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ORIGINAL

Depression and anxiety are not related to nummular headache

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Abstract Nummular headache (NH) is a clinical picture characterized by head pain that is exclusively felt in a round, elliptical, or oval area of the head. Although there is evidence supporting an organic origin for NH, some authors question this origin, hypothesizing a potential role for psychological factors. Our aims were to investigate the differences in anxiety and depression between NH patients and healthy controls, and to analyse if these conditions were related to pain parameters in NH patients. The Beck depression inventory (BDI-II) and the trait anxiety scale from state-trait anxiety inventory (STAI) were administered to 26 patients with NH and 34 comparable matched controls. No significant interactions between group (NH patients, controls) in either depression ($U = 391$; $p = 0.443$) or anxiety levels ($U = 336$; $p = 0.113$) were found. Both groups showed similar scores in the BDI-II (patients: 3.9 ± 2.9; controls: 3.46 ± 3.15) and STAI (patients: 17.23 ± 10.3; controls: 13.5 ± 7.9). Moreover, neither depression nor anxiety showed association with mean pain intensity, pain intensity in exacerbations, size of pain area, or pain frequency. Our study demonstrated that self-reported depression and anxiety were not related to the presence of NH. Further, longitudinal studies are still needed to elucidate the role of mood state in the course of NH.

Keywords Nummular headache · Depression · Anxiety

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Introduction

Nummular headache (NH) is a well-defined clinical picture characterized by local pain that is exclusively felt in a round, elliptical, or oval area of the head, typically 1–6 cm in diameter [1]. The symptomatic area does not change in shape and size with time and may show a variable combination of symptoms and signs of sensory dysfunction, such as hypoesthesia, paresthesia, dysesthesia, or tenderness [2, 3]. NH was first described in 2002 [1] and it was subsequently included in the appendix of the 2nd edition of the International Classification of Headache Disorders [4]. Several clinical series have been published since then [5–9], but population epidemiological data are still lacking.

The aetiology and pathogenesis of NH are largely unknown, though it has been regarded as an *epicrania*, i.e. an "in situ" headache probably stemming from epicranial

tissues [10]. The confinement of pain and sensory symptoms to a small cranial area apparently reflects a non-generalized and rather limited disorder. In fact, there is some evidence supporting this hypothesis. For instance, NH patients did not show increased peri-cranial tenderness to palpation when compared to healthy control subjects [11]. Furthermore, evidence of increased mechanical pain sensitivity (lower pressure pain thresholds) restricted to the symptomatic area in NH has been found [12]. Finally, we have demonstrated that patients with NH show similar topographical pressure pain sensitivity maps of the head when compared to healthy controls, with local decrease of PPT levels restricted to the symptomatic zone in comparison with the non-symptomatic symmetrical point [13].

The characteristics of clinical observations suggest a non-psychogenic origin, not of NH, since the majority of patients with NH have no previous diagnoses of another psychopathological disease [6]. Further, there are few patients who reported a mild head trauma previous to the onset of NH, establishing a possible relationship between the trauma and NH, so the relation with post-traumatic stress seems very unlikely [1, 6]. Despite all the evidences supporting an organic source for NH, Cohen has questioned the organic origin of NH, suggesting a potential role for psychological and psychiatric factors. Indeed, he reported some evidence of depression, bipolar disease, and anxiety in a few patients with NH. However, such disturbances were only present in 4 patients out of 10, and their psychiatric diagnoses were not conclusive [14]. The association between anxiety and depression with different headaches has been explored in the peer-reviewed literature [15, 16]. This association has been focussed mainly in tension type headache [17] and migraine [18, 19]. To the best of authors' knowledge no study has previously investigated the association of self-reported anxiety and depression with NH. Our aims were to investigate the differences in anxiety and depression between patients with NH and healthy controls, and to analyse if these states were related to clinical pain parameters in NH. Our hypothesis was that neither anxiety nor depression was significantly different between NH patients and healthy controls and that these psychological conditions were not related to headache clinical parameters.

Materials and methods

Subjects

As much as 26 patients with NH, 16 men and 10 women, aged from 28 to 84 years old (mean: 52 ± 15 years), and 34 comparable healthy controls, 16 men and 18 women, aged from 24 to 89 years old (mean: 44 ± 18 years), participated in this study. There were no significant differences for gender ($p = 0.2$) and age ($p = 0.1$) between groups. NH patients were recruited from the Neurology Department of Fundación Hospital Alcorcón. The diagnosis of NH was made when head pain was exclusively felt in a small rounded or elliptical area of the head, and not attributed to another disorder. Patients had to outline the painful area, which was also drawn in detail by palpation and by means of a pointed probe. Various signs of sensory dysfunction, i.e. hypoesthesia, hyperesthesia, or allodynia were usually present in the symptomatic pain area. Otherwise the neurological examination was normal in all patients. There were no abnormalities in routine blood analyses with ESR or urine analyses. A CT scan or MRI of the head was invariably performed and did not show structural lesions. Other concomitant primary or secondary headaches were excluded in all cases. Healthy controls were subjects from the same area who responded to a local announcement. They had no history of any primary headaches, chronic pain conditions, or psychiatric disorders. They were matched as much as possible with NH patients for both age and sex. Ethical approval was granted by the local Ethics Committee. An informed consent was obtained from all the participants, and all the procedures were conducted according to the Declaration of Helsinki.

