (35%)<sup>18</sup>. There is a high frequency of asymptomatic patients and brain calcifications due to NCC in endemic areas<sup>1,3,17,18</sup>. In our study, all cases with NCC have intra-parenchyma calcifications.

NCC is a leading cause of seizures and epilepsy in the developing world and is an increasingly important health issue in developed countries, such as the United States. Because millions of people have immigrated from Latin America in recent years, NCC has become an increasingly important cause of seizures in the United States<sup>19</sup>. For example, between 1994 and 1998, an average of 120 patients with cysticercosis were admitted to the Los Angeles County/USC Medical Center per year<sup>20</sup>. These numbers represent a substantial increase from 1983, when 80 cases were identified in all four Los Angeles County hospitals<sup>21</sup>. Cysticercosis now accounts for up to 10% of emergency room visits for seizures in the southwestern United States<sup>19</sup>.

Due to population migration from endemic areas, cysticercosis also has importance as a traveler's disease<sup>19,21</sup>.

In the present study, the frequency of depression in groups with epilepsy (groups 1 and 3) was 86%, higher than described in the literature. However, a comparison between group 1 (an association of two factors, NCC and epilepsy) and groups 2 and 3 reveals that the incidence of depression was not higher nor there was higher number of cases with more severe depression levels in groups 2 and 3.

The prevalence of interictal depressive illness in epileptic patients is between 50% and 60%<sup>22,23</sup>. Other studies have shown a frequency of up to 75% of depression in groups of epilepsy and an increase of depressive symptoms in epileptic patient when compared to normal control<sup>24,25</sup>.

When patients receive the diagnosis of epilepsy, some can react with a period of sadness before the adaptation. After elaborating this situation, they tend to come back to the normal mood. However, there are those that develop a depressive picture with morbidity characteristics.

The physician must differentiate between a depression of organic characteristics or a psychogenic reactive depression, or one without pathological characteristics. The depression, then, can be concomitant to, precede, or follow the epileptic picture<sup>26</sup>. Post-ictal depressive episodes must also be considered, which disappears in few hours.

In this study, the group with epilepsy had a higher number of moderately depressed patients and in the group of NCC without epilepsy 41.2% were slightly depressed.

The group with chronic headache had a higher number of patients seriously depressed, (42%), in agreement with previous studies<sup>27</sup>. These authors demonstrated that these patients have significant limitations in life quality relative to the healthy population and when compared with other chronic illnesses, such as arthrosis and diabetes.

The analyses of the scores of depression did not present significant difference between groups of NCC and other groups. It is possible that, in a general way, patients with a chronic illness will have depression in a similar intensity. In chronic conditions, the emotional, familiar, social, physical and functional aspects are compromised, influenced by the type and degree of illness compromise, and period of the illness.

The risks and factors contributing to major depressive episodes in NCC infection remain unclear. The immunologic response and incidence of depression in NCC must be evaluated. There is a strong suggestion that cytokines have a role in the biology of depression<sup>28</sup>. Th1 cytokines are predominant in the immunological response elicited by *Cysticercus cellusae* and include gamma interferon, interleukin-18 (IL-18), and the immunosuppressive, fibrosis-promoting cytokine transforming growth factor beta. The Th2 cytokines IL-4, IL-13, and IL-10 were also present, though to a lesser extent<sup>29,30,31</sup>. Monocyte stimulation by *T. solium* larval antigen results in a differential secretion profile of chemokines: CCL3/MIP-1alpha after 8 hours, CXCL8/IL-8 after 24 hours, and CCL2/MCP-1 after 48 hours<sup>32</sup>. Some of these immunological factors are described when depression is associated with infectious diseases such as HIV<sup>33</sup> and HCV<sup>28</sup>.

Although immunological factors could be related with the development of depression, higher frequencies were found, in our study, in groups without infectious diseases such as epilepsy and chronic headache. These data lead us to hypothesize about the association of other factors such as genetic predisposition, or social and cultural factors. Patients with chronic illnesses possess peculiarities that must be considered in the evolution of the disease and its treatment, such as presence of depressive phenomena or anxiety on a large scale, beside acute reduction or loss of work capacity that will interfere in life quality. This study have some limitations: the participants were not evaluated by a psychiatrist, other psychiatric diagnosis instru-

ments as DSM-IV criteria, MINI plus or SCID were not used. Previous personal or family psychiatric story including depression story or anti-depressive medication use was not collected. Delirium was not evaluated. No information about the use of prophylactic pain medication as tricyclic antidepressants was collected. Cognitive status, alcohol or substance abuse was not assessed. There are few studies addressing the topic depression among patients with NCC, besides the limitations of the study this association is shown; although other studies are necessary for definitive conclusions.

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