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Personality in patients with migraine evaluated with the "Temperament and Character Inventory"

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M. Hernández • A. Resendiz U.M. Guevara-López Pain and Palliative Medicine Clinic, National Institute of Medical Sciences and Nutrition "Salvador Zubirán", Mexico City, Mexico Abstract The objective of this study was to assess the personality profile of a sample of Mexican patients with migraine using the Temperament and Character Inventory (TCI). A cross-sectional study was performed including adult migraine patients identified from the outpatient neurology clinics of two large teaching hospitals in Mexico City. Patients were asked to voluntarily participate in the study. A physician conducted a standardised diagnostic interview adhering to the criteria of the International Headache Society (IHS). Patients were interviewed and administered the TCI. We used two healthy controls groups and a third group of non-migraine pain controls. One hundred and fortytwo subjects with migraine, 108 healthy blood donors, 269 young healthy controls and 30 patients with non-migraine pain (NMP) were included in the study. Patients with migraine had higher scores in the dimension harm avoidance (HA) and all its sub-dimensions (p < 0.05) than healthy patients. Patients with non-migraine pain had high scores in HA and low scores in novelty seeking, self-directedness and cooperativeness. Blood donors had high scores in the following subdimensions: HA1, HA4 and C3 (Cooperativeness). Personality features consistent with migraine are avoidance, rigidity, reserve and obsessivity. Our study shows that patients with chronic pain share some of the personality features of patients with migraine but their TCI profile could be indicative of cluster C avoidant personality. Blood donors were shown to have more energy, with a tendency to help other people and be more optimistic. The results support serotoninergic involvement as explaining the physiopathology of migraine.

Keywords Personality • Migraine • Headache • TCI • Temperament • Character • Harm avoidance

Introduction

Early clinical descriptions of the personality of patients with migraine (PWM) performed by Wolf [1] included such characteristics as ambitiousness, extreme tidiness, perfectionism, inflexibility, resentment and aggression. Later authors corroborated these observations [2, 3], although their evaluations lacked standardised questionnaires and control groups.

Accordingly, Köhler and Kosanic [4] created an instrument to measure the personality variables initially reported by Wolf. Their data suggested there was no evidence of a single modal personality profile among migraine patients. Most studies in this clinical population have evaluated personality using either the Minnesota Multiphasic Personality Inventory (MMPI) [5-10], the Eysenck Personality Questionnaire [11, 12] or the Zuckerman-Kuhlman's Personality Questionnaire [13]. In general these studies tend to find differences between PWM and controls in the scales related with neuroticism, stress, depression, anxiety and hostility [5, 11, 13]. However, others have failed to find these patterns [14, 15]. Furthermore, higher MMPI scores for neuroticism can be explained, at least partially, by the content of certain scale items that inquire about stomach and headache symptoms [16] and potentially as a consequence of the type of pain in migraineurs and the chronicity of this condition, as some authors have suggested [17]. In a similar fashion, controlled studies using the Eysenck Personality Questionnaire (EPQ) have found higher scores for neuroticism in PWM relative to controls [18, 19]. Other studies suggest this pattern of neuroticism could be typical of patients with tension-type headache but not with migraine [20].

These traditionally utilised measures do not adequately account for the biological and social determinants of personality, factors considered important in the assessment of migraine patients. A more recently used scale is the Temperament and Character Inventory (TCI). In this instrument Cloninger et al. [21] proposed 7 independent dimensions: four related with the character and three with the temperament. The character dimensions of personality explain the heritance of information processing [22] and have a strong correlation with various mechanisms in the central nervous system related to the activation, inhibition or maintenance of a behaviour. These mechanisms are novelty seeking (NS), which has been related with the onset and activation of behaviours (associated with dopaminergic activity), harm avoidance (HA), related with the termination of behaviour (associated with serotoninergic activity), reward dependence (RD), involved in the maintenance of behaviour (associated with noradrenergic activity) and persistence (P) (associated with glutamatergic activity) [21, 23, 24]. In addition, the TCI evaluates three character dimensions of personality: acceptance of the individual self (Self-directedness, SD), acceptance of other people (Cooperativeness, C) and acceptance in general (Self-transcendence, ST) [21, 23, 24].

Nylander et al. [23] evaluated the personality profile of 26 members of a family with migraine and 87 controls and only the subscale levels NS1 (exploratory excitability) and the NS2 (impulsivity) were higher in migraine patients compared to controls. These authors concluded that somatic anxiety and especially impulsivity could be part of the personality profile of migraine patients [23].

