Research article
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Relationship of intensity and special characteristics of migraine to depressive and anxious features

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Mood and pain are interrelated to each other in a mutual and complex manner. Patient populations in headache clinics exhibit more emotional disturbance than general practice patients. Nonetheless, the degree of psychological illness among headache patients is less than maybe found in psychiatric outpatients. However, it is a fact that several psychiatric disorders appear to be comorbid with primary headache syndromes such as migraine. Still, prospective standardized studies are sparse. We aimed to investigate whether migraine per se or specific migraine characteristics are associated to depression and anxiety. In a single center study (Department of Neurology of the University of Athens) migraineurs were asked for several headache features such as pain intensity, attack frequency, average attack duration, prodromal symptoms and the presence of aura. We assessed 50 consecutive headache patients who were referred to our headache outpatient clinic. Patients diagnosed with non-migraine syndromes, mixed non-migraine and migraine syndromes, or patients with previously diagnosed systemic disease known to precipitate psychiatric disorders (such as systemic lupus erythematodes) were excluded from the study. Furthermore, we did not include any subjects who were already on antidepressive or other psychiatric medication. Twenty four patients met the inclusion criteria. The data were then correlated with scores obtained by the Beck Depression Inventory and the Hamilton's scales for Depression and Anxiety. Our results showed an increased frequency of mild and moderate depression compared to what was expected from the normal population which is in line with past observations on headache patients. In an analogous manner, mild and moderate anxiety appeared more frequently among migraineurs than healthy subjects. However, we did not find any significant relation between depression or anxiety and parameters such as pain intensity, monthly attack frequency, attack duration, presence or absence of aura, appearance of pre-ictal prodromal symptoms and migraine career duration (age of assessment minus age of migraine onset). These findings suggest that migraine, although often comorbid with depression and anxiety, has no specific headache characteristics causally related to mood abnormalities. Larger samples will be required in future studies to address the question of a link between more specific mood and mental disturbances with primary headache syndromes.

Key words: Migraine, primary headaches, depression, anxiety

Introduction

It is widely accepted that emotional disorders promote pain and pain promotes emotional disorders. Patient populations in headache clinics exhibit more emotional disturbance than general practice patients. Nonetheless, the degree of psychological illness among headache patients is less than maybe found in psychiatric outpatients.[1]

An interesting finding is that certain features of the abnormal sensory processing prevalent among migraineurs proved to be manifestations of concomitant depressivity.[2] The comorbidity of headache and depression might suggest commonalities in the pathophysiology of these disorders, in particular a dysfunction of the serotoninergic system.[3] This fact is also reflected by the more or less successful use of antidrepressants with serotoninergic mode of action in headache prophylaxis.[4]

Although the evidence of the association of headache with mood abnormalities is robust, studies on the correlation of specific headache characteristics with depression and anxiety are sparse.[5]

In the present study we investigated the link between specific migraine features such as pain intensity, the presence of aura and mean attack duration and mood abnormalities measured by standard questionnaires.

Material and method

Three questionnaires were devised as the basic instruments of the survey: The Beck Depression Inventory (BDI),[6] the Hamilton Anxiety Scale (HAM-A)[7] and the Hamilton Depression Rating Scale (HAM-D).[8] Migraine was diagnosed according to the Second Edition of the International Classification of Headache Disorders.[9] We assessed 50 consecutive headache patients who were referred to our headache outpatient clinic. Patients diagnosed with non-migraine syndromes, mixed non-migraine and migraine syndromes, or patients with previously diagnosed systemic disease known to precipitate psychiatric disorders (such as systemic lupus erythematodes) were excluded from the study. Furthermore, we did not include any subjects who were already on antidepressive or other psychiatric medication. All patients gave written informed consent for participation in the study which was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of the Department of Neurology of the University of Athens. Beside the above mentioned psychometric tests, headache characteristics were obtained by one neurologist who interviewed the patients. The parameters under study were: Age of migraine onset, migraine "career" (age at the time of assessment minus are of migraine onset), average migraine attack frequency (events per month) in the last year, average migraine intensity-categorial (three-scaled variable: mild, moderate, severe), average migraine intensity-continuous (according to the visual analog scale-VAS), average attack duration, presence or absence of aura, presence or absence of prodromal symptoms (such as irritability, excessive sleepiness, craving for certain food, altered mood, depression or euphoria, fatigue, yawning neck muscle stiffness, dizziness, hot ears, constipation or diarrhoea, increased or decreased urination and other visceral symptoms),[10] and the level of education (years of education).

