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Depression Following Traumatic Brain Injury

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ABSTRACT:

DEPRESSION FOLLOWING TRAUMATIC BRAIN INJURY

BACKGROUND: Depression is the most frequent psychiatric disorder after Traumatic Brain Injury (TBI) and hampers community re-entry for trauma patients. The prognosis is worse in TBI patients with depressive symptoms compared to those without depression. Estimating the risk of depression after TBI could help to improve the prognosis of these patients.
OBJECTIVE: To determine the factors that increase the risk of depression after TBI. To examine if the symptomatology of depression is different in cases with and without TBI. To see if the Rivermead Post-concussion symptoms Questionnaire, RPQ , is answered differently by depressed patients with and without TBI in the past.
METHODS: A community-based retrospective cohort study of the inhabitants of Nijmegen. A total of 5424 inhabitants filled out 3 different questionnaires, including the RPQ, between 2002 and 2008. TBI was diagnosed if there was a self-reported brain concussion or –contusion. Depression was diagnosed using the Beck Depression Inventory (BDI) with a cut-off score of more than 9.
RESULTS: People with a history of TBI did not have a significantly higher risk of developing a depression later on in life. The most important risk factors for depression were: history of depression, employment status, marital status, and level of education.
Four different groups of symptoms were discovered in the RPQ using $\chi 2$ analysis to test for differences.
Depressed participants with TBI had significantly more trouble falling asleep than depressed participants without TBI ($\chi 2$ (3) = 8,639, $p < 0.05$).
CONCLUSION: A history of TBI does not have predictive value for the development of a future depression. More important factors for developing depression are history of depression, employment status marital status, and level of education. There is no difference in the symptomatology of depressed patients with and without a TBI.

Introduction

Traumatic Brain Injury (TBI) is a major health problem with an incidence of 235 per 100,000 hospitalizations in Europe per year[1]. 24% to 31% of all severe trauma patients survive their trauma and have to deal with long-term disabilities[2]. Cognitive and neurobehavioral problems are the most common after TBI. Depressive symptoms together with anxiety comprise the most common complications after TBI[3], with prevalence rates of depressive symptoms ranging between 10% and 77%[4]. Research shows that TBI patients who develop a depression have a worse prognosis. They have many psychosocial problems that complicate community re-entry, and hamper resuming a productive life and maintaining satisfactory interpersonal relations[5-9]. Researchers have consistently suggested that the psychosocial problems associated with TBI may be the major challenge facing rehabilitation.[10-15]

Many risk factors for depression named in literature are inconsistent. Gender is a good example of this; some studies show that females are at higher risk[16-18], while other studies show that men are more at risk[19] and there are even reports that found that gender is no risk factor at all[3, 20-26]. The question arises: what are the risk factors for developing a depression after TBI? If patients who are at high risk for depression can be identified and get immediate intense counseling by a psychiatrist, this may decrease their risk of developing a depression.
One test that might differ between those who develop depression and those who do not, is the Rivermead Postconcussion Questionnaire (RPQ)[27], a short questionnaire to measure the severity of post-concussion symptoms. Many sections of this questionnaire compromise depressive symptoms. The question arises, whether the risk of depression could be estimated with the results of the RPQ? Also the people who get depressed after TBI might have a different kind of depression, which would need a different kind of treatment.
The aim of this study is to find the factors that might increase or decrease a person's risk of getting a depression after TBI. Also to check if the Rivermead Postconcussion Questionnaire can differ between those who will develop depression after TBI and those who will not. Furthermore, we will compare the symptoms of depressed patients with and without TBI, to see if symptoms differ.

Methods

Participants

All participants were selected from the Nijmegen Biomedical Study (NBS); this is a population-based survey conducted by the Department

of Epidemiology and Biostatistics and the Department of Clinical Chemistry of the Radboud University Nijmegen Medical Centre. This study was approved by the Institutional Review Board.
A random sample from the register of the population of Nijmegen, stratified on sex and 5-year age groups was taken in 2002. People were included if they were aged over 18, not living in institutions and rest homes, and able to fill out a Dutch questionnaire. Per 5 year age category 750 men and 750 women were included. All people above 85 were included, because of the shortage of people above this age.

