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Alexithymia profile across migraine subtypes: a cross-sectional study

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ABSTRACT

Background: Migraine is a prevalent neurological disorder, with chronic migraine (CM) and medication overuse headache (MOH) often comorbid with psychiatric conditions. Patients with CM may experience social cognitive impairments, including alexithymia, which could contribute to their condition's severity and prognosis. This study aims to characterize alexithymia in patients with episodic migraine (EM) and CM and explore differences in alexithymia between patients with and without aura.

Methods: This cross-sectional study included adult patients with EM, CM (with or without MOH), and healthy controls (HCs), conducted at two tertiary headache centers in Italy. Participants completed the Toronto Alexithymia Scale-20 (TAS-20) to assess alexithymia levels. Demographic, clinical, and cognitive functioning data were collected. Migraine features, including frequency, aura symptoms, and medication usage, were also recorded.

Results: The cohort included 200 migraine individuals and 79 HCs. Patients with CM exhibited significantly higher alexithymia scores (56.0±13.2) compared to EM patients (47.8±12.0, p<0.001) and HCs (44.5±11.9, p<0.001). A higher proportion of CM patients (32.0%) had pathological alexithymia compared to EM patients (16.0%) and HCs (9.0%) (overall difference, p<0.001). No significant differences were found in TAS-20 scores between migraine individuals with aura (45.2±9.9) and those without aura (49.5±13.0, p=0.182).

Conclusions: Patients with CM exhibit higher levels of alexithymia compared to those with EM and HCs. These findings suggest that alexithymia may be a more specific trait of CM. Future research should investigate the role of alexithymia in migraine management, particularly in relation to its impact on quality of life and treatment outcomes.

Key words: theory of mind, migraine, medication overuse headache, alexithymia.

Introduction

Migraine is one of the most common debilitating diseases affecting over one billion people worldwide. It is frequently comorbid with psychiatric conditions such as anxiety disorders and major depression, with a negative impact on quality of life and severity of migraine. (1) The burden of migraine is worsened by its frequent association with other comorbidities, leading to a greater overall impairment in functioning. (2)

Psychiatric disorders seem to be more prevalent in patients with chronic migraine (CM) and medication overuse headache (MOH) than in those with episodic migraine. (3,4) Furthermore, a growing amount of evidence shows that patients with migraine, especially CM, present an impairment of social cognition, a cognitive/psychological domain that refers to the ability underlying social interaction, based on the recognition of others' emotions, representation of others' affective and cognitive mental states, that allows one to navigate into the social environment. (5,6) These impairments may hinder individuals with migraine in their ability to fully engage in social environments, potentially exacerbating the impact of the disorder on their daily lives.

Alexithymia is a personality trait defined by difficulty in identifying and describing one's emotions, along with an excessive focus on physical symptoms. (7) Since the ability to recognize others' emotions and feelings depends on accurately identifying one's own, alexithymia is closely linked to social cognitive functioning. (8)

A few studies on alexithymia and primary headaches have been conducted, mostly including small sample sizes. (9) They showed that alexithymia may be considered a potential characteristic trait of migraine, especially in CM. (10,11) However, characterization of alexithymia across different forms and subtypes of migraine, and in particular in CM and MOH, and migraine with and without aura, is currently under-recognized and underreported. At the same time, they could represent determinant factors contributing to diagnosis, prognosis, and potentially treatment response. (11)

The primary aim of this study was to characterize the alexithymia trait through the Toronto Alexithymia Scale-20 (TAS-20) in a cohort of adult patients with episodic migraine (EM) and CM, comparing the findings with healthy controls (HC). Finally, we also compared alexithymia levels in patients with migraine with aura and without aura.

Results

The study cohort involved 200 migraine individuals with a mean age of 34.8±12.0 years (156 females [78%]) and 79 age-matched HCs (37.2±12.6 years). The migraine cohort included 153 patients with EM (76.5%) and 47 patients with CM (23.5%); 18 had migraine with aura (10.0%). In the CM group, 40 patients had MOH (85.0%).

For the overall migraine cohort, the mean monthly headache days (MHDs) were 13.4±9.0, and the mean total number of analgesics per month (AMNs) was 17.5±26.1. The mean values of the Headache Impact Test-6 (HIT-6) and the Migraine Disability Assessment (MIDAS) questionnaire scores were 61.6±8.5 and 51.6±54.4, respectively.

The mean Montreal Cognitive Assessment (MoCA) score was 26.4±3.0 for HCs, 24.2±3.4 for EM, and 24.6±4.2 for CM (overall difference, p=0.073). After correction, no migraine individuals or HCs had a MoCA score below the cut-off for cognitive impairment. (12)

The clinical and demographic characteristics of the cohort are summarized in **Table 1**.

