Psychological Correlates of Idiopathic Intracranial Hypertension

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Abstract

Background: Idiopathic intracranial hypertension, also known as pseudotumor cerebri, is a relatively rare disorder of increased intracranial pressure >250 mm water, with a normal neuroimaging and normal cerebrospinal fluid content.

Objectives: To examine whether hostility, anxiety and autobiographical memory (a correlate of depression) are associated with IIH[1].

Methods: Using a case-control cross sectional design, 20 patients with IIH were compared with 9 healthy controls of similar age, weight and height, and 11 headache controls. Patients were assessed for hostility and anxiety. The Autobiographical Memory Test was used to assess episodic memories.

Results: The IIH group reported significantly more anxiety and more general episodic memories than the healthy controls, but not the headache control group. The headache control patients reported more general memories than did the healthy controls.

Conclusions: Patients with headaches, whether of general origin or related to IIH, have a poor psychosocial profile. While the study design does not permit any conclusions regarding causality, our results support the need to consider psychological factors in evaluating and treating IIH and headache patients.

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Idiopathic intracranial hypertension, also known as pseudotumor cerebri, is a relatively rare disorder of increased intracranial pressure >250 mm water, with a normal neuroimaging and normal cerebrospinal fluid content [1]. The Modified Dandy Criteria are used to diagnose this condition [Table 1]. The annual incidence rate of IIH in the general population is 0.9 per 100,000 people [2]. In Israel, although the population consists of individuals from many different origins (eastern and western countries), the IIH incidence per year is similar to that of western countries [3].

Case-control studies performed to date have shown a substantial association between IIH and obesity [4,5]. Obesity is indeed a significant risk factor for IIH. Among obese women the prevalence of IIH is approximately 4 per 100,000, and among women with body mass index above 20% the prevalence is 19 per 100,100 [2].

Although extensive research has been conducted regarding the accurate diagnosis and appropriate treatment of IIH, the psychosocial impact of this condition has not been systematically studied, nor has the possibility that psychosocial factors play an etiologic role in IIH. Only one systematic study has investigated the relationship between psychological factors and IIH [6]. In this study, Kleinschmidt et al. [6] compared IIH patients to age- and weight-matched controls and to an additional age-matched normal-weight control group. Significantly higher levels of anxiety and depression were found among the patients with IIH than among both control groups. Furthermore, the IIH group reported being significantly more affected by the burden related to health problems than either of the control groups. Their findings suggest a high degree of distress in IIH.

While Kleinschmidt's study included adequate control groups and measures, it had a few conceptual and methodologic limitations. From a conceptual point of view, certain psychological factors were not tested, namely hostility and anger, that had been previously associated with headache conditions. For example, aggressive and anger-related contents in dreams were found to precede migraine attacks [7]. Hence, hostility may be related to IIH as well. From a methodologic point of view, Kleinschmidt et al. [6] included only self-reported questionnaires, which may have been affected by presentation biases. An indirect measure that assesses episodic memory, the Autobiographical Memory Test [8], may be less affected by presentation biases. In the AMT, participants provide memories from their lives in response to word cues, and non-specific responses (over-general memory bias) have been found to correlate with depression [9]. The purpose of the present study was to replicate the findings of Kleinschmidt and associates [6] in another culture, and extend the study by assessing additional psychological constructs (hostility) using alternative forms of assessment (the AMT). We hypothesized that patients with IIH would score higher on hostility, anxiety and general episodic memory than headache controls and a non-headache overweight control group.

Table 1. Modified Dandy's criteria for diagnosing idiopathic intracranial hypertension

- Symptoms and signs of increased intracranial pressure in an awake and alert patient
- No abnormal neurologic signs other than abducens nerve paresis
- Normal neuroimaging except for empty sella
- Cerebrospinal fluid opening pressure >200 mm H_20 in non-obese and >250 mm H_20 in obese patients
- Normal composition of cerebrospinal fluid
- No other known causes of intracranial hypertension

Data taken from Rhadhakrishnan et al. [2].