Using the same instrument Di Piero et al. [25] found high HA scores and low scores in the NS dimension in PWM. These authors suggested that the TCI supports a role of the serotonergic system in migraine pathophysiology and a possible dysfunction of dopaminergic and glutamatergic pathways as a specific feature of migraine [25]. In a subsequent study Mongini et al. [6] corroborated the presence of higher scores of HA in PWM compared with controls. Also the same study found higher scores of PE and lower scores of SD in PWM compared with controls [6]. On the other hand other studies have not shown the association of HA in PWM when it is controlled with the presence of depression measured with the Beck Depression Inventory, as Boz et al. pointed out [26]. Although Boz et al. [26] did not find an association between the HA and migraine, this dimension was associated with tension-type headache, indirectly supporting serotonin involvement in this type of headache, as other authors have described extensively [27].

Although there are already studies in migraine patients using the TCI, there are none that have investigated personality dimensions using different type of controls and our study is the first using the TCI to evaluate personality in patients with chronic pain. The objectives of the present study are: (1) to assess personality in a sample of Mexican PWM, using the TCI; and (2) to compare their profiles with two healthy controls and a group of non-migraine pain controls. We hypothesised that the TCI domains altered in PWM will have a strong correlation with the mechanisms of migraine in the central nervous system.

Methods

Methods and sample design

The current study was a cross-sectional study performed in two large teaching hospitals in Mexico City (National Institute of Medical Sciences and Nutrition and National Institute of Neurology and Neurosurgery). The Institutional Review Boards of both institutions approved the research protocol. The investigation was carried out in accordance with the latest version of the Declaration of Helsinki.

Migraine patients

Adult patients with migraine were identified from the outpatient neurology clinic of the two mentioned hospitals. Daily clinical charts of patients with potential diagnosis of migraine attending appointments on study days were reviewed. After their clinic appointment, 143 consecutive patients were approached and asked to voluntarily participate in the study. Informed consent of the participants was obtained after the nature of the procedures had been fully explained. A physician conducted a standardised diagnostic interview adhering to the criteria of the International Headache Society (IHS), evaluating the presence of headache and its subtypes in the previous year. The headache test contains 51 questions and classifies headache into the seven subtypes accepted by the IHS. This test assesses the type and frequency of headache medications and it includes a brief neurological exam to rule out secondary causes. It has been previously validated in a Mexican population [28-30]. None of the patients were evaluated during a migraine episode. We used the MIDAS questionnaire to evaluate headache-related disability [31]. The MIDAS score was classified into four grades of severity: I, scoring 0-5 (minimal or infrequent disability) - these migraine sufferers tend to have little or no treatment needs; II, scoring 6-10 (mild or infrequent disability) - these migraine sufferers tend to have moderate treatment needs; III, scoring 11-20 (moderate disability) and IV; scoring 21 and over (severe disability) - grade III and IV migraine sufferers have high disability and tend to have urgent treatment needs [31]. Patients were then interviewed and administered the TCI. The comorbidity of migraine was evaluated with single questions (self reported prevalence) asking for the presence of other specific medical conditions.

Control groups

We used three controls groups to evaluate the personality of PWM. The first control group was a group of healthy people obtained from a sample of adult patients attending the blood donor bank (BD, blood donors) of the hospitals on the same days as the migraine case recruitment. Those controls participated voluntarily and had a general examination and answered a standardised questionnaire to rule out other relevant medical conditions. None of these controls had migraine and were attending the clinic for clinical reasons, and all were determined to be healthy. The process of headache ascertainment was performed with the segment of the questionnaire used in the Latin American study of prevalence of migraine and tensional headache [28]. We performed the TCI to 150 BD and finally 108 BD were matched by age and gender with PWM. For the matching process we stratified and plotted both samples and randomly some controls were excluded till there were no statistical differences in both populations in the two mentioned variables. The selection of age and gender for the matching process was performed according to international recommendations for assessing personality in populations [32].

The second group was a historical group of healthy people (HGHP) used to validate the TCI in Mexican population. This group was made up of 269 participants: 125 were aspiring to enter a medical school in Mexico City and 144 were people

attending a cultural event [24]. None of these patients had a physical examination or blood work to rule out medical conditions including migraine.

