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Cluster headache and anxiety: Results of the EUROLIGHT cluster headache project – An Internet-based, cross-sectional study of people with cluster headache

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Abstract

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Keywords

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Introduction

Anxiety disposes towards defensive behaviours.[1–4] Inducing preoccupation, restlessness, irritability, hypervigilance and a sense of fear, it aims at increasing the odds of surviving under threat.[1–4]

The extent of objective danger necessary to provoke anxiety varies individually. Very low thresholds are the prerequisite for anxiety disorders that are characterised by a strong propensity towards defensive behaviour.[1] They impose a tremendous burden that often adds to that of co-morbid diseases.[5]

Cluster headache (CH) and anxiety frequently co-occur in the same individuals[6–8]; Jorge et al. found that an anxiety disorder often preceded the onset of CH.[6] While we do not

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Table 1. Numbers of participants and demographic characteristics per country.[a]

Country	Participants. *n* (%)	Sex (% male)	Age (years), mean (SD)	Employed or student (%)	Married or living with partner (%)
Austria	34 (3.1)	64.7	38.1 (9.0)	88.2	73.5
Belgium	29 (2.7)	69.9	42.5 (9.2)	82.1	85.2
Czech Republic	–	–	–	–	–
Denmark	11 (1.0)	63.6	41.3 (15.8)	72.7	63.6
Finland	46 (4.2)	57.8	42.9 (13.0)	73.9	78.3
France	210 (19.3)	72.9	39.4 (10.3)	79.3	71.4
Germany	264 (24.3)	71.9	43.2 (9.7)	82.2	71.3
Ireland	5 (0.5)	60.0	47.0 (11.6)	80.0	100
Italy	81 (7.4)	70.4	40.2 (10.3)	91.3	85.2
Luxembourg	1 (0.1)	100	46	100.0	100
The Netherlands	16 (1.5)	62.5	40.9 (13.2)	81.3	68.8
Norway	18 (1.7)	61.1	39.8 (10.4)	81.3	77.8
Poland	8 (0.7)	62.5	46.8 (7.7)	75.0	50.0
Spain	90 (8.3)	78.9	39.1 (9.2)	76.7	78.4
Sweden	43 (3.9)	62.8	43.0 (13.2)	76.7	78.0
Switzerland	42 (3.9)	78.6	40.1 (11.2)	85.4	69.0
United Kingdom	191 (17.5)	62.8	46.3 (11.2)	70.9	71.4
Total	1089	69.5	42 (11)	79.5	73.9

HADS-A: anxiety subscale of the Hospital Anxiety and Depression Scale; SD: standard deviation.
[a]Even though participants from the Czech Republic had filled in the questionnaire,[9] none of them completed the HADS-A.

know whether one condition causes the other, we expect them to influence each other.

The aim of this study is to test the hypothesis of anxiety affecting the burden of CH.

Methods

Design and sampling methods have already been published.[9,10] Patient associations and national headache societies in several European countries were notified about the study and asked to inform patients. The study was cross-sectional and Internet-based. A self-reported diagnosis of CH and a residency in a European country were required for participation. Before completing the questionnaire, patients were informed about the purpose of the survey and asked to provide informed consent.

Participants were included into further analysis if the diagnosis could be validated according to the criteria published by the International Headache Society.[11] The survey consisted of a modified version of the EUROLIGHT questionnaire.[9,12] If at least one attack had occurred within 30 days prior to the survey participants with episodic CH were considered 'in-bout'. The National Research Ethics Committee Luxembourg had approved the study.

Anxiety was measured with the anxiety subscale of the Hospital Anxiety and Depression Scale (HADS-A)[13]; scores below eight points indicate the absence of an anxiety disorder.[14]

Statistical analysis

We analysed the data using SPSS version 25 (IBM, USA). Categorical variables are described as proportions, and continuous variables as means and standard deviations. We used a two-tailed χ^2 test to test for association. Correlation between ordinate variables was measured using two-tailed Spearman's rho. The extent of association in contingency tables was measured calculating odds ratios (OR) and their 95% confidence intervals (CIs). Sixteen p values were corrected for multiple testing according to Bonferroni; values below 0.05 were considered as significant. We will refer to missing data as 'not reported' (n.r.).

Results

The questionnaire was completed by 1514 individuals.[9] The diagnosis of CH was validated in 1165 participants, of whom 1089 (93.5%) responded all items of the HADS-A, and data of only these participants were taken for further analysis. Chronic CH was present in 233 participants (21.4%).

Mean age was 42 $\pm$ 11 years (five n.r.), 69.5% of the participants were male (755 of 1087; 2 n.r.), 73.9% were married or living with a partner (788 of 1067; 22 n.r.), and 79.5% were studying, employed or self-employed (851 of 1071; 18 n.r.). Table 1 summarises demographic data.