Comparing migraine individuals, regardless of their phenotypes, with HCs, the migraine group exhibited significantly higher levels of alexithymia (49.7±12.8 *vs.* 44.5±11.9, p<0.001) (**Figure 1**).

When subdividing the migraine group by MHD frequency (EM or CM), CM exhibited significantly higher levels (56.0±13.2) compared to EM (47.8±12.0) (p<0.001) and to HCs (44.5±11.9) (p<0.001). At the same time, there was no significant difference in the comparison between EM and HCs (p=0.148) (**Figure 1**).

Respectively, in the EM group and the CM group, 24 patients (16.0%) and 15 patients (32.0%) exhibited pathological alexithymia, compared to 7 subjects (9%) in the HC group (overall difference, p<0.001).

No significant differences were found in the TAS-20 scores between migraine individuals with aura (45.2±9.9) and those without aura (49.5±13.0) (p=0.182).

In the migraine group, no sex differences in TAS-20 were found comparing females (50.4±13.2) and males (47.3±10.8) (p=0.482) (**Table 2**).

Table 1. Patients' demographic and clinical features at baseline.

Variable	Overall population (n=200)	
Age, years (mean, SD)	34.8	12.0
Disease duration (mean, SD)	15.6	11.7
MoCA (mean, SD)*	24.4	4.0
Sex, F (n, %)	156 (78%)	
MHDs (mean, SD)*	13.4	9.0
AMNs (mean, SD)*	17.5	26.1
Aura, yes (n, %)	18 (10%)	
HIT-6 (mean, SD)*	61.6	8.5
MIDAS (mean, SD)*	51.6	54.4
TAS-20 (mean, SD)	49.7	12.8

SD, standard deviation; MoCA, Montreal Cognitive Assessment Test; F, female; MHDs, monthly headache days; AMNs, total number of analgesics per month; HIT-6, Headache Impact Test-6; MIDAS, Migraine Disability Assessment; TAS-20, Toronto Alexithymia Scale-20. *Available data for 40 episodic migraine patients and 41 chronic migraine patients.

Discussion

Our study showed that alexithymia levels, assessed using the TAS-20 scale, are significantly higher in migraine individuals compared to healthy controls. When considering different migraine subtypes, the total TAS-20 score and the proportion of patients exhibiting pathological alexithymia were higher in the CM group (85.0% with MOH) than those with EM. This finding suggests that alexithymia may be a specific trait of this migraine phenotype.

These results contribute to the existing literature on alterations in social adaptation among individuals with migraine. (6,10,11,13) This highlights the complexity of migraine as not only a physical condition but also one with significant psychological and social implications.

In particular, alexithymia-related impairments indicate difficulties in experiencing and expressing emotional states, along with an excessive preoccupation with physical symptoms. (8)

The most notable finding of this study is the greater degree of alexithymia impairment observed in patients with chronic migraine, consistent with previous literature based on smaller sample sizes, usually including not more than 100 patients. (10) In our investigation of patients diagnosed with CM, the majority of whom also presented with concomitant MOH (85.0%), the worst performance was observed on the TAS-20 scale, consistent with existing literature. (11,14) This suggests

Table 2. Socio-demographic description of the sample and Toronto Alexithymia Scale-20 results.

Variable	HC (n=79)		EM (n=153)		CM (n=47)		p	Pairwise comparisons		
								HC *vs.* EM p^{Bonf}	HC *vs.* CM p^{Bonf}	EM *vs.* CM p^{Bonf}
Age, years (mean, SD)	37.19	12.58	33.97	11.25	37.49	13.95	0.153^	n.s.	n.s.	n.s.
Disease duration (mean, SD)	N/A	N/A	14.9	11.0	17.8	13.9	0.447§			
MoCA (mean, SD)*	26.4	3.0	24.2	3.4	24.6	4.2	0.073§	n.s.	n.s.	n.s.
Sex, F (n, %)	40 (51%)		118 (77%)		38 (81%)		<0.001°	<0.001	<0.001	n.s.
MHDs (mean, SD)*	N/A	N/A	6.2	5.6	20.1	5.9	<0.001§			
AMNs (mean, SD)*	N/A	N/A	5.7	4.9	28.3	32.4	<0.001§			
Aura, yes (n, %)	N/A		15 (10%)		3 (8%)		0.761°			
HIT-6 (mean, SD)*	N/A	N/A	59.89	8.17	63.53	8.50	0.005§			
MIDAS (mean, SD)*	N/A	N/A	31.03	39.16	75.33	60.08	<0.001§			
TAS-20 (mean, SD)	44.5	11.9	47.8	12.0	56.0	13.2	<0.001#	n.s.	<0.001	<0.001