Finally the third control group was made up of patients with non-migraine chronic pain (NMCP). This sample was obtained from the pain clinic of the same institutions and was matched by age and gender with PWM. Daily clinical charts of patients with an established diagnosis of a pain disorder, including radiculopathies, peripheral neuropathies and osteoarthritis, attending appointments on study days were reviewed. The median duration of pain in the group was 6 (1–30) years. None of these controls had migraine or tension-type headache and were ascertained with the same questionnaire as used for the blood donors. After their clinic appointment, 30 consecutive patients were approached and asked to voluntarily participate in the study. The main focus of our analysis was directed to the groups collected during the study (BD, NMCP and PWM). The study of the HGHP [24] was added to enrich the observations of this article.

TCI

The TCI is composed of 240 items that evaluate 7 dimensions of personality: four of temperament and three of character. Each dimension has between three and five sub-dimensions. The total store is calculated by a computer program, which also assigns a score to the sub-dimensions.

The scales and subscales of temperament measured by the TCI are as follows. Novelty Seeking (NS): NS1, Exploratory excitability *vs.* rigidity; NS2, Impulsiveness *vs.* reflection; NS3, Extravagance *vs.* reserve; NS4, disorderliness *vs.* regimentation. Harm Avoidance (HA): HA1, Anticipatory worry *vs.* optimism; HA2, Fear of uncertainty *vs.* confidence; HA3, Shyness *vs.* gregariousness; HA4, Fatigability and asthenia *vs.* vigour. Reward Dependence (RD): RD1, Sentimentality *vs.* insensitivity; RD3, Attachment *vs.* detachment; RD4, Dependence *vs.* independence. PE, Persistence *vs.* irresoluteness.

The scales and subscales of character measured by the TCI are as follows. Self Directedness (SD): SD1, Responsibility vs. blaming; SD2, Purposeful vs. goal-undirected; SD3, Resourcefulness vs. apathy; SD4, Self-acceptance vs. self-striving; SD5, Congruent second nature. Cooperativeness (C): C1, Social acceptance vs. intolerance; C2, Empathy vs. social disinterest; C3, Helpfulness; vs. unhelpfulness; C4, Compassion vs. revengefulness; C5, Purehearted vs. self-serving. Self-transcendence (ST): ST1, Self-forgetful vs. self-conscious; ST2, Transpersonal identification; ST3, Spiritual acceptance vs. materialism. This instrument was validated previously in the general Mexican population [24], where it was shown that despite cultural differences the instrument had a good validity and reliability. The instrument has not been used to evaluate other samples of patients in the Mexican population.

Analysis

We used descriptive statistics to assess frequencies and distributions. As appropriate, proportions were compared with either a chi square test or a Fisher's exact test. One way ANOVA analysis was used to compare the scores of TCI in the following groups: PWM, BD and NMCP. For the post hoc analysis, Bonferroni's correction for equal variances and the Games-Howell's Test for unequal variances were used. All analyses were performed using SPSS version 10 (SPSS Inc., Chicago, IL). To compare the TCI scores of PWM, NMCP and HGHP used in the original validation of the TCI in the Mexican population [24], we used the formula to compare median and standard deviations proposed by Machin et al. [33] and Cohen [34] as independent samples. This formula has been included in the statistical program EPIDAT 3.0 [35], which was utilised in our study. Cronbach's alpha was calculated to evaluate the reliability of the TCI in our study.

Results

General description

We studied 142 PWM, 108 BD and 30 PNMP. Also we utilised a historical cohort of 269 people used to validate the TCI in the Mexican population (see description in Methods) [24]. The percentage of PWM who refused to participate was 5% (7 patients); none of the BD and NMCP refused to participate. Of the PWM, 58 patients did not have aura while 84 did. The most frequent clinical findings were nausea in 83% of patients and photophobia in 85%. The most important triggers included stress 23%, food 8% and menstruation 6%. The most frequently associated chronic conditions were hypotension or hypertension (7%), epilepsy (2%) and irritable bowel syndrome (3%). Seven percent of patients had mild or minimal disability, 51% moderate and 42% had severe according to the MIDAS scale (see Table 1). In the group of PWM 112 (79%) were females, in the blood donors 74 (69%), in the non-migraine pain controls 24 (80%) and in the study of Sanchez de Carmona et al. [24], 269 (54%). The difference of proportion of females in the first three groups was not statistically significant (p=0.36). The age of PWM was 36.7±13, in the BD 35.8±13, in the NMCP 40.9±15 and in the HGHP from the study of Sanchez de Carmona [24], 25.6±8.8 years. The differences in ages between the first three groups were not statistically significant (p=0.18).