Data analysis was performed using linear regression analysis or analysis of variance (ANOVA) were appropriate. Significance was set to 0.05.

Results

Twenty four migraine patients (21 females, age range 21 to 69 years) met the criteria presented in Methods and took part in the study. Patient data and clinical characteristics are given in table 1. All migraineurs had concordant results in the BDI, the HAM-D and the HAM-A scale. Linear regression analysis showed a significant correlation between BDI and HAM-D (R^2=0.227, F= 5.585, p<0.05), BDI and HAM-A (R^2= 0.202, F= 4.818, p<0.05) and HAM-D and HAM-A (R^2= 0.529, F= 22.429, p<0.001). Mean BDI score was 8.2 (±6.4) (range 0–23) and the majority of the patients were categorized in the lowest level of depression (low level depression: 86.4%, moderate depression: 13.6%, significant depression: 0%) (table 2). On the HAM-A scale subjects scored on average 8.9 (±8.0) (range 0–29) and most of them were categorized as normal (normal: 73.9%, mild anxiety: 17.4%, moderate anxiety: 8.7%, significant anxiety: 0%) (table 3). Finally, the mean HAM-D score was 7.1 (±4.6) (range 0–21) and most migraineurs fell in the category of "normal" (normal: 54.5%, mild depression: 36.5%, moderate depression: 4.5%, severe depression: 4.5%, very severe depression: 0%) (table 4) .

Table 1. Patient's demographic and clinical characteristics

Number of migaineurs	24
Female gender	21 (87.5%)
Migraine with aura	6 (25%)
Prodromal symptoms	5 (20.8%)
Age range (years)	21–69 (mean: 44.6, SD: 12.7)
Education (years)	6–23 (mean: 13.4, SD: 4.6)
Age of migraine onset (years)	7-36 (mean: 18.3, SD: 7.6)
Attack frequency (episodes per month)	0.33–25 (mean: 5.1, SD: 5.2)
Mean attack duration (hours)	2–120 (mean: 27.3, SD: 26.6)
Attack intensity	low=0 (0%), moderate=7 (29.2%), high=17 (70.8%)
VAS	5–10 (mean: 7.5, SD: 1.7)

Table 2. BDI score and disease severity categorization (N=22). Low level depression: 0–16, moderate depression 17–30, significant depression ≥31.

Low level depression	*Moderate depression*	*Significant depression*
19 (86.4%)	3 (13.6%)	0 (0%)

Table 3. HAM-A score and disease severity categorization (N=23). Normal: 0–13, mild anxiety 14–17, moderate anxiety 18–24, significant anxiety ≥25.

Normal	*Mild anxiety*	*Moderate anxiety*	*Significant anxiety*
17 (73.9%)	4 (17.4%)	2 (8.7%)	0 (0%)

BDI score was not significantly affected by average pain intensity during an attack [ANOVA: NS (non significant)], the presence or absence of aura (ANOVA: NS) or other prodromal symptoms (ANOVA: NS). The same was true for HAM-A scores (pain intensity ANOVA: NS, prodromal symptoms ANOVA: NS, aura ANOVA: NS) and HAM-D scores (pain intensity ANOVA: NS, prodromal symptoms ANOVA: NS, aura ANOVA: NS).

The lifetime duration of migraine (migraine career) had no effect on the BDI (linear regression, R^2=0.043, NS), the HAM-A (R^2=0.001, NS) or the HAM-D scale (R^2=0.048, NS). No effect showed also the reported level of education (for BDI: R^2=0.033, NS, for HAM-A: R^2=0.030, NS and for HAM-D: R^2=0.085, NS).

We also found no influence of the age of migraine onset (for BDI: R^2=0.002, NS, for HAM-A: R^2=0.040, NS ,and for HAM-D: R^2=0.029, NS).

Finally, neither attack frequency, nor attack average duration or intensity judged on the visual analog scale affected significantly the scores of BDI (frequency: R^2=0.030, NS, duration: R^2=0.073, NS and VAS: R^2=0.023, NS), HAM-A (frequency: R^2=0.092, NS, duration: R^2=0.072, NS and VAS: R^2=0.052, NS) and HAM-D (frequency: R^2=0.005, NS, duration: R^2=0.000, NS and VAS: R^2=0.001, NS).