IIH = idiopathic intracranial hypertension
AMT = Autobiographical Memory Test

Methods

Patients

Twenty patients with IIH, 10 patients with chronic headaches (headache controls), and 9 healthy controls participated voluntarily in the study. The IIH patients met the Modified Dandy Criteria [2] as mentioned above. The patients were recruited from the Neuro-Opthalmology Unit, Sourasky Tel Aviv Medical Center, Israel. Healthy controls were a convenience sample of healthy women selected according to age and weight to match the IIH group. We deliberately recruited only women for the healthy control group since nearly all the IIH group included women. Patients' age, weight and gender were recorded. In the IIH group, acetazolamide (Diamox®) was recorded since it may be correlated with psychological parameters such as depression [10]. Informed consent was given and the study was approved by the local Human Research Ethics Committee (Helsinki Committee).

Instruments

In general, we used brief psychological instruments to reduce subject fatigue and potential non-compliance when completing the questionnaires. To assess hostility, we used the recently developed 8-item New-Buss scale. This scale is strongly associated with antagonistic behavior and has been shown to significantly correlate with severity of atherosclerosis in young men [11]. To assess anxiety, we used the 6-item version of the State-Trait Anxiety Inventory (state version) [12]. For the purposes of the present study this measure was used as a trait measure, and participants were asked to respond to each item as relating to themselves "in general." Finally, to assess episodic memory, a correlate of depression [9], we used the AMT [8]. In the AMT, 10 cue words are provided to the participants who are asked to provide a specific event from their life corresponding to each cue word. The original test evaluated generality vs. specificity of each response using a categorical scoring (i.e., general or specific). To increase reliability, we analyzed each response in relation to generality vs. specificity concerning three dimensions: time (e.g., a year ago), place (e.g., my home) and people (e.g., my brother). Each response was scored: 0 for a general response and 1 for a specific answer relating to the three dimensions (place, time, people). Scores for all items were summed across the three dimensions, yielding a possible range of scores between 0 and 30. A higher score indicated a more specific response (hence, lower risk for depression). To test for inter-observer reliability, 11 AMT scores of the total sample were analyzed separately by two of the investigators (A.K., Y.G.). Using the Pearson correlation, a high level of agreement between both raters was shown ($r = 0.86$, $P < 0.001$). The three instruments were translated from English to Hebrew. The first two were used in previous Israeli studies by our research team and have adequate reliability and validity in this culture [11].

BMI = body mass index

Statistical analysis

We first compared all three groups in relation to age, body mass index and education using analyses of variance (ANOVA). Any differences between groups on these background variables were then taken into consideration in further analyses using an analysis of covariance (ANCOVA). We then performed the main ANOVA (or ANCOVA) by examining the effects of group (IIH, headache controls, healthy controls) on each of the three psychological measures (AMT, anxiety, hostility). We used planned contrasts between the IIH and healthy controls, as well as between the IIH and headache controls in relation to hostility, anxiety and the AMT scores. Due to the exploratory nature of the study and the small sample size, we did not correct for multiple tests. Finally, we examined the correlations between scores on the psychological measures using Pearson correlations.

Results

Table 2 shows mean and standard deviation (SD) of the IIH, headache controls and healthy controls in relation to age, BMI, gender, anxiety, hostility and total AMT scores. While no differences were found between the IIH and healthy controls for age and BMI, the headache controls were significantly higher on age [$t(36) = 2.29$, $P < 0.05$] and lower on BMI [$t(37) = 5.17$, $P < 0.001$] than were IIH patients. Within the IIH group, there was no difference in any psychological variables for patients taking or not taking the prescription drug acetazolamide (Diamox®). Therefore, the following comparative analyses of the psychological variables were conducted with and without controlling for effects of age and BMI.

Patients in the IIH group reported significantly higher levels of anxiety than did healthy controls [$t(37) = 2.14$, $P < 0.05$]. In addition, the IIH group scored significantly lower on specificity for the AMT test than did healthy controls [$t(37) = 12.38$, $P < 0.001$]. These latter findings indicate that the IIH group reported more general episodic memories (over-general memory bias) than the healthy control group. The differences between these two groups in relation to anxiety and AMT scores remained significant, after controlling statistically for the effects of age and BMI [$F(1,25) = 4.93$, $P < 0.05$ for anxiety; $F(1,25) = 178.98$, $P < 0.001$ for AMT scores]. No differences between the IIH and healthy controls were found regarding hostility.