Depression: Beck depression inventory (BDI-II)

The BDI-II is a 21-item self-report measure assessing affective, cognitive, and somatic symptoms of depression [20]. Patients choose from a group of sentences which best describes how they have been feeling in the past 2 weeks. For example, to assess sadness, patients can choose either: "I do not feel sad", "I feel sad much of the time", "I am sad all the time", or "I am so sad or unhappy that I can't stand it". Higher scores indicate higher levels of depressive symptoms [18]. The BDI-II has shown good internal consistency (alpha coefficient 0.90) and adequate divergence and divergent validity [21].

Trait-anxiety: state-trait anxiety inventory (STAI)

The STAI is a self-report assessment device which includes separate measures of state and trait anxiety [22]. In the present study, the trait-anxiety subscale was used, which denotes relatively stable anxiety proneness and refers to a general tendency to respond with anxiety to perceive threats in the environment. Sample items include "I feel well", "I am a quiet and calm person", or "I am a stable person". Participants use a four-point response scale ranging from "almost never" to "almost always", indicating the extent to which they experience each emotion. The trait-anxiety subscale of the STAI questionnaire has

shown good internal consistency (alpha coefficient 0.83). Higher scores indicate greater trait anxiety [22].

Statistical analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS-16.0). For quantitative data, mean, standard deviation (SD), and 95% confidence intervals (95% CI) are given. Previously, outlier analysis and non-normality tests were conducted. Given the presence of non-normality, the decision was made to deal with non-normal data using Mann–Whitney *U* test for the association analyses at univariate level, and logistic regression for the multivariate analysis of association [23]. Logistic regression is a multivariable method devised for dichotomous outcomes [24] and particularly appropriate for models involving disease states [25]. Hierarchical logistic regression method was employed in order to control potential confounding variables (age and sex) in a first block, and to analyse depression and trait anxiety in a second and third blocks. To test the association between mood state (i.e. depression and anxiety) and headache severity, linear regression analyses were done for continuous variables (mean pain intensity, pain intensity in exacerbations, and size of pain area) and discriminate analysis for categorical variables (pain frequency).

Results

Headache features

Within the patient group, the length of headache history was 45.5 ± 49.8 months (95% CI 25.7–65.4 months). As much as 19 patients reported pain confined to a circular area of 1–4 cm, and the remaining 7 patients had pain in a single elliptical area with diameters of 1.5–6 × 2–9 cm. The symptomatic area was located in parietal ($n = 7$), temporal ($n = 6$), occipital ($n = 4$), frontal ($n = 4$), and temporo-parieto-occipital ($n = 5$) regions. The right side was affected in 16 patients and the left side in 10. The temporal pattern was chronic and continuous in 9 patients, chronic but intermittent in 12 patients, and episodic in the remaining 5. Baseline pain intensity was mild ($n = 6$), moderate ($n = 12$), or severe ($n = 8$), with a mean pain intensity of 5.2 in a 10-point scoring rate (95% CI 4.2–6.2). Exacerbations upon the background mean pain—either spontaneous or precipitated by stimuli on the symptomatic area—were reported by 20 patients (pain intensity in exacerbations: 7.3, 95% CI: 6.3–8.2).

Preliminary analyses

Initially, both DfBetas and Mahalanobis distances (critical value $\chi^2 = 13.81$, $p < 0.001$) outlier analyses were conducted, and 2 outliers emerged using the latter criterion. Skewness and kurtosis indices were calculated for each variable separately for both groups. Troublesome skewness and kurtosis values were evident for depression and for trait anxiety within the healthy sample (see Table 1).

Association between depression, anxiety, and presence of nummular headache (NH)

No significant interactions between group (patients, controls) and depression ($U = 391$, $p = 0.443$) or between group and trait anxiety ($U = 336$, $p = 0.113$) were found in the univariate analyses. The results of the logistic regression showed no association between any of the variables in the model and group, neither at individual level nor at multivariate level. Table 2 shows Wald statistics (test for the null hypothesis that a coefficient in the regression model is zero), betas, and odds ratios for each variable. Chi-square values for the blocks and for the final model were non-significant (block 1: $\chi^2 = 4.600$, *df* 2, $p = 0.10$; block 2: $\chi^2 = 0.243$, *df* 1, $p = 0.622$; block 3: $\chi^2 = 1.439$; *df* 1; $p = 0.230$; and final model: $\chi^2 = 6.281$; *df* 4; $p = 0.179$).