Measurements and data analysis
22,451 inhabitants of the municipality of Nijmegen received the first (NBS1) postal questionnaire, 9350 inhabitants responded. The second questionnaire (NBS2) was sent, in October/November 2005, to all participants of NBS1, who had given permission for further research. The NBS2 questionnaire included questions about, health and disease, pregnancy, mood and behavior, traumatic brain injuries, daily activities, and memory. 7986 participants received the NBS2 questionnaire and 70% (N=5594) filled in the questionnaire. A few questions still remained after NBS1 and NBS2, so participants were again contacted in 2008 to fill out an additional questionnaire (NBS4). 8109 people received the NBS4 questionnaire and 69% (N=5613) completed the questionnaire.

The study population were all patients that answered the NBS1 questionnaire (N=5594) minus 170 persons who were included in a pilot study for the NBS2 questionnaire. So the real study population existed of 5424 participants. All the participants (n=5424) filled in all three questionnaires (NBS1, NBS2 and NBS4). TBI was diagnosed if there was a self-reported case of brain concussion or contusion. The severity of trauma was determined by the time that participants were unconscious (no unconsciousness, 0-30 minutes, 31-360 minutes, >360 minutes)

Risk factors
Literature shows that many variables might be a confounder in the relation between TBI and depression, shown in appendix 1. Most of the risk factors named in appendix 1 are questions of the NBS 1, 2, and 4. Appendix 2, 3, and 4 show the NBS questionnaires.
The relationship between TBI and depression was expressed as an Odds Ratio (OR).

First an univariate model was made for all variables to check their predictive value for depression. Second all variables with a p-value lower than .1 were used to build a multivariate model (model 1). Using backward stepwise selection, the variables with a p-value higher than 0.1 were removed and the variables with a p-value lower than 0.05 were entered. All remaining variables were classified as being a risk factor.

Rivermead
The RPQ scores the 16 most common post-concussion symptoms at a scale from 0 to 4, 0 being no problems and 4 being a severe problem. The questionnaire is used in the first 7-10 days after injury to rate the severity of post-concussion symptoms.[27] For this study the RPQ was slightly altered because the time between injury and the questionnaire was generally more than 7-10 days. The questions of the RPQ are found in NBS2 question B12. The variable blurred vision is not included in the NBS2 questionnaire but is present in the original RPQ. The participants were asked if the suffered from the 15 items in the last 6 months. Answers on these questions could be yes or no.
TBI history and depression at the time of interview were used to make four categories, 1) never had a TBI, not depressed (N=3468), 2) ever had a TBI, not depressed (N=933), 3) never had a TBI, depressed (N=765), 4) ever had a TBI, depressed (N=258). $\chi 2$ tests were used to check if participants in different categories answered differently on the RPQ. Based on the differences in the 15 RPQ items between the groups, different groups of answering patterns were produced. Each group had his own pattern of significance when the four former groups, TBI/depression groups, were compared.

Symptomatology
The NBS2 questionnaire contained an altered version of the Beck Depression Inventory (BDI) for self-administration (Appendix 3 questions D8 t/m D29). The BDI contains 21-items, rated from 0 to 3 in terms of intensity. The ratings were summed to calculate total depression scores, which ranged from 0 to 63[28].
A cut-off score for depression was set at a total score of 10 or higher; all participants with this score were diagnosed as being depressed at the time of the interview. After that, the 21 items of the BDI were categorized as being somatic or cognitive using the original Beck classification[29].
$\chi 2$ tests were used to check if there was a difference in the severity of symptoms between those who were depressed with TBI and without. Secondly, Mann-Whitney U tests were used to check if there was any difference in somatic or cognitive symptoms between those two groups.

Results

Demographics
Table 1 shows the demographic characteristics of the study population at the time of interview.
The ethnic diversity of the study population was close to the ethnic diversity of Nijmegen. Approximately 85% of the inhabitants of Nijmegen are of Caucasian origin, 8% is black and 1% is of Asian origin[30].
In this study of 5424 participants, 1191 ever had a self-reported brain contusion or concussion. This means that there is a prevalence of 21,958 per 100,000 (22%).
A total of 1023 participants had a BDI cut-off score of 9 or more and are diagnosed as being depressed at the time of interview. The prevalence of depression in this study population is 18,661 per 100,000 (19%).
Table 2 shows the distribution of the cases in the categories TBI and depression. People who had a TBI have a significantly higher risk of developing a depression later on in life, OR 1.25, 95%CI [1.1-1.5].