Table 2. IIH and control groups in relation to all measured variables (mean and SD)

Variable	IIH-group (n=20)	Headache controls (n=10)	Healthy controls (n=9)
Age (yrs)	27.4 ± 8.2	34.5 ± 9.4*	28.8 ± 5.5
BMI	32.2 ± 5.7	22.3 ± 5.1**	32.8 ± 3.3
Gender			
Women	18	9	9
Men	2	0	0
Anxiety	15.4 ± 3.5	15.1 ± 3.7	12.4 ± 3.1*
Hostility	18.1 ± 5.9	18.0 ± 6.1	17.5 ± 4.5
AMT total	5.1 ± 3.0	6.4 ± 3.7	20.1 ± 2.0**

* $P < 0.05$, ** $P < 0.001$ (contrasts are between the corresponding group and the IIH group).
IIH = idiopathic intracranial hypertension, AMT = autobiographical memory test.

In contrast, the IIH and headache controls did not differ on the AMT score, anxiety or hostility scores ($P > 0.05$) and these results remained intact after statistically controlling for age and BMI. Finally, the healthy controls had a significantly higher BMI [$t(37) = 4.6$, $P < 0.001$] and a significantly more specific AMT score [$t(37) = 10.0$, $P < 0.001$] as compared to the headache controls. However, the healthy controls and headache controls did not differ in relation to anxiety or hostility scores. The significant differences in AMT scores between these two groups remained significant after controlling statistically for the effects of age and BMI [$F(1,15) = 18.56$, $P = 0.001$]. The mean AMT scores as a function of study group (IIH, healthy controls, headache controls) are depicted in Figure 1.

Finally, we examined the associations between the psychological measures using Pearson correlations. While hostility was positively and significantly correlated with anxiety ($r = 0.50$, $P = 0.001$), hostility was unrelated to the AMT test ($r = -0.04$, not significant). In contrast, anxiety levels tended to be inversely significantly correlated with degree of specificity of the AMT scores ($r = -0.24$, $P < 0.07$).

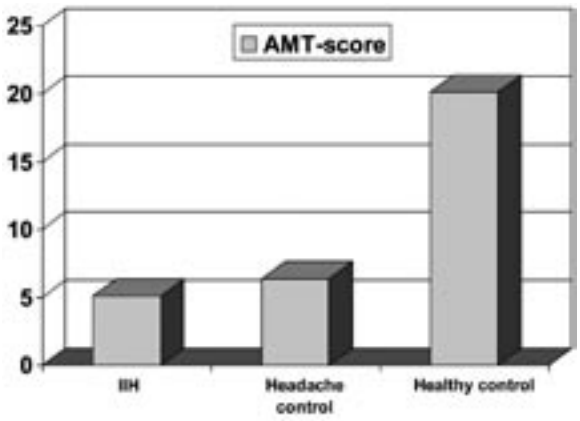

Figure 1. Autobiographical memory test (AMT) scores (vertical axis) as a function of study group.

Discussion

The present study wished to replicate and extend the findings of a previous study on psychological correlates of IIH to another culture, using additional psychological measures and methods. Patients with IIH scored higher on anxiety and presented an over-general memory bias compared to obese controls of similar weight and height. In contrast, hostility scores were not higher among patients with IIH. These results partly support the findings demonstrated by Kleinschmidt et al. [6] regarding anxiety and extend them to the Israeli population. Unlike the latter study, the present work did not include a direct measure of depression. However, our finding that IIH patients reported more general autobiographical memories, a reliable correlate of depression [9], is in line with the observation of higher depressive symptoms in IIH reported by Kleinschmidt's team [6]. However, when including patients with chronic headaches as a pain-control group (headache controls), the IIH group did not differ from these patients on any of the psychological variables. This differs from Kleinschmidt's finding [6] that the IIH group scored higher on depression than both the headache controls and the healthy controls. It is possible that our use of a correlate of depression, which is not biased by presentation biases, yielded these discrepancies. In fact, similar to the IIH, the headache controls also reported less specific memories on the AMT test than did the healthy control group. Hence, these results suggest that less specific AMT scores may characterize people with chronic headache conditions, whether IIH, migraine or tension headaches. In contrast, the fact that there was no difference in feelings of anxiety between the healthy controls and the headache controls, and that anxiety was higher among IIH patients than among healthy controls alone, suggest that anxiety may be a more severe problem in IIH patients. This will be discussed below. Regarding the AMT, it is important also to mention that reduced recall of specific autobiographical memory is correlated with depression as well as with other psychological conditions including previous trauma and post-traumatic stress symptoms [13,14]. Thus, the fact that both clinical samples reported less specific autobiographical memories than the controls did may imply greater general psychological distress than depression alone.