The median score reached in the HADS-A was eight; Figure 1 depicts the frequency distribution.

Ictal burden

We refer to stresses and strains that occur during an attack as 'ictal burden'; it is opposed to the 'interictal burden' that is present in the absence of acute headache. Interictal burden may occur inside as well as outside cluster bouts.

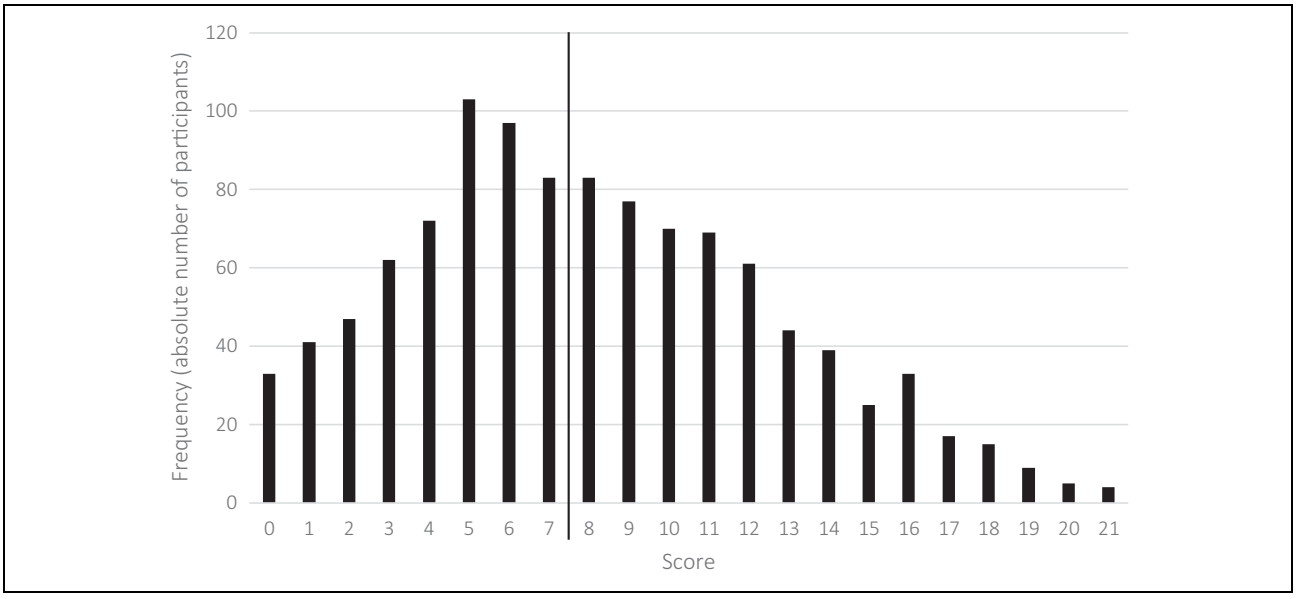

Figure 1. Frequency distribution of the scores in the anxiety subscale of the Hospital Anxiety and Depression Scale; the vertical black line indicates the cut-off above which an anxiety disorder is assumed. Eight or more points were reached by 50.6% of the participants.

The score of the HADS-A correlated negatively with disease duration ($r = -0.09$, $p = 0.033$) and positively with the number of attacks in the last 30 days ($r = 0.17$, $p < 0.001$). Scores of eight and more occurred more frequently in chronic CH than in episodic ($p = 0.037$, OR = 1.58, 95% CI 1.18–2.12; 50 n.r.). The frequency of scores above the threshold did not differ significantly between the in-bout and the out-bout period in episodic CH ($p = 0.974$, OR = 0.76, 95% CI 0.57–1.01).

About one-third (36.2%; 384 of 1062; 27 n.r.) of the participants reported having hurt themselves during an attack. This was more common among those in whom the HADS-A indicated an elevated anxiety level (OR = 2.63, 95% CI 2.03–3.41, $p < 0.001$, 27 n.r.). In addition, patients scoring eight or more were significantly more likely to have sought medical advice of a general practitioner, a headache specialist, or in an emergency department within the last 12 months (OR = 1.85, 95% CI 1.45–2.37, $p < 0.001$). Furthermore, in the group of participants taking preventive drugs (50.1%; 546 of 1089), anxiety levels above the threshold were more common (OR = 1.55, 95% CI 1.22–1.97, $p = 0.01$).

Inter-ictal burden

Avoiding telling others about CH was reported by 51.1% of the participants (542 of 1060; 28 n.r.); 77.5% (815 of 1051; 28 n.r.) felt that their family and friends accept and understand their disease, and 54.2% (456 of 842; 247 n.r.) did not feel understood by colleagues and employers.