Risk factors
Almost all variables show a significant relation with depression when they were analyzed in a univariate binary logistic model. Table 3 lists all variables and their significance in the univariate model. Only the variables race and severity of trauma were not significant and so were not used in model 1. In the backward selected binary logistic model the next variables came out significant: depression before trauma, depression after trauma, employment, and education (Table 4).

Table 1: Demographics and psychiatric variables of Community-Based Sample of Persons with and without TBI at Time of Interview

Variable	TBI (N=1191)	No TBI (N=4233)	*p*
Mean age ± SD	55.5 ± 16.4	57.9 ± 17.4	<0.05
Gender, n (%)			
Male	550 (46.2)	1930 (45.6)	0.720
Race, n (%)			
White	941 (79.0)	3288 (77.7)	0.355
Black	2 (0.2)	6 (0.1)	
Asian	5 (0.4)	40 (0.9)	
Other	10 (0.8)	36 (0.9)	
Severity of trauma, n (%)			
Mild	1025 (86.1)	-	-
Moderate	78 (6.5)	-	
Severe	44 (3.7)	-	
Depressed, n (%)	258 (21.7)	765 (18.1)	<0.05
Depression before trauma, n (%)	44 (3.7)	-	-
Depression after trauma, n (%)	182 (15.3)	-	-
Other psychiatric illness, n (%)	65 (5.5)	137 (3.2)	<0.05
Family depression history, n (%)	324 (27.2)	921 (21.8)	<0.05
Family psychiatric history, n (%)	369 (31.0)	1080 (25.5)	<0.05
Marital Status, n (%)			
Married	797 (66.9)	2880 (68.0)	0.216
Divorced	73 (6.1)	263 (6.2)	
Widow	104 (8.7)	417 (9.9)	
Alone	211 (17.7)	653 (15.4)	
Employed, n (%)	603 (50.6)	1960 (46.3)	<0.05
Education, n (%)			
Elementary education	97 (8.1)	367 (8.7)	0.534
Junior secondary education	189 (15.9)	596 (14.1)	
Senior vocational education	328 (27.5)	1225 (28.9)	
Higher general secondary education	123 (10.3)	448 (10.6)	
Higher Vocational Education/University	452 (38.0)	1579 (37.3)	

* All categorical variables are tested with χ^2 tests, mean age is tested using the Mann-Whitney U test

Model 1 resulted in the following equation:
Odds ratio to develop depression = -0.998 + 1.428*depression before trauma + 1.384*depression after trauma - 0.594*employed + 0.657*divorced + 0.796*widow + 0.652*alone - 0.655*junior secondary education - 0.966*senior vocational education - 1.305*higher general secondary education - 1.209* Higher Vocational Education/University.

Rivermead

Based on the differences in answering patterns between the four categories of patients, different groups were conducted. Each group has its own pattern of significance between the four categories. Four different groups of answering patterns were found. All four groups are described below with the variables of the RPQ that belong to it.

Group 1:
Headaches (Figure 1)
No significant difference in the percentages of headaches between those with only TBI or only depression was found. The difference between depressed cases without TBI and TBI cases without depression versus those with TBI and depression was significant.

Group 2:
Double vision (Figure 2), light sensitivity (Figure 3), forgetfulness/poor memory (Figure 4), being irritable (Figure 5), fatigue (Figure 6), sleep disturbance (Figure 7), noise sensitivity (Figure 8), nausea/vomiting (Figure 9), dizziness (Figure 10)
The differences between all patient categories are significant. Patients with TBI seem to suffer more from these symptoms than the general population. People with depression seem to suffer more from these symptoms than people with only TBI and people with both a

	Depressed	Not Depressed	Total
TBI	258	933	1191
No TBI	765	3468	4233
Total	1023	4401	5424

Table 2: TBI and depression cases

depression and TBI suffer the most.

Group 3:
Restlessness (Figure 11), frustration (Figure 12), depressed or tearful (Figure 13), poor concentration (Figure 14)
In this group the difference between cases with only depression or with depression and TBI is not significant. The main source of restlessness, frustration, tearfulness, and poor concentration seems to be the depression, TBI adds nothing to the amount of complaints.

Group 4:
Taking longer to think (Figure 15)
TBI has no significant effect on the time to think in individuals without depression. However, when someone is depressed, TBI has an additional effect.