SD, standard deviation; HC, healthy controls; EM, episodic migraine; CM, chronic migraine; MoCA, Montreal Cognitive Assessment Test; F, female; MDHs, monthly headache days; AMNs, total number of analgesics per month; HIT-6, Headache Impact Test-6; MIDAS, Migraine Disability Assessment; TAS-20, Toronto Alexithymia Scale-20; N/A, not applicable; n.s., not significant; #ANOVA; °chi-squared X2 test; ^Kruskal-Wallis test; §Mann-Whitney U test; *available data for 40 EM patients and 41 CM patients. Pairwise comparisons were adjusted using the Bonferroni correction (pBonf).

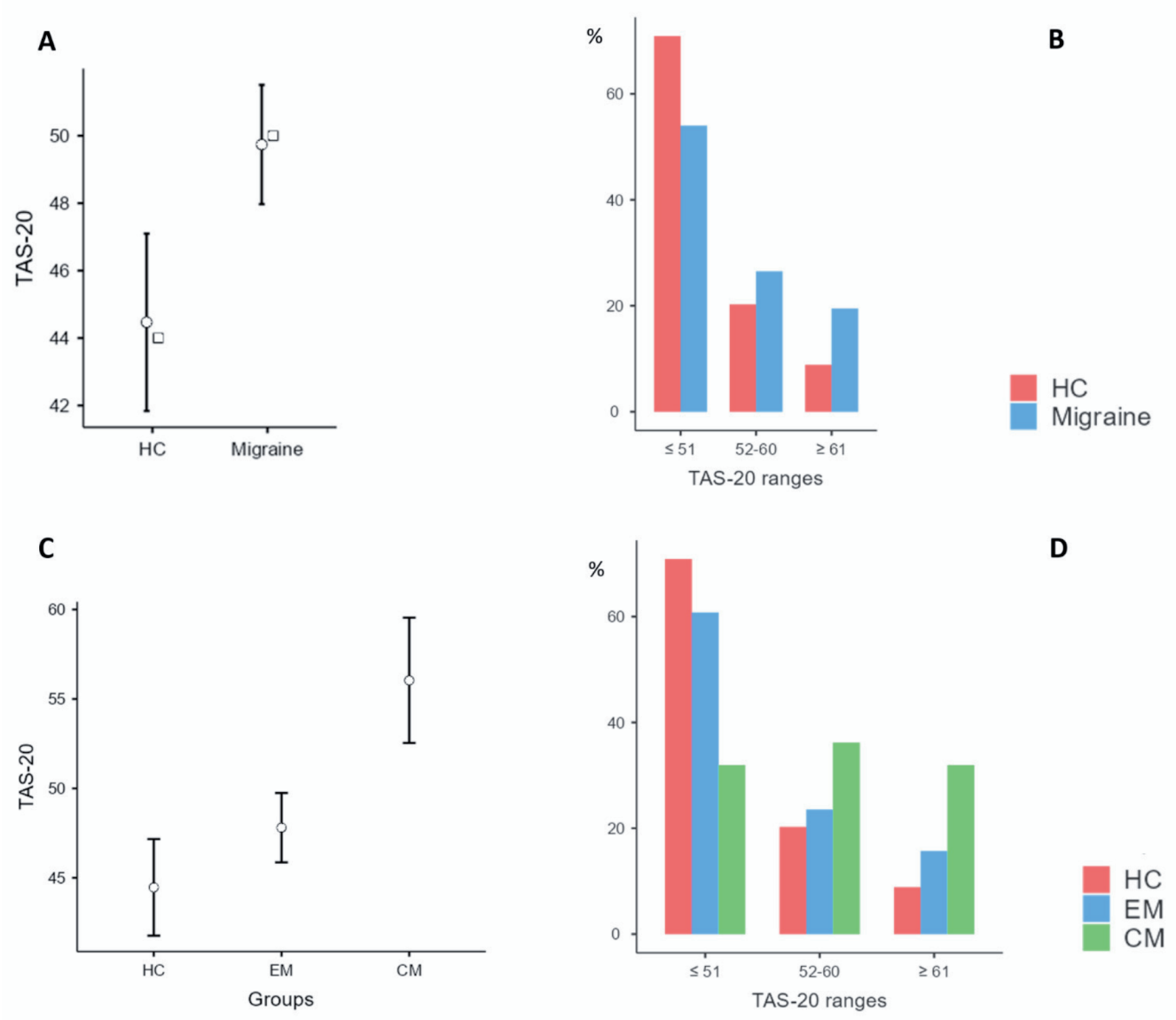

Figure 1. Performances in TAS-20 of migraine group compared to healthy controls (A,B) and in the HC, episodic migraine, and chronic migraine groups (C,D). CM, chronic migraine; EM, episodic migraine; HC, healthy controls; TAS-20, Toronto Alexithymia Scale-20. The white square represents the median value.

that CM with MOH may share an underlying pathophysiological or psychological mechanism that exacerbates emotional dysregulation.