Discussion

The clinical impression of migraineurs is often considered as anxious, depressive, neurotic or even hostile and rigid, although these features were not obtained by systematic studies.[11] There are convincing data supporting a comorbidity of depression and anxiety with migraine.[12–14] More detailed analyses suggested that the presence of neuroticism, as evaluated with the Eysenck Personality Questionnaire, might be more critical when considering psychiatric comorbidity in migraine.[15] Still, mood and mental abnormalities have not been systematically correlated with the core characteristics of migrainous pain.

In this study using the scoring on BDI and HAM-D we found a slightly increased frequency of mild and moderate depression compared to what was expected from the normal population[16]which is in line with past observations on headache patients.[12–14] This could point to a biological factor predisposing for both migraine and depression. Alternatively, the slightly increased depressivity indices in migraineurs could be the result of long standing suf-

Table 4. HAM-D score and disease severity categorization (N=22). Normal: 0–7, mild depression: 8–13, moderate depression: 14–18, severe depression: 19–22, very severe depression: ≥23.

Normal	*Mild depression*	*Moderate depression*	*Severe depression*	*Very severe depression*
12 (54.5%)	8 (36.4%)	1 (4.5%)	1 (4.5%)	0 (0%)

fering from chronic headaches, and could be related to disease duration, intensity and attack frequency. In an analogous manner, mild and moderate anxiety appeared more frequently among migraineurs than healthy subjects.[17] We further examined the association of specific features of migraine attacks to depression and anxiety. We did not find any significant relation between depression or anxiety and parameters such as pain intensity, monthly attack frequency, attack duration, presence or absence of aura, appearance of pre-ictal prodromal symptoms and migraine career duration (age of assessment minus age of migraine onset). Thus, although our sample as a whole exhibited slightly increased BDI, HAM-D and HAM-A scores, those patients that scored higher had no differences in any of the analyzed specific headache parameters. A possible interpretation is that migraine is comorbid with depression and anxiety in a categorial yes-or-no manner without showing a monotonous quantitative correlation between core features such as pain intensity or attack frequency with mood abnormalities. The lack of association of migraine features with mood favors the hypothesis of comorbidity and may serve as an argument against the hypothesis of depression emerging secondary to a long standing, intense, migraine career. It should be noted, however, that our results are based on a rather small sample. Hence, in order to verify the lack of correlation found in our analysis in a statistical robust manner, larger samples might be necessary. Nonetheless, the reported non significant results did not display any obvious trend. As can be derived from the results of Radat et al,[18] it is difficult to find robust prospective studies on this topic for comparison. These authors studied retrospectively 87 headache patients looking on depression and generalized anxiety among other psychiatric disorders. They clearly demonstrated that in retrospective analyses the International Classification Criteria for Headache Disorders (second edition)[9] are not strictly applied, a fact that significantly hampers causative comparisons between headache features and mood abnormalities.

The main weakness of our study was the relatively small sample size, partly dictated by the trade-off between detailed migraine feature assessment and the number of patients willing to participate and complete the study. Clearly, larger samples will be required in future studies to address the question of a link between more specific mood and mental disturbances such as anhedonia, coping difficulties and personality profiles[19]on the one side and primary headache syndromes on the other side.

Η σχέση της έντασης και των ειδικών χαρακτηριστικών της ημικρανίας με καταθλιπτικά και αγχώδη στοιχεία

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Η διάθεση και ο πόνος αλληλοεξαρτώνται και αλληλεπιδρούν με έναν σύνθετο τρόπο. Ο πληθυσμός των ασθενών που επισκέπτεται ειδικά ιατρεία κεφαλαλγίας παρουσιάζει μεγαλύτερο επιπολασμό διαταραχών διάθεσης σε σύγκριση με ασθενείς γενικών εξωτερικών ιατρείων. Ωστόσο, η βαρύτητα ψυχιατρικών νοσημάτων σε κεφαλαλγικούς ασθενείς φαίνεται ότι είναι σαφώς χαμηλότερη εάν συγκριθεί με τη βαρύτητα νόσου ασθενών σε αμιγώς ψυχιατρικά εξωτερικά ιατρεία. Είναι εντούτοις γεγονός ότι πλήθος ψυχιατρικών διαταραχών παρουσιάζουν συννοσηρότητα με πρωτοπαθή κεφαλαλγικά σύνδρομα όπως η ημικρανία. Ωστόσο ελεγχόμενες τυχαιοποιημένες μελέτες με αυτό το αντικείμενο σπανίζουν. Ο σκοπός της παρούσας εργασίας ήταν να μελετήσουμε εάν η ημικρανία καθ'