Symptomatology
Depressed participants with TBI complained significantly more about having trouble falling asleep than depressed participants without TBI ($\chi 2$ (3) = 8.639. $p < 0.05$). No significant difference in other items of the BDI were found.
Because none of the other items was significant the 21 items were divided into two factors: somatic symptoms and cognitive symptoms, according to Beck & Steel[29]. The difference in cognitive and somatic symptoms between depressed patients with and without TBI, was tested using the Mann-Whitney U test.

Discussion

Risk factors
Patients with TBI showed a higher risk to develop depression compared to patients without a history of TBI, which is consistent with literature[31-36], after adjustment for confounding this result was no longer significant.
The univariate modeling shows that many factors increase the risk for depression: a depression before the trauma, a previous depression after trauma, unemployment, divorce, being widowed, living alone, and education level. Many of these factors are classic risk factors for depression[37]. Other factors that are described in literature show no significant effect in this sample. This could be because literature describes variables that are measured at the time of trauma and are risk factors for depression after TBI. Because this study is a retrospective cohort study the variables measured at the time of interview may not be applicable for the time of trauma. The variables found in this study might therefore be interpreted as risk factors for a depression but not as a risk factor for a depression after TBI.

Literature shows that cases that had mild TBI are more at risk for depression than cases with a moderate/severe TBI[18]. In the univariate analysis severity of trauma showed no significant effect on depression. But the slope of mild TBI is positive towards depression while the slopes for moderate and severe TBI are negative. This is in agreement with the existing literature. In our study the results are not significant, but there is a tendency showing that mild TBI patients might have a higher risk of depression than patients with moderate/severe TBI.
Model 1 shows that history of depression, employment status, marital status, and level of education are the most important factors for developing a depression. TBI is not a significant factor in this model. This means that corrected for all other factors TBI is no risk factor for developing a depression.
As found in this research divorced people, widows, and people who are alone are more at risk than people who are married. Other studies suggest that marital status is no risk factor for depression after TBI [3, 20-22, 26, 38]. These studies measured marital status directly after the trauma, whereas in this study it is measured at a random time after trauma.

In this model higher education and employment decrease the risk of depression. This can be explained because higher education as well as employment usually contribute to more social stability, which may therefore be the true influencing variable. A history of depression is a well- known risk factor for a new episode of depression[3, 17, 21, 39]. In this study both depression before and after trauma have shown to be a risk factor for a new episode of depression. The time between trauma and depression, at time of interview, is long in this study (32.5 years ± 17.9). Literature describes the highest rates of depression in the first 3-5 years after trauma[19]. The cause of the depression at time of interview might therefore not be the trauma but a depressive episode that happened earlier after trauma.

Another shortcoming of this study is that all the questionnaires are self-administered. This leads to an overestimation of depression and TBI cases. All questions were clearly formulated to minimize misinterpretation and overestimation. But still an overestimation of the amount of TBI cases should be taken into account. The BDI, has shown to have a high specificity (80%) but a low sensitivity (36%)[40]. In research of Beck, the cut-off score of more than 9 was shown to identify the correct amount of cases of depression in a general population, corresponding to the general incidence of depression[28]. But in this study an old population is used, so the cut-off score might not be correct for this sample. People who get older have more physical disabilities and might therefore rate some items of the BDI higher possibly leading to an overestimation of the prevalence of depression in this sample. With a point-prevalence of 19% in this sample compared to a life time prevalence of 18.7% in the Netherlands[37], there still is a overestimation.

Rivermead
Different groups of items of the RPQ are found based on the significance between different categories. The items that are in group 2, are the more vegetative symptoms of the RPQ. Depressed partici-

pants complain about these symptoms while most of them are no classic depression symptoms. This could be explained by the fact that depressed patients will complain more about their general state of mind as a result of their disease. It seems to be that TBI and depression together have a additional effect in this group.
The variables summed up in group 3 are the variables of the RPQ that describe the mood symptoms. Depressed participants seem to be bothered a lot more by these symptoms than TBI cases. These symptoms are classic depression symptoms. The amount of complaints that TBI contributes to the people who are already depressed is very small and therefore not significant.

