Journal of Psychosomatic Research 79 (2015) 458–463

Contents lists available at ScienceDirect

Journal of Psychosomatic Research

Symptom dimensions of affective disorders in migraine patients

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ARTICLE INFO

Article history:
Received 24 April 2015
Received in revised form 8 September 2015
Accepted 27 September 2015

Keywords:
Migraine
Depression
Anxiety
Affective disorders
Comorbidity
Tripartite model

ABSTRACT

Objective: A strong association has been established between migraine and depression. However, this is the first study to differentiate in a large sample of migraine patients for symptom dimensions of the affective disorder spectrum.
Methods: Migraine patients (n = 3174) from the LUMINA (Leiden University Medical Centre Migraine Neuroanalysis Program) study and patients with current psychopathology (n = 1129), past psychopathology (n = 477), and healthy controls (n = 561) from the NESDA (Netherlands Study of Depression and Anxiety) study, were compared for three symptom dimensions of depression and anxiety. The dimensions —lack of positive affect (depression specific); negative affect (nonspecific); and somatic arousal (anxiety specific)— were assessed by a shortened adaptation of the Mood and Anxiety Symptom Questionnaire (MASQ-D30). Within the migraine group, the association with migraine specific determinants was established. Multivariate regression analyses were conducted.
Results: Migraine patients differed significantly ($p < 0.001$) from healthy controls for all three dimensions: Cohen's *d* effect sizes were 0.37 for lack of positive affect, 0.68 for negative affect, and 0.75 for somatic arousal. For the lack of positive affect and negative affect dimensions, migraine patients were predominantly similar to the past psychopathology group. For the somatic arousal dimension, migraine patients scores were more comparable with the current psychopathology group. Migraine specific determinants for high scores on all dimensions were high frequency of attacks and cutaneous allodynia during attacks.
Conclusion: This study shows that affective symptoms in migraine patients are especially associated with the somatic arousal component.

Introduction

Migraine and depression are both rated among the top 20 of most disabling disorders by the World Health Organisation [1]. Previous studies showed that persons with migraine have a fivefold higher risk of first-onset major depression than persons without migraine. In addition, persons with a lifetime depressive disorder have a threefold higher risk of first-onset migraine than persons without a depression diagnosis [2,3]. This bidirectional association suggests a shared etiology, which is supported by several studies indicating shared genetic factors in migraine and depression [4,5]. Besides depression, there is an association between anxiety disorders and migraine as well [6]. The economic impact of migraine is significantly compounded in patients with comorbid psychiatric conditions [7]. Understanding the mechanisms underlying the comorbidity is important in order to gain more insight into the mechanism of both migraine and depression/anxiety and to develop specific preventive treatments.

Previous studies in migraine defined depression using either categorical DSM-IV (Diagnostic and Statistical Manual of Mental Disorders) diagnoses or self-reported questionnaires. However, although DSM-IV categories are of great use in clinical practice, they have arbitrary boundaries, and show much overlap and comorbidity. Moreover, high heterogeneity of symptoms and severity within one diagnostic category is possible [8]. Depression and anxiety severity scales based on self-reported questionnaires also have limitations: two similar scores may indicate different clinical subtypes due to the heterogeneity of the covered range of symptoms as multidimensionality of symptomatology is not taken into account. Consequently, measuring affective disorders with these tools may provide suboptimal phenotyping for clinical and biological (e.g. genetic) research. Thus, in a research setting, it may be more appropriate to study dimensions of depressive and anxiety

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http://dx.doi.org/10.1016/j.jpsychores.2015.09.014
0022-3999/

symptoms in migraine patients as these seem to reflect more homogeneous disease entities.

Several attempts have been made to develop a dimensional model for depression. Within a dimensional approach, a patient is described in terms of scores on a range of coexisting different symptom domains, and not in terms of presence or absence of psychopathology [9]. A well-known model is the tripartite model that accounts for the overlap between depression and anxiety [10]. In this model the broad symptom dimension of negative affect covers symptoms of general psychological distress (e.g. lack of concentration or pessimism). High negative affect has often been indicated as a central clinical feature of both anxiety and depression, accounting for the high rates of comorbidity [11–14]. The lack of positive affect covers anhedonic symptoms, which are mainly specific for depression. The somatic arousal dimension comprises symptoms of hyperarousal which are anxiety specific.

The aim of the present study is to investigate whether migraine patients are characterized by different symptom patterns of depressive and anxiety symptomatology compared with healthy controls, and persons with a current or past depression and/or anxiety disorder. Furthermore, we investigate which migraine specific characteristics are associated with the affective symptom dimensions of the tripartite model.

Methods

Study design and population

Four groups were differentiated for comparison: i) migraine patients, ii) healthy controls without psychopathology and without migraine, iii) persons with 'current psychopathology', a 6-month diagnosis of major depressive disorder, dysthymia or anxiety disorder and without migraine, and iv) persons with 'past psychopathology', a lifetime (but no current) diagnosis of major depressive disorder, dysthymia or anxiety disorder and without migraine.