Analysis of personality (migraine patients vs. BD)

Regarding temperament, PWM had a higher scores in the HA dimension and all its sub-dimensions, except HA3. Lower scores in PWM were identified in the RD3 subdi-

Table 1 Clinical characteristics of migraine patients (n=142)

Variable	Frequency	%
Migraine type		
With aura	58	59
Without aura	84	41
Disability		
Mild or minimal	10	7
Moderate	73	51
Severe	59	42
Clinical manifestations		
Nausea	118	83
Vomiting	85	59
Phonophobia	95	67
Photophobia	121	85
Others	8	6
Triggers		
None	57	40
Stress	33	23
Food	12	8
Menstruation	9	6
Alcohol	8	5
Exercise	6	4
Others	2	1
Associated conditions*		
Hypertension	10	7
Epilepsy	3	2
Irritable bowel syndrome	4	3
Peptic disease	2	1
Depression	12	8
Asthma	3	2
Allergies	4	2

*Self-reported prevalence

mension. Regarding the character scores, PWM had lower scores in the SD5 subdimension, as well as the subdimension C3 (see Table 2a,b).

Analysis of personality (migraine patients *vs.* the HGHP from the study of Sanchez de Carmona et al. [24])

Regarding temperament, PWM have lower scores in the NS dimension and its NS1 and NS4 subdimensions and higher scores in the dimension HA and all its subdimensions. Higher scores were seen in the subdimension RD1 and P, and lower scores in RD3. Regarding character, PWM had higher scores in the C dimension and its subdimensions C1, C4 and C5 (see Table 3a,b).

Subscales	Temperament scales	Migraine (<i>n</i> =142)	BD (<i>n</i> =108)	NMCP (<i>n</i> =30)	C Bonfer (df=2, 2	One-way ANOVA, Bonferroni's post hoc analysis (df=2, 277) (M vs. C vs. NMCP)	
					F	p	
	Novelty seeking	17.9±5.0	18.1±4.9	18.1±5.8	0.056	0.946	
NS1	Exploratory excitability vs. rigidity	6.2±1.8	6.4±2.0	5.3±2.5	3.22	0.037 (BD>NMCP)	
NS2	Impulsiveness vs. reflection	3.5±2.4	3.3±2.1	5.3±2.2	9.58	<0.001 (NMCP>M, BD)	
NS3	Extravagance vs. reserve	4.3±2.1	4.6±1.9	3.5±1.5	3.59	0.024 (BD>NMCP)	
NS4	Disorderliness <i>vs</i> . regimentation	3.8±1.9	3.9±1.8	4.0±1.5	0.135	1.0	
	Harm avoidance	17.2±6.1	14.1±6.2	16.2±5.3	8.248	<0.01 (M and NMCP>BD)	
HA1	Anticipatory worry vs. optimism	4.6±2.3	3.9±2.1	5.0±2.4	4.49	0.029 (M and NMCP>BD)	
HA2	Fear of uncertainty vs. confidence	4.5±1.6	4.0±1.7	3.2±1.7	9.25	<0.05 (M>BD and NMCP)	
HA3	Shyness vs. gregariousness	3.7±2.3	3.0±2.0	3.7±1.5	3.21	0.332	
HA4	Fatigability and asthenia vs. vigour	4.3±2.4	3.2±1.9	4.4±1.9	9.61	<0.05 (M and NMCP>BD)	
	Reward dependence	14.6±3.9	15.3±3.4	14.4±3.3	1.40	0.724	
RD1	Sentimentality vs. insensitivi	ty 6.9±2.1	6.7±2.0	7.1±1.7	0.618	0.919	
RD3	Attachment vs. detachment	4.2±2.4	4.9±2.2	4.8±1.5	3.14	0.05 (BD>M)	
RD4	Dependence <i>vs</i> . independence	3.5±1.6	3.8±1.3	2.5±1.7	7.59	0.004 (M and BD>NMCP)	
RD2	Persistence	5.1±1.7	5.2±1.8	4.0±1.5	6.34	0.004 (M and BD>NMCP)	

Table 2a Comparative analysis of scores of *temperament* dimensions and subdimensions between patients with migraine *vs.* blood donors (BD) and non-migraine chronic pain controls (NMCP)

BD, blood donors; NMCP, non-migraine chronic pain

Analysis of personality (migraine patients vs. NMCP)

Patients with migraine showed higher scores in the subscales of temperament HA2 and RD4 than NMCP (see Table 2a). Patients with NMCP had lower scores in the following subdimensions: P, SD, SD1, SD3, C, C1, C4 and C5 than PWM. Higher scores in the subdimension NS2 were found in NMCP than PWM and BD (see Tables 2a,b). Analysis of personality (NMCP *vs.* the HGHP from the study of Sanchez de Carmona et al. [24] and blood donors)