Association between depression, anxiety, and headache severity

In regression analyses, once socio-demographic (sex and age) and medication variables (analgesic, antidepressant, and anxyolitic medication) were controlled, neither depression nor anxiety showed association with mean pain intensity (depression: $\beta = 0.18$, $t = 0.086$, $p = 0.933$; trait-anxiety: $\beta = 0.455$, $t = 1.642$, $p = 0.116$), pain

Table 1 Descriptive statistics for anxiety and depression in patients with nummular headache and healthy controls

Sample	Variable	Mean	SD	95% CI	Skewness	Kurtosis
Nummular headache	Depression	3.89	2.89	2.72–5.05	0.372	−0.636
	Trait-anxiety	17.23	10.29	13.07–21.38	0.148	0.456
Healthy controls	Depression	3.47	3.15	2.37–4.57	1.06	0.744
	Trait-anxiety	13.47	7.90	10.71–16.23	1.03	0.611

Table 2 Regression coefficients, Wald statistics and Odds Ratios of independent variables

Block	Variable	B	Wald	*df*	*p* value	OR	95% CI
1	Sex	0.485	0.786	1	0.375	1.62	0.55–4.74
	Age	0.029	3.155	1	0.080	1.03	0.99–1.06
2	Sex	0.566	0.971	1	0.324	1.76	0.57–5.42
	Age	0.028	2.769	1	0.096	1.03	0.99–1.06
	Depression	0.047	0.244	1	0.622	1.05	0.87–1.26
3	Sex	0.561	0.940	1	0.332	1.75	0.56–5.44
	Age	0.025	2.187	1	0.139	1.02	0.99–1.06
	Depression	−0.005	0.002	1	0.966	0.99	0.81–1.23
	Trait-anxiety	0.041	1.362	1	0.243	1.04	0.97–1.12

intensity in exacerbations (depression: $\beta = -0.350$, $t = -1.581$, $p = 0.148$; trait-anxiety: $\beta = -0.948$, $t = -1.913$, $p = 0.088$) or size of pain area (depression: $\beta = -0.090$, $t = -0.422$, $p = 0.677$; trait-anxiety: $\beta = -0.013$, $t = -0.047$, $p = 0.963$). Discriminate analysis showed lack of association between depression and anxiety with pain frequency (1 to 2 function: Wilks' Lambda = 0.887, $\chi^2_4 = 2.95$, $p = 0.567$; 2: Wilks' Lambda = 0.998, $\chi^2_1 = 0.48$, $p = 0.826$).

Discussion

The aims of the present study were to analyse the association between anxiety and depression and NH, and to evaluate if the level of anxiety/depression was related to clinical parameters of NH. With regard to the first objective, our results showed that self-reported depression and anxiety do not appear to be distinct features of NH. For the first time, we have shown that NH is not associated to either depression or anxiety. The scores of both NH patients and controls were within normal ranges. Accordingly, anxiety and depression do not seem to put people at different risk of being afflicted by NH than people without this kind of mood states. Given that anxiety and depression are the most prevalent mood state disorders [26], this absence of association would constitute first evidence favouring the hypothesis that NH is not a psychogenic disorder.

Regarding our second objective, we found no relation between depressive symptoms or anxiety levels and headache clinical parameters in NH patients. Once the effects of socio-demographic characteristics and medication were controlled, neither the intensity of the pain nor the size of the pain area was associated with patient's mood state. These results further support that self-reported depression and anxiety are not related to the presence of NH. Moreover, the lack of relation between level of depression and anxiety and headache severity suggests that mood states do not play a relevant role in the maintenance of NH, in contrast to other headaches like tension type headache [17] or migraine [18, 19].

Finally, we should recognize some limitations in this study. First, the sample size ($n = 26$) was relatively small, though it is the greatest reported sample, and it seems sufficiently representative of this headache condition. Second, a correlational design is not a clear-cut method to assess a pathogenic relationship between psychological variables and headache. Third, only depression and anxiety were investigated, but other psychological or personality variables may influence pain perception. Future studies with greater samples and follow-up designs may further elucidate the influence of psychological variables on the course of NH.

Conclusions

According to this study, NH is not associated with depression and anxiety, since patients with NH showed similar mood states to those of healthy controls. Furthermore, in NH patients neither depressive symptoms nor anxiety levels were related to headache clinical parameters. Our findings support that depression and anxiety do not have a significant influence on the presence or the severity of NH.

Conflict of interest None.

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