Migraine patients were collected as a part of the Leiden University Medical Centre Migraine Neuro-analysis Programme (LUMINA) project, a well-defined web-based migraine population, the details of which are reported elsewhere [15]. The LUMINA project is an ongoing cohort study, designed to investigate migraine, its comorbidities, and its long-term course. Participants were Dutch adults aged 18 to 74 years with migraine with or without aura according to the International Classification of Headache Disorders (ICHD-III beta) criteria [16]. The LUMINA study population recruitment is still ongoing, but we included participants recruited between 2008 and 2011. Participants were recruited via nationwide public announcement, advertising in lay press and via the research website, inviting migraine patients to participate in migraine research (see supplementary). In addition, patients attending our dedicated headache clinic were also invited to participate in this survey. This latter group, however, comprises only 3.5% of the total LUMINA population. On the website, patients were asked to fill out a screening questionnaire that has been validated priorly [17]. Firstly, if patients fulfilled the screening criteria, they received a web-based extended migraine questionnaire, based on the ICHD-III beta criteria [15,16]. This questionnaire was previously validated by a semi-structured telephone interview in 1038 patients who had filled out the extended migraine questionnaire [15]. The specificity of the questionnaire was 0.95. Participants without the needed internet skills could fill out the questionnaires on paper. Secondly, all applicable migraine patients were selected for a web-based questionnaire on symptoms of affective disorders. Patients were enrolled in this study after completion of the affective disorders questionnaire. The response rate to the depression questionnaire was 80%.

Healthy controls and patients with psychopathology were derived from The Netherlands Study of Depression and Anxiety (NESDA), which is an ongoing cohort study designed to investigate the long-term course and consequences of depressive and anxiety disorders. Participants were adults aged 18–65 recruited from community (19%), general practice (54%), and secondary mental health (27%) facilities. A total of 2981 participants, including persons with current or past depressive and/or anxiety disorders and healthy controls, were assessed at baseline between 2004 and 2007. Exclusion criteria for the NESDA study were inability to speak Dutch and a known clinical diagnosis of other psychiatric conditions, such as bipolar disorder, obsessive-compulsive disorder, severe addiction disorder, psychotic disorder or organic psychiatric disorder. A detailed description of the NESDA study design can be found elsewhere [18]. In summary, the baseline assessment was comprised of a face-to-face interview, including a standardized diagnostic psychiatric interview, a medical assessment, computer tasks, written questionnaires, and biological measurement. For the current study, migraine patients, identified through a screening migraine questionnaire largely in accordance with the ICHD-III beta criteria for migraine (described in detail elsewhere) [19], were excluded from the NESDA population.

The LUMINA project was approved by the medical ethics committee of the Leiden University Medical Centre. The NESDA research protocol was approved by the Ethical Committee of participating universities. All respondents provided written informed consent.

Measurements

In the NESDA study, the presence of psychiatric disorders was determined by using the Composite International Diagnostic Interview (CIDI, version 2.1). The CIDI is a standardized psychiatric diagnostic interview that follows the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) criteria to establish diagnoses. The CIDI is a highly reliable and valid instrument for assessing depressive and anxiety disorders [20] and was administered by specially trained research staff. Psychopathology (major depressive disorder, dysthymia, anxiety disorder) status was categorized as follows: current diagnosis (i.e., past 6 months), past diagnosis (i.e., lifetime diagnosis but not in the past 6 months), controls (no lifetime diagnosis). In both the LUMINA and NESDA studies, a 30-item adaptation of the Mood and Anxiety Symptoms Questionnaire (MASQ-D30) was used to measure the tripartite dimensions of depression. On the MASQ-D30, participants were asked to rate to what extent in the past week they had experienced 'feelings, sensations, problems and experiences that people sometimes have' on a 5-point scale, with 1 being 'not at all' and 5 being 'extremely'. The three 10-item subscales are 'general distress' (lack of positive affect), 'anhedonic depression' (negative affect) and 'anxious arousal' (somatic arousal). The MASQ-D30 scales showed adequate psychometric characteristics and showed good reliability and validity within the NESDA study [21].

In the LUMINA population, we predefined migraine specific characteristics to be examined: migraine subtype (migraine with or without aura), frequency (migraine days per year), and cutaneous allodynia. Cutaneous allodynia, the perception of pain in response to non-noxious stimuli to the normal skin, is a common feature accompanying migraine attacks. A significant part of migraine patients experience an increased sensitivity of the skin for common daily activities during attacks, such as combing of hair, taking a shower, touching the periorbital skin, shaving, or wearing earrings during migraine attacks. Cutaneous allodynia was measured using a validated questionnaire [22]. These migraine specific characteristics are shown to be associated with depression [23,24].

Data analysis and statistics

Baseline characteristics were reported as mean ± standard deviations (SD) or percentages. Analysis of covariance (ANCOVA) models were used to test the association between the four different groups and MASQ-D30 symptom profiles, adjusting for gender and age. Post-hoc analyses were run in case of significant findings, performing ANCOVA analysis to test for differences between the migraine group and the three remaining