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Psychiatric disorders and pain location in unilateral migraineurs

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Abstract To explore the relationship between the side of pain during attacks and psychopathological features in strictly unilateral migraine, we recruited 35 patients affected by migraine with and/or without aura diagnosed according to the revised ICHD-II criteria. Seventeen patients had right side-locked pain (R-SUM), 11 had left side-locked (L-SUM) and 7 had side-shifting pain (SSM). Patients were administered the Hamilton Anxiety Scale, the State and Trait Anxiety Inventory-State Anxiety, the Beck Depression Inventory and the 20-

item Toronto Alexithymia Scale. Statistical analyses showed that the L-SUM group was significantly more anxious and depressed than the other two groups of patients. Our preliminary data suggest that strictly left unilateral migraine is associated with more severe anxiety and depression. This finding appears to be consistent with studies that reported a higher degree of these disorders in patients with left cerebral hemispheric damage.

Key words Unilateral migraine • Psychiatric disorder • Alexithymia

Introduction

Psychiatric disorders are often associated with primary headaches, both migraine and tension-type headaches. Although the relationship between psychological factors and headache still has to be further elucidated [1, 2], psychological distress is certainly present in headache patients suffering from chronic daily attacks [3]. Psychiatric disorders have also been described in patients with episodic forms of primary headache, such as migraine without aura (MO) and migraine with aura (MA). To the best of our knowledge, no studies reported a correlation between pain location and psychopathological features in migraineurs. From a neurobiological perspec-

tive, a correlation between psychiatric symptoms, i.e., anxiety and depression, and laterality of vascular brain lesions (mainly involving left cerebral hemisphere) has been shown in previous studies [4]. Also, in depressed patients hypoactivity of the left frontal cerebral regions due to metabolic dysregulation has been evidenced by functional neuroimaging studies [5]. Given that a cerebral metabolic dysregulation is reported in migraine too [6], it is possible that a metabolic imbalance in migraine patients with left strictly unilateral attacks is likely related to a higher expression of these psychopathological conditions. Therefore, the present study was aimed at investigating depression, anxiety and alexithymia in a population of unilateral MO and/or MA patients with side-locked and side-shifting pain during attacks.

Materials and methods

Thirty-five patients affected by side-locked or side-shifting unilateral MO and/or MA participated in the study (28 women and 7 men). Side-locked unilateral migraine (SLM) was defined according to the presence of the pain on the same side of the head during the attack, whereas in side-shifting unilateral migraine (SSM) attacks the pain shifted from side to side during attack.

Mean age of the patients at the time of observation was 38.02 ± 9.26 years (range: 20–56) [39.07 ± 8.94 (range: 20–56) in females, $n=28$; 33.85 ± 10.04 (range: 22–51) in males, $n=7$]. Thirty patients were affected by MO (24 females and 6 males), 2 by MA (1 female and 1 male) and 3 by both MO and MA (all females). Diagnosis was made according to the revised ICHD-II criteria [7]. Mean age at onset of the disease was 19.34 ± 7.70 (range: 7–34) [19.96 ± 7.63 (range: 7–34) in females; 16.85 ± 8.07 (range: 8–30) in males]. During attacks the pain was right side-locked in 17 patients (13 F and 4 M), left side-locked in 11 patients (9 F and 2 M) and side-shifting in 7 patients (6 F and 1 M). The attack frequency over the 12-month period preceding the evaluation ranged from 2 to 8 attacks per month. The mean disease duration was 18.48 ± 9.49 years (range 1–37) [18.85 ± 10.13 in females and 17 ± 6.70 (range: 10–28) in males]. Patients were not under preventive medication during the study period.

In all patients anxiety and depression were evaluated using the Hamilton Anxiety Rating Scale (HAMA) [8], the State and Trait Anxiety Inventory-State Anxiety (STAY-S) [9] and the Beck Depression Inventory (BDI) [10] according to Endler et al. [11] to consider psychological and somatic symptoms of depression separately. Alexithymia was evaluated by using the 20-item Toronto Alexithymia Scale (TAS-20) [12]. Psychopathological evaluation was executed by a specialist that was blind to the headache diagnoses. Patients were divided into three subgroups according to pain location (R-SLM, L-SLM and SSM). One-way ANOVAs were performed to compare scores obtained in the three groups of patients. Post-hoc analyses with LSD method were also performed whenever the group effect was significant. Finally,

Spearman's rho correlations were performed to investigate the relationship between some demographic and clinical variables (such as sex, age at observation, age at onset, illness duration and mean frequency of attacks) and psychopathological features.