Compared with the HGHP of the study of SC, NMCP showed lower scores in the dimension NS and higher scores in HA. The subscales with lower scores in NMCP were NS1, NS2 and NS3. The subscales with higher scores were HA1, HA3 and HA4 (see Tables 3a,b). Regarding character, two

Subscale	Character scales	Migraine (<i>n</i> =142)	BD (<i>n</i> =108)	NMCP (<i>n</i> =30)	One-way ANOVA with Bonferroni's post hoc analysis (df=2, 277) (M vs. C vs. NMCP)	
					F	p
	Self-directedness	29.5±7.8	32.3±5.7	25.4±9.0	11.69	<0.05 (M and BD>NMCP)
SD1	Responsibility vs. blaming	5.4±2.1	6.3±1.5	3.6±2.5	24.63	<0.001 (M and BD>NMCP)
SD2	Purposeful vs. goal-undirected	5.4±2.1	5.8±1.7	5.3±1.5	1.87	0.156
SD3	Resourcefulness vs. apathy	3.9±1.7	4.2±1.5	2.1±1.5	19.65	<0.001 (M and BD>NMCP)
SD4	Self-acceptance vs. self-striving	6.2±2.5	6.7±2.3	6.1±2.6	1.37	0.255
SD5	Congruent second nature	8.6±2.4	9.3±2.0	8.3±2.2	4.23	0.05 (BD>M)
	Cooperativeness	30.3±6.0	32.0±4.1	25.4±6.6	16.84	<0.001 (M and BD>NMCP)
C1	Social acceptance vs. intolerance	6.0±1.9	6.5±1.3	4.6±1.6	14.31	<0.001 (M and BD>NMCP)
C2	Empathy <i>vs</i> . social disinterest	4.6±1.4	4.6±1.2	4.0±1.5	2.59	0.076
C3	Helpfulness <i>vs</i> . unhelpfulness	5.6±1.3	6.1±1.1	6.0±1.4	6.89	0.001 (BD>M)
C4	Compassion vs. revengefulness	7.9±2.5	8.4±1.8	5.4±2.1	21.10	<0.001 (M and BD>NMCP)
C5	Pure-hearted <i>vs</i> . self-serving	6.3±1.7	6.3±1.7	5.3±1.5	4.63	0.05 (M and BD>NMCP)
	Self-transcendence	16.6±6.2	17.1±6.2	17.0±6.6	0.167	0.846
ST1	Self-forgetful vs. self-conscious	6.1±2.7	5.6±2.5	6.0±3.0	1.05	0.350
ST2	Transpersonal identification	4.1±2.2	4.7±2.2	4.9±2.1	2.52	0.082
ST3	Spiritual acceptance vs. materialism	6.4±3.0	6.8±2.8	6.0±2.8	1.00	0.369

Table 2b Comparative analysis of scores of the *character* dimensions and subdimensions of the TCI between patients with migraine *vs*. blood donors (BD) and non-migraine chronic pain controls (NMCP)

BD, blood donors; NMCP, non-migraine chronic pain

scales had lower scores in SD and C. The subdimensions with lower scores were SD1, SD3, C1 and C4. Compared with blood donors NMCP had lower scores in the temperament subdimensions NS1 and NS3, but higher in NS2.

NMCP had higher scores in the dimension HA and its HA1 and HA4 subdimensions. In character scales SD and C dimensions had lower scores in NMCP. The subscales with lower scores in NMCP were SD1, SD3, C1, C4 and C5.

Subscales	Temperament scales	Migraine patients, mean±SD (<i>n</i> =142)	SC controls*, mean±SD (<i>n</i> =269)	NMCP, mean±SD (<i>n</i> =30)
	Novelty seeking	17.9±5.0ª	20.2±5.1	18.1±5.8 ^a
NS1	Exploratory excitability vs. rigidity	6.2±1.8 ^a	6.9±2.2	5.3±2.5ª
NS2	Impulsiveness vs. reflection	3.5±2.4	3.9±2.5	5.3±2.2 ^a
NS3	Extravagance vs. reserve	4.3±2.1	4.7±2.0	3.5±1.5 ^a
NS4	Disorderliness vs. regimentation	3.8±1.9 ^a	4.5±2.0	4.0±1.5
	Harm avoidance	17.2±6.1ª	12.6±7.1	16.2±5.3ª
HA1	Anticipatory worry vs. optimism	4.6±2.3