It is well established that this specific patient population (CM with or without MOH), particularly those with MOH, has a specific psychological profile characterized by a higher presence of psychiatric comorbidities and obsessive-compulsive traits. (4,15) Furthermore, the presence of alexithymia in this group may play a role in emotional avoidance, making it harder for patients to cope effectively with their condition. These features may contribute to the compulsive overuse of symptomatic medications and the persistent seeking of pain relief. (4,15) They may also exhibit deficits in emotional awareness and recognition, both of their own emotions and those of others. (6) These findings suggest that MOH patients may experience impaired social adaptation and limited self-awareness. (6) In addition, MOH patients seem to be characterized by a neurotic profile with concerns about physical symptoms and low self-esteem. (16) This may be closely linked to alexithymia. Individuals with alexithymic traits exhibit heightened activity in brain regions associated with physical sensation and somatosensory amplification. (17) Moreover, alexithymia is linked to an increased tendency to overreport physical symptoms. (18) As a result, individuals with high levels of alexithymia may perceive bodily signals in an altered way, interpreting low-intensity stimuli as significantly more intense, in line with what happens in migraine and especially in chronic forms. (19)

This impairment of different facets of socio-cognitive functioning may also be associated with limited insight into illness and reduced perception of the somatic and psychological consequences of excessive symptomatic medication use. (11)

The mechanisms through which psychological mechanisms and psychiatric comorbidities influence migraine phenotype, severity, and disability are largely unknown and unexplored. A dysfunction of the dorsal anterior cingulate cortex (dACC), which is part of the limbic system, has been proposed

as one of the main mechanisms of alexithymia. (20) This area is involved in numerous emotional functions, including evaluating pain (*i.e.*, assessing pain as unpleasant), evaluating socially relevant information, and reward mechanisms. (21) A neurolimbic model of migraine has been proposed based on the presence of limbic abnormalities in individuals with migraine (22) and alexithymia, as a marker of emotional dysregulation, which may further support this notion.

Alexithymia is also highly correlated with depression and anxiety in migraine individuals. (22-24) Similar to the patterns observed for depression and anxiety, higher levels of alexithymia are linked to a reduced quality of life and greater disability. (22-25) This highlights the potential for a more integrated treatment approach, where both the physical and psychological aspects of migraine are managed.

Depression and anxiety are also known risk factors for the transformation of episodic into chronic migraine. Similarly, MOH seems to be prompted and sustained by psychological disturbances and psychiatric comorbidities. (3,26) Psychopathological dysfunctions are also possible predictors of relapses and scarce response to treatments, even if this concept is debated, especially when considering the novel preventive treatments for migraine. (27-29) Thus, psychiatric comorbidities, as well as impairment of social cognition domains, may affect the prognosis and treatment response of these patients. In fact, a recent study from Bottiroli *et al.* showed that in a cohort of patients treated with erenumab, non-responders were characterized by a higher prevalence of anxiety disorders and alexithymic traits than responders. (30)

This finding suggests that psychiatric comorbidities may not only affect migraine severity but also influence how well patients respond to new treatments. Future studies should prioritize evaluating the alexithymia profile, both independently and in association with comorbid depression and anxiety, to determine its potential role in influencing migraine severity, disability, and treatment response.

Our study has notable strengths. It includes a large sample size of patients, and migraine phenotypes were accurately differentiated. Nonetheless, some limitations should be acknowledged. First, we did not explore the sub-items of alexithymia, and we only focused on alexithymia without integrating data on other psychological variables (*i.e.*, anxiety and/or depression), which could play a mediating role in influencing alexithymia levels. Second, due to small numbers, CM and CM with MOH could not be analyzed separately, potentially limiting phenotypic characterization. Lastly, while our study provides a robust characterization of alexithymia across migraine subtypes, the cross-sectional design inherently limits a deeper clinical characterization of individual migraine features beyond what was collected for this specific research question. Future longitudinal studies would allow for a more comprehensive understanding of the dynamic interplay between alexithymia and various clinical aspects of migraine.