Reduced earnings and an impaired career due to the disease were reported by 58.0% (580 of 1000; 89 n.r.) and 58.6% (624/1064; 25 n.r.), respectively; 13.2% (134 of 1014; 75 n.r.) recounted a failed relationship, and 13.6% (140 of 1028; 61 n.r.) declared having had less or no children because of CH. The association between anxiety levels and inter-ictal burden is summarised in Figure 2.

Discussion

A high level of anxiety affected half of the participants of this study. It correlated, though weakly, with both the number of the attacks and disease duration. Given the small correlation coefficient, it is unlikely that anxiety is just a consequence of the number of suffered attacks – or vice versa. This seconds the findings of Jorge et al. who concluded from their data that an anxiety disorder frequently preceded the first manifestation of CH.[6] Anxiety and CH must hence be viewed as co-morbidities.

While anxiety levels are significantly higher in chronic than episodic CH, the influence of these subtypes on anxiety is small. The association between anxiety and both inter-ictal and cumulative burden is more marked (see Figure 2). Clearly, the repercussions of CH in daily life are either more severe or experienced as more severe in the presence of anxiety.

Donnet et al. investigated a large sample of 2074 patients suffering from chronic CH and found high levels of anxiety in 75.7% of them.[15] Other studies with considerably smaller sample sizes reported anxiety to be present in between 8% and 23.8% of patients with episodic CH and between 11.8% and 19% of patients with chronic CH.[8]

Anxiety is not rare in the general population as well. Using the HADS-A, an elevated level of anxiety was identified in 21%.[16] Most likely, however, not all of them suffer from an anxiety disorder. The 12-month prevalence of anxiety disorders and of subthreshold anxiety disorders in the general population is 12% and 3.9%, respectively.[17,18] The latter is