Results

Results of one-way ANOVAs and post-hoc analyses are reported in Table 1. As shown in the table, the L-SLM group obtained significantly higher scores compared to the R-SLM group on BDI, HAMA and STAY-S. The L-SLM group achieved higher scores than the SSM group in cognitive-affective BDI sub-scale scores and STAY-S scores. No statistically significant results were found between groups on TAS-20 scores. In the overall group of patients, no significant correlations (i.e. all $p > 0.10$) were found with demographic variables, clinical features of migraine and psychopathological measures. A significant positive correlation between mean monthly frequency of attacks and TAS-20 total score ($\rho = 0.68$; $p = 0.032$), partial score on F1 subscale of TAS-20 ($\rho = 0.75$; $p = 0.013$) and somatic subscale of HAMA ($\rho = 0.69$; $p = 0.020$) were found in SSM patients. In the same group a significant linear correlation between age at onset of migraine and partial score on F2 subscale of TAS-20 ($\rho = 0.70$; $p = 0.023$) was also found.

Discussion

The majority of clinical and population studies [1–3, 13–15] suggest the presence of a close relationship

Table 1 Comparisons between scores obtained by strictly unilateral migraineurs with right side-locked, left side-locked and side-shifting pain on psychopathological scales

Psychopathological scales	L-SLM	R-SLM	SSM	<i>F</i> (2,32)	<i>p</i>
BDI-Tot	13.27 (10.3)	6.92 (4.32)	7.82 (6.98)	2.45	n.s
BDI-Cogn	8 (5.98)*°	3.15 (2.23)	3.91 (4.86)	3.81	0.033
BDI-Phy	4.82 (3.21)	3.31 (2.13)	3.64 (2.06)	1.16	n.s.
STAY-S	42.73 (7.21)**°°	35.38 (6.67)	30.73 (4.49)	10.26	<0.001
HAMA-Tot	10.18 (5.72)*	4.38 (4.40)	8.63 (5.81)	3.90	0.030
HAMA-Psy	7.55 (4.08)*	3.77 (3.91)	5.64 (3.80)	2.75	0.079
HAMA-Som	2.64 (2.11)*	0.62 (0.87)	3.00 (3.63)	3.48	0.043
TAS-20 Tot	49.55 (12.82)	44.54 (13.93)	43.8 (10.26)	0.67	n.s

L-SLM, left side-locked unilateral migraine; R-SLM, right side-locked unilateral migraine; SSM, side-shifting unilateral migraine; n.s., statistically not significant

*Post-hoc analyses with LSD method indicating a significant difference between L-SLM and R-SLM groups with $p < 0.05$; **Post-hoc analyses indicating a significant difference between L-SLM and R-SLM groups with $p < 0.01$; °Post-hoc analyses indicating a significant difference between L-SLM and SSM groups with $p < 0.05$; °°Post-hoc analyses indicating a significant difference between L-SLM and SSM groups with $p < 0.01$

between migraine, depression and anxiety disorders. These studies considered MO and MA both together and separately, without any specification on the side of the pain. In a study that attempted to differentiate between the two migraine subtypes [2], MA patients were found to have higher rates for major depression (45.5 vs. 31.9%), dysthymia and manic episodes compared with MO patients. These findings have been supported by further studies [13, 14] reporting that anxiety disorders and major depression co-existed in 30% of migraine patients. Breslau et al. [1] reviewed the lifetime prevalence rates of major mood disorders in patients suffering from MA and MO, underlining that the onset of anxiety generally precedes onset of migraine, which in turns precedes the onset of depression. This pattern seems to be the result of a two-way "bi-directional" relationship between the two conditions, ruling out the possibility that mood disturbances could be secondary to repeated migraine attacks. These psychopathological findings in migraine patients appear to be confirmed by further clinical studies [3, 15]. In the present study, we investigated the relationship between pain location and anxiety, depression and alexithymia in strictly unilateral migraineurs. Alexithymia, substantially defined by difficulty in identifying and describing own feelings and by an externally oriented cognitive style [16], has been previously investigated in headache patients [17], in particular in those with chronic tension-type headache [18]. Recent data showed that alexithymia is more frequent in MO patients compared to healthy subjects [19]. Our data do not show a relationship between

side-locked pain and alexithymia in migraineurs. However, we cannot make assumptions on the prevalence of alexithymia in these patients. On the contrary, the results of the present study evidence that L-SLM patients are more anxious and depressed than the other two groups. This finding could be interpreted from a neurobiological perspective. Indeed, it could be argued that the recurrence of pain on the left cerebral hemisphere could be likely related to a hemispheric biochemical dysfunction. As a matter of fact, proposed pathogenetic hypotheses on migraine indicated an impaired cerebral metabolism underlying cortical spreading depression and the related headache, suggesting an unmasking dysfunction of brain mitochondria [6]. Furthermore, PET studies during migraine attacks demonstrated episodic dysfunction of certain brainstem areas [20]. Our data are consistent with these reports and with previous studies showing a relationship between anxiety and depression with vascular left cerebral lesions [4] and with metabolic alteration in left frontal regions [5]. Therefore, the correlation between left unilateral migraine, anxiety and depression we found in migraineurs offers new clues on the role of left cerebral hemisphere in these disorders.

Although the absence of a control group of healthy subjects and the small size of our sample represent an important limitation of the study, our preliminary data seem to indicate that the investigation of the relationship between head pain location and psychopathological alterations in strictly unilateral migraine may be a field of interest for further research.

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