Conclusions

This study contributes to a better understanding of the psychological profile of patients with migraine and, more specifically, CM. Given its ease of assessment in clinical practice, TAS-20 could serve as a valuable screening tool for identifying patients with a complex psychological profile, potentially associated with greater disease severity or reduced response to preventive treatments. Its clinical relevance underscores the need to consider psychological factors, including alexithymia, in headache management, particularly when integrating non-pharmacological approaches.

Materials and Methods

Setting and participants. This cross-sectional observational study was conducted in two headache tertiary centers (Fondazione Policlinico Universitario A. Gemelli IRCCS in Rome, Italy, and Sapienza University of Rome, Polo Pontino, Latina, Italy) from November 2020 to December 2024.

We included patients with a diagnosis of EM, CM (with or without concomitant MOH diagnosis), and HCs who completed the TAS-20 questionnaire. Inclusion criteria were age >18 years, informed consent to participate, and fulfillment of the criteria of The International Classification of Headache Disorders 3rd edition (ICHD-3) for migraine. (31) In particular, MOH was defined as a headache occurring on 15 or more days per month in a patient with a pre-existing headache disorder, associated with regular overuse of one or more medications typically used for acute and/or symptomatic treatment of headache for more than 3 months. Healthy controls reported no previous diagnosis of headache disorders and did not meet the criteria for primary headache disorders after a detailed interview conducted by headache specialists. We excluded patients with a diagnosis of a secondary headache, subjects who refused to give informed consent, patients with cognitive decline or mental illness, and non-Italian native speakers.

Medication overuse headache was defined as a chronic headache that occurs more than 15 days/month in patients who regularly overuse headache medications (more than 10 or 15, depending on the medication) for more than 3 months. (31)

The study was reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.

The study adheres to the ethical guidelines of the 1975 Declaration of Helsinki, as reflected in the prior approval granted by the institution's human research committee at each participating study site. The study was approved by the Ethics Committee of Fondazione Policlinico A. Gemelli IRCCS.

Assessment of migraine features. Migraine features were collected from a neurologist and headache specialist through a structured interview. Information about socio-demographic data, general medical history, age at onset of headache, frequency of headache (MHD), aura symptoms, history of acute and preventive medication use, and total number of analgesics per month (AMNs).

The severity and the headache-related disability were assessed through HIT-6 and MIDAS scales.

Cognitive functioning screening and assessment of alexithymia. All subjects were screened for cognitive impairment with the MoCA. (32) Its total score ranges from 0 to 30, with higher scores indicating better performance. After adjusting for age and education, the cut-off for cognitive impairment is 17.54, according to Italian normative data. (14)

The TAS-20 (33) is a 20 multiple-choice self-report questionnaire developed to evaluate alexithymia. The scale included three core components: Difficulty Identifying Feelings (DIF), Difficulty Describing Feelings (DDF), and Externally Oriented Thinking (EOT). The cut-off for alexithymia on the TAS-20 total score is ≥61, out of a total score of 100. Scores ≤51 indicate the absence of alexithymia, and scores ranging from 52 to 60 suggest possible alexithymia.

Statistical analyses. Descriptive statistics were used to describe the demographic and clinical features of the sample. Numerical variables were described using mean and standard deviation. Categorical variables were presented as absolute numbers (n) and percentages (%). The distribution of each

numerical variable was checked with the Shapiro-Wilk Test, and parametric or non-parametric analyses were performed according to the distribution. The comparison between two groups (migraine group and HCs, as well as EM and CM) for non-normally distributed data was performed using the Mann-Whitney U test, while normally distributed data were compared using the *t*-test. Categorical variables were compared using the chi-square test.

Comparisons among the three groups (EM, CM, and HCs) were conducted using a one-way analysis of variance (ANOVA) or a Kruskal-Wallis test, depending on whether the data were normally or non-normally distributed, with Bonferroni *post hoc* correction. Categorical variables among the three groups were analyzed using the chi-square test. A two-tailed p-value <0.05 was considered significant for all variables. All data were analyzed using SPSS software version 26.0 (IBM Corp., Armonk, NY, USA).

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Conflict of interest: the authors have no conflict of interest to declare.

Ethics approval and consent to participate: this study adheres to the ethical guidelines of the 1975 Declaration of Helsinki, as reflected in the prior approval granted by the institution's human research committee at each participating study site. The study was approved by the Ethics Committee of Fondazione Policlinico A. Gemelli IRCCS. Written informed consent was obtained from all participants.

Availability of data and materials: the datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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