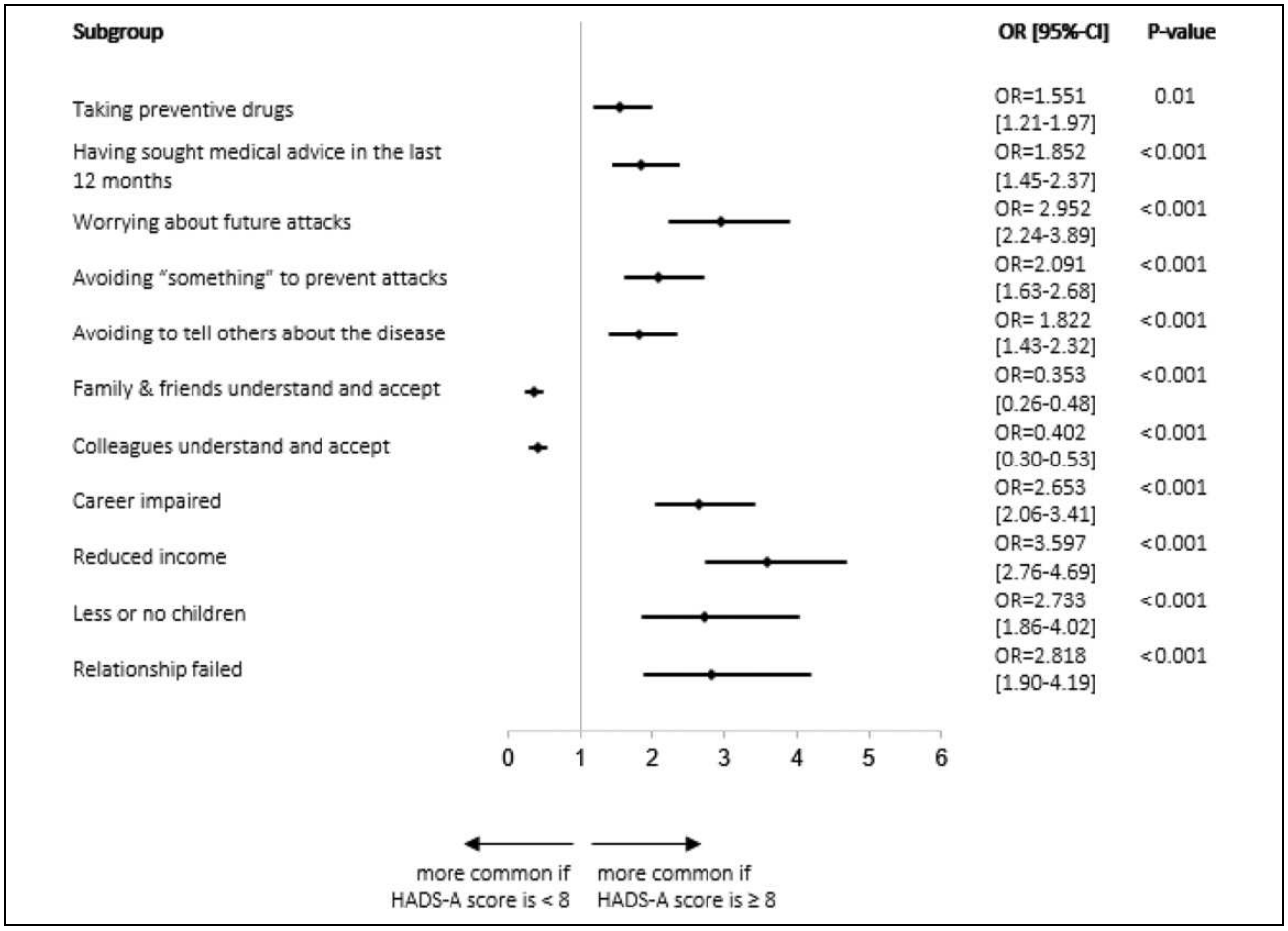

Figure 2. Differences in inter-ictal burden between patients who scored less than eight points and those who scored eight points and more in the HADS-A. An OR below 1.0 indicates that we found higher odds for that attribute to be present in participants with lower scores. Conversely, an OR higher than 1.0 indicates that the odds are higher for participants with higher scores. The reported *p* values were corrected for multiple testing. OR: odds ratio; CI: confidence interval; HADS-A: anxiety subscale of the Hospital Anxiety and Depression Scale.

defined as recurrent psychopathological symptoms that are typical for anxiety disorders but not sufficiently severe to make the diagnosis. Evidently, when assessing anxiety, different measuring methods may yield different results.

The HADS-A was designed to quantify anxiety and not to diagnose a specific disease.[13] It focuses on the repercussion of anxiety on mood and – to a lesser extent – on behaviour and cognition.[3] Yet, a score of eight and more hints at a generalised anxiety disorder (GAD) with a sensitivity of 89% and a specificity of 75%.[19] Thus, many participants who reached higher scores probably suffered from GAD. This could explain why the disease state (in-bout/out-bout, episodic/chronic) influences anxiety levels little.

Long-lasting and pervasive worrying is the hallmark of GAD.[4] Often, though, worrying is not recognised as an issue by patients suffering from that disorder; contrarily, they tend to see it as a helpful instrument to prevent unpleasant experiences.[20] What they commonly do is complain about physical symptoms, particularly chronic pain.[4] The reason for the latter is unknown; studies suggest that anxiety does not affect the pain threshold.[21,22]

Anxiety may be linked to a sense of helplessness.[4] That feeling perhaps explains the higher odds of consulting doctors in the group of anxious persons. Seeking medical advice might be a way to cope with helplessness, given that family, friends, colleagues and employers often do not seem to understand and accept their disease.

Loneliness, work loss and reduced productiveness at work can be associated with GAD.[23,24] Therefore, we must consider that not CH but anxiety compromised relationships, understanding by others and job opportunities. Not only relations to others may be troubled; anxious persons often are not safe from themselves either. Patients suffering from anxiety disorders are prone for self-harm.[25] Concordantly, in our study, people with higher levels of anxiety report hurting themselves during CH attacks more frequently. In addition, both anxiety disorders and CH are associated with a higher likelihood of suicidality.[25,26] Thus,

suicidal ideation should be assessed regularly in anxious patients with CH.

The strengths of this study are the large sample size and the rather high number of countries of origin of the participants. Some limitations should be noted. Firstly, as stated before,[9] it is likely that women and patients with chronic CH were over-represented. Secondly, the self-reported diagnosis of CH might lead to a measuring bias. Addressing that issue, we included only patients whose diagnosis could be validated based upon their responses in the questionnaire. Thirdly, the sample is not population based. Therefore, we cannot deduce prevalence and incidence from our data. Instead, we focused on studying subgroups and their relationships. Finally, the study design does not allow conclusions about cause and effect.

Conclusions

Anxiety is a physiological reaction to threat that aims at reducing danger by increasing vigilance and preparing for escape. It is based upon the notion of being confronted with stronger forces that make offensives futile.

When anxious persons are struck with CH, their reaction comprises worrying and the attempt to avoid potential triggers. Instead of finding help in others, they feel misunderstood and withdraw; relationships fail and difficulties at work arise. Anxiety complicates dealing with CH and aggravates its burden. Therefore, we recommend screening every patient for anxiety. We would like to encourage future research investigating the influence of the treatment of anxiety on the burden of CH.

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