The methodology used in the present study may be unique in several ways. We used the AMT test, which is less affected by presentation biases than commonly used questionnaires [15]. This stems from the fact that patients' responses are not rated in relation to their emotionally negative or positive contents but rather to their specificity. Patients may be less prone to respond in a socially desirable manner in relation to response specificity than to emotional valance of responses. In addition, we examined the association of another variable, hostility, in relation to IIH, which was not previously tested. Although hostility is associated with migraines and headaches [7,16,17], hostility was unrelated to IIH in the present study. This finding needs to be confirmed in larger studies.

It appears that a relationship exists between IIH and anxiety. In other types of pain conditions such as abdominal pain, it was found that anxiety and distress predict onset of pain [18]. Future studies need to examine more closely whether episodes of anxiety may exacerbate the onset of IIH in initially healthy people or predict future painful attacks in patients with this disorder. What could be the mechanism/s linking anxiety to this disorder? If anxiety is a consequence of IIH, it may result from the inability to predict or control symptomatic painful episodes in IIH patients. Controllability and control were also found to mediate the relation between pain and depression in other painful disorders [19]. This may also be the case for anxiety. Future studies need to examine whether control over pain mediates the relation between IIH and anxiety observed in the present study. Alternatively, anxiety may lead to IIH via common underlying biological mechanisms such as elevated catecholamines [20]. The latter were found to play a role in hemodynamic changes in an animal model of IIH [21] and are

also strongly correlated with anxiety in various patient groups [22]. Future studies may try to verify whether anxiety is an etiologic or prognostic factor in IIH, or whether it results from this disorder. Nevertheless, should the results observed in the present study be replicated in a prospective design and demonstrate that anxiety predicts future painful episodes, interventions aimed at reducing anxiety symptoms may improve the prognosis and well-being of patients with IIH.

Although over-general memory biases were found in both the IIH and headache controls compared to healthy controls, this may be due to different causes. In the IIH group, an over-general memory bias may result from intracranial hypertension causing mild brain damage that may interfere with accessing or retrieving memories. Alternatively, biological factors common to both IIH and other headaches, such as pain-induced subclinical inflammation, may account for memory problems and anxiety. Reichenberg and colleagues [23] found that subclinical inflammation elicited by a small peripheral dose of lipopolysaccharide induced significant reductions in memory and elevations in anxiety in healthy volunteers. This may apply to IIH patients as well and may partly explain our findings.

The major methodologic limitations of the present study are its limited sample size and its cross-sectional design, and results should therefore be interpreted with caution. In addition, our argument that anxiety may be especially severe in IIH needs to be considered carefully because the IIH group did not report statistically significantly higher anxiety scores than did the headache controls but only more severe anxiety levels than found among healthy controls. An additional limitation of the present study is that the headache controls had a lower mean BMI than did IIH patients, which could reflect the fact that the former patients were not selected to match IIH in weight as were the healthy controls. These variables need to be considered in future studies. Nevertheless, this study dealt with a condition that has been investigated mainly from the medical/physiological perspective. Recently, there has been heightened awareness and empiric evidence that quality of life, depression and anxiety are critical outcomes of medical treatment and have prognostic importance in several diseases [24,25]. We recommend that psychological tests enter in the evaluation of IIH patients. According to our results, obesity alone, a well-known risk factor for IIH, may not fully explain the association between anxiety and IIH.

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