Symptomatology
No difference was found in the expression of depression in cases with and without TBI. Cases with TBI had only significantly more trouble falling asleep than cases without TBI. The group of depressed TBI cases was slightly older than those without TBIwhich was a significant difference (Mann-Whitney U: z=-2.876. p<.05). Trouble falling asleep is a problem than develops at a later age, so the fact that TBI patients were older may be the explanation for the found difference in trouble falling asleep. Concluding, the symptomatology of depression does not differ between cases with and without TBI.

Conclusion

We showed that a history of TBI does not have a predictive value for the development of a future depression. Other factors have proven to be more predictive: a history of depression, employment status, marital status, and level of education.
The RPQ is answered differently by those who had a TBI and are now depressed compared to those depressed without TBI or those who are not depressed. Further research will show is the RPQ can be used to predict depression after TBI.
Based on the different items of the BDI, the symptomatology of depression does not differ in those with or without TBI.

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Table 3: Univariate analysis of risk factors for depression

	OR	95,0% C.I. for OR	
		Lower	Upper
TBI	1.254	1.070	1.469
Female	1.712	1.486	1.971
Age at time of interview	1.017	1.012	1.021
Age at trauma	1.009	1.000	1.017
History of depression before trauma	4.375	2.413	7.931
History of depression after trauma	3.330	2.461	4.506
Other psychiatric disease	3.475	2.606	4.633
Family history of depression	1.680	1.445	1.954
Family psychiatric history	1.554	1.343	1.798
Race			
White (reference category)			
Black	2.852	0.680	11.961
Asian	1.538	0.776	3.049
Other	1.320	0.652	2.673
Severity of trauma			
No coma (reference category)			
1-30min coma	1.060	0.790	1.422
31min-6hr coma	0.616	0.325	1.165
>6hr coma	0.695	0.319	1.514
Employed at time of interview	0.468	0.405	0.540
Marital status			
Married (reference category)			
Divorced	2.171	1.683	2.801
Widow	2.827	2.308	3.463
Alone	1.586	1.319	1.907
Education			
Elementary education (reference category)			
Junior secondary education	0.663	0.510	0.861
Senior vocational education	0.677	0.537	0.854
Higher general secondary education	0.520	0.388	0.696
Higher Vocational Education/University	0.348	0.275	0.442

Table 4: Variables used in model 1, with their OR's and slope

Variables	B	Exp(B)	95.0% C.I.for EXP(B) Lower	Upper
Depression before trauma	1.428	4.169	1.998	8.699
Depression after trauma	1.384	3.990	2.715	5.864
Marital Status				
Married				
Divorced	.657	1.930	1.033	3.607
Widow	.796	2.216	1.302	3.774
Alone	.652	1.919	1.251	2.944
Education				
Elementary education				
Junior secondary education	-.655	.519	.277	.973
Senior vocational education	-.966	.381	.211	.686
Higher general secondary education	-1.305	.271	.129	.569
Higher Vocational Education/ University	-1.209	.298	.164	.543
Employment	-.594	.552	.382	.798
Constant	-.998	.369		

The next 15 figures (Fig 1 t/m Fig 15) are all graphs of the percentage of participants that answered yes to the question in the RPQ about the topic mentioned in the title of the figure.

Category 1:

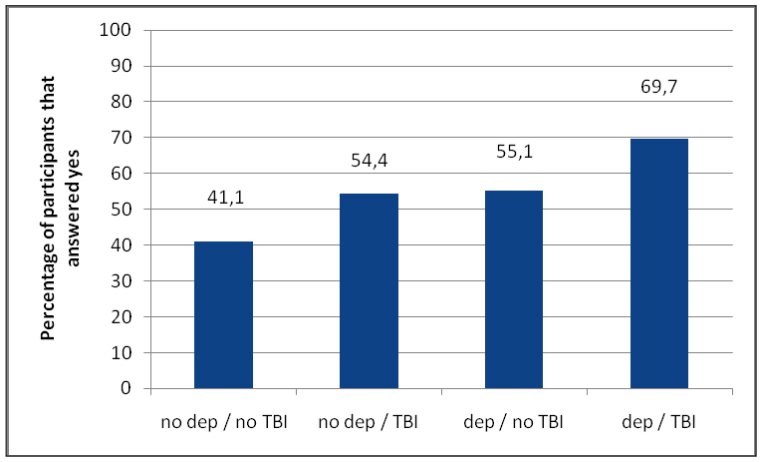

Figure 1. Headaches

Category 2:

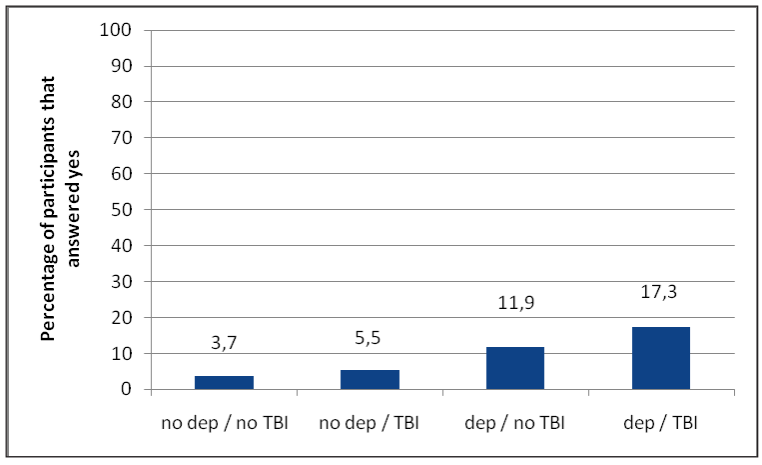

Figure 2. Double Vision

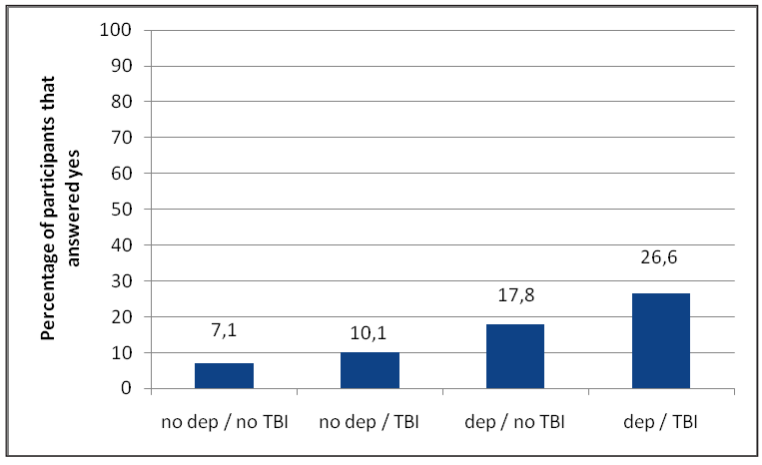

Figure 3. Light Sensitivity. Easily upset by bright light

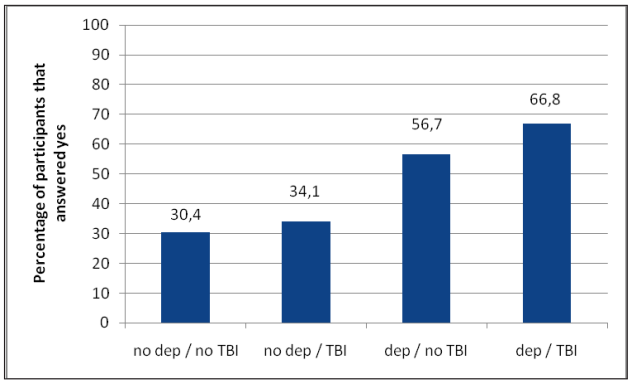

Figure 4. Forgetfulness. poor memory

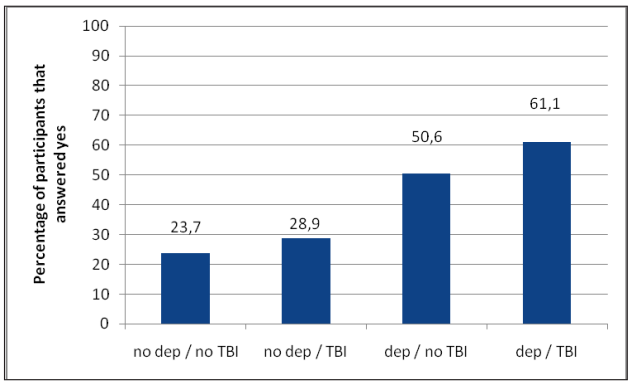

Figure 5. Being Irritable. easily angered

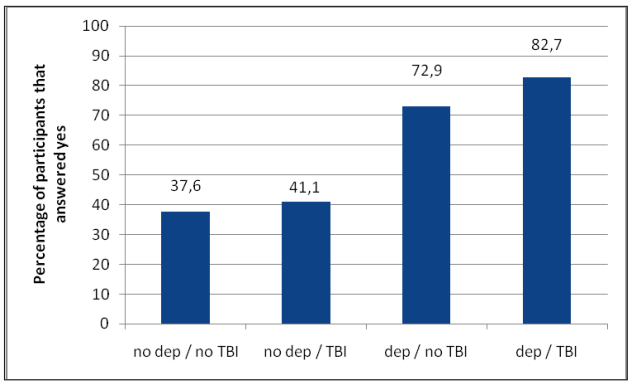

Figure 6. Fatigue. tiring more easily

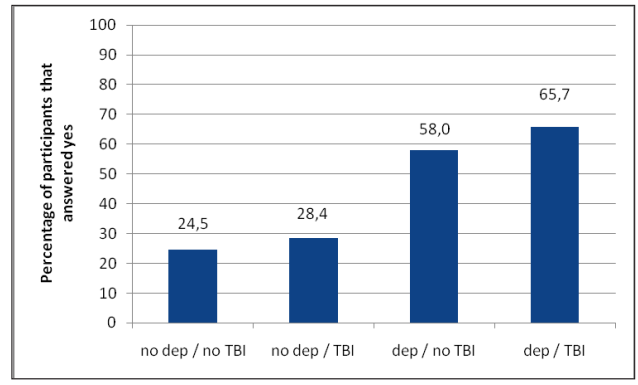

Figure 7. Sleep Disturbance

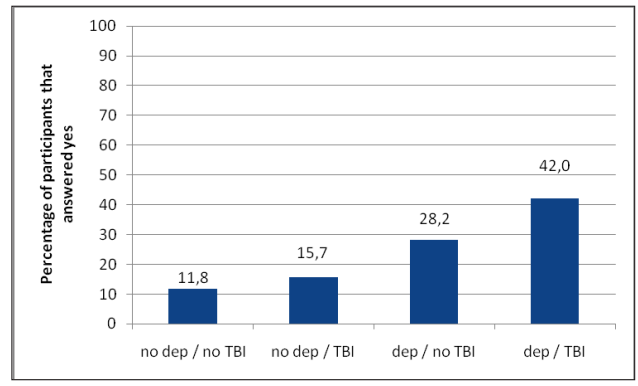

Figure 8. Noise Sensitivity. easilly upset by loud noise

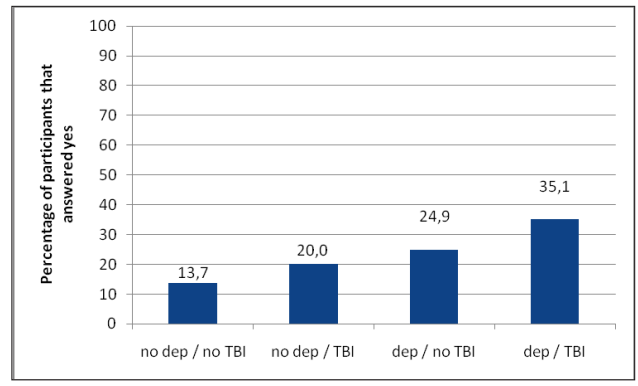

Figure 9. Nausea and/or Vomiting

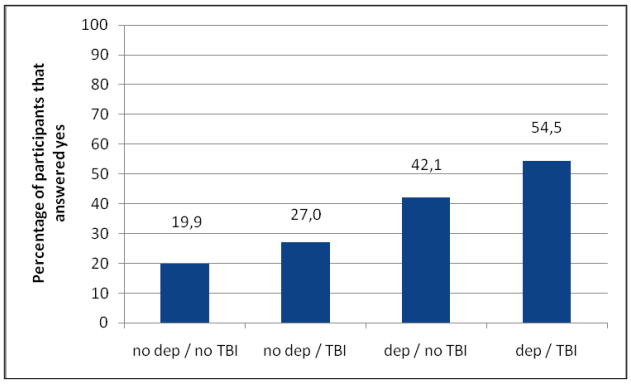

Figure 10. Feelings of Dizziness

Category 3:

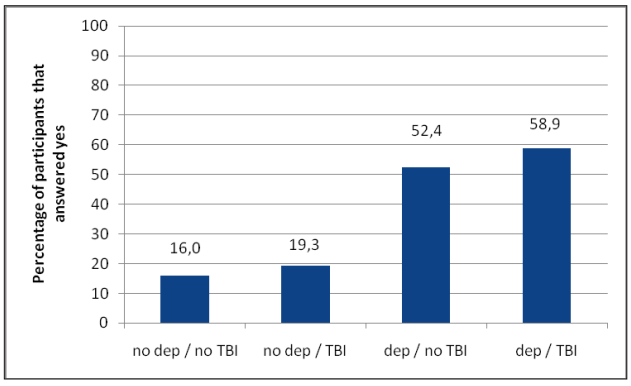

Figure 11. Restlessness

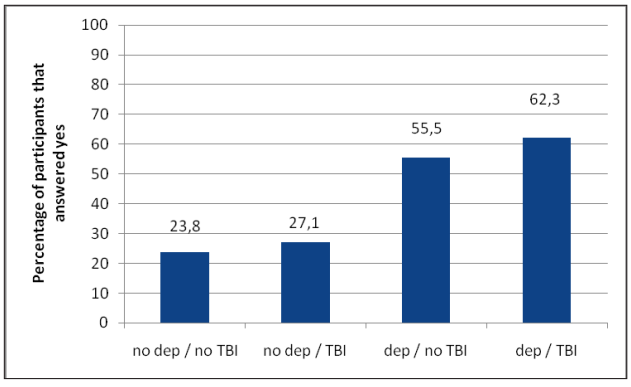

Figure 12. Feeling Frustrated or Impatient

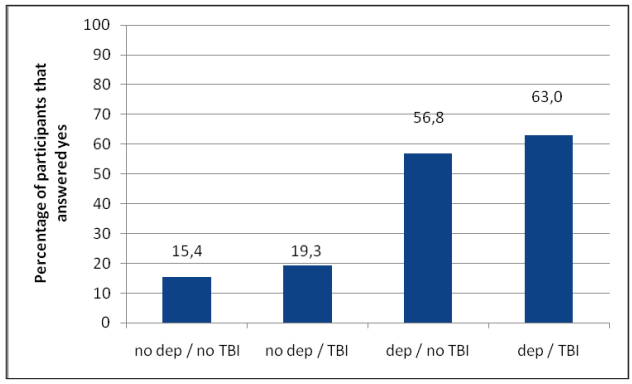

Figure 13. Feeling Depressed or Tearful

Category 4:

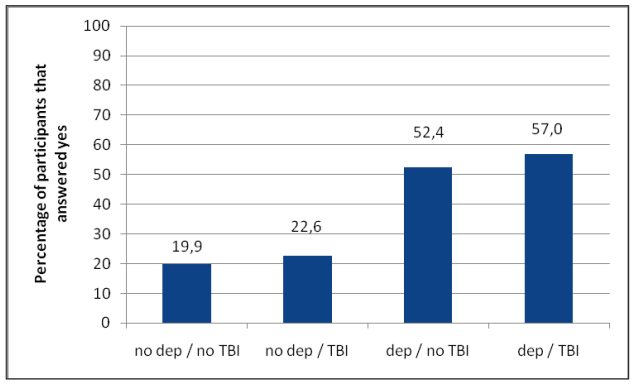

Figure 14. Poor Concentration

Category 5:

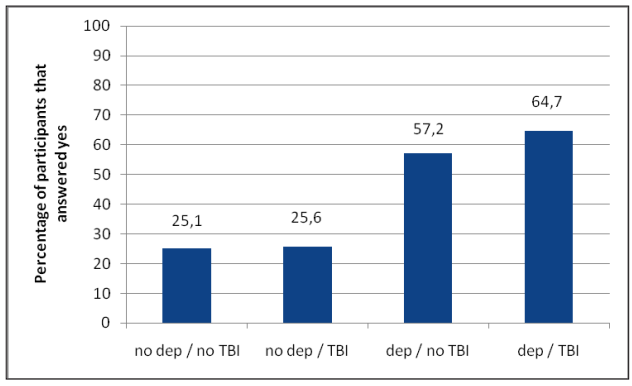

Figure 15. Taking Longer to Think