αυτή αλλά και εάν συγκεκριμένα ημικρανικά χαρακτηριστικά σχετίζονται με κατάθλιψη ή/και άγχος. Στη μονοκεντρική αυτή μελέτη (Ειδικό Ιατρείο Κεφαλαλγίας της Νευρολογικής Κλινικής του Πανεπιστημίου Αθηνών), ημικρανικοί ασθενείς βαθμολογήθηκαν βάσει τυποποιημένων ερωτηματολογίων ως προς παραμέτρους όπως ένταση του ημικρανικού πόνου, μηνιαία συχνότητα κρίσεων, μέση διάρκεια κρίσης, πρόδρομα συμπτώματα και παρουσία αύρας. Αξιολογήθηκαν 50 διαδοχικοί ασθενείς που είχαν παραπεμφθεί στο ειδικό ιατρείο κεφαλαλγίας της κλινικής μας. Ασθενείς που εν τέλει έλαβαν άλλες διαγνώσεις όπως μη-ημικρανική κεφαλαλγία, μικτή ημικρανική και μη-ημικρανική κεφαλαλγία, ή ασθενείς με συστηματικά νοσήματα που είναι γνωστό ότι προδιαθέτουν για κεφαλαλγίες (όπως ο ερυθηματώδης λύκος) αποκλείσθηκαν από τη μελέτη. Τέλος δεν συμπεριελήφθησαν ασθενείς που ελάμβαναν αντικαταθλιπτική ή άλλη ψυχιατρική αγωγή. Εικοσιτέσσερεις ασθενείς πληρούσαν τα κριτήρια και συμπεριελήφθησαν στις αναλύσεις. Τα δεδομένα συσχετίσθηκαν με τις βαθμολογίες της κλίμακας κατάθλιψης του Beck, της κλίμακας άγχους του Hamilton και της κλίμακας κατάθλιψης του Hamilton. Τα αποτελέσματά μας κατέδειξαν αυξημένη συχνότητα ήπιας έως μέτριας κατάθλιψης σε σύγκριση με την αναμενόμενη συχνότητα από τον γενικό πληθυσμό, εύρημα που ήταν σύμφωνο με παλαιότερες μελέτες. Αντίστοιχα, αυξημένη συχνότητα ήπιου και μέτριου άγχους αναδείχθηκε στους ημικρανικούς ασθενείς. Εντούτοις, δεν βρέθηκε καμία σημαντική συσχέτιση μεταξύ κατάθλιψης ή άγχους από τη μία πλευρά και παραμέτρων όπως ένταση του ημικρανικού πόνου, μηνιαία συχνότητα κρίσεων, διάρκεια κρίσης, παρουσία ή απουσία αύρας, εμφάνισης πρόδρομων συμπτωμάτων και ημικρανική «καριέρα» (ηλικία κατά την εξέταση μείον ηλικία έναρξης της νόσου). Το κύριο αποτέλεσμα ήταν ή απουσία οποιασδήποτε σημαντικής συσχέτισης των ημικρανικών παραμέτρων με τις μετρήσεις κατάθλιψης και άγχους. Τα ευρήματα αυτά υποδεικνύουν ότι η ημικρανία, πέραν της τεκμηριωμένης συννοσηρότητας με κατάθλιψη και άγχος, δεν παρουσιάζει ειδικά ημικρανικά χαρακτηριστικά σχετιζόμενα αιτιακά με τη διαταραχή της διάθεσης. Μελλοντικά είναι σκόπιμο να αναλυθούν μεγαλύτερα δείγματα προκειμένου να τεκμηριωθεί πιθανή συσχέτιση μεταξύ πιο συγκεκριμένων ψυχιατρικών διαταραχών με διάφορα πρωτοπαθή κεφαλαλγικά σύνδρομα.

Λέξεις ευρετηρίου: Ημικρανία, πρωτοπαθείς κεφαλαλγίες, κατάθλιψη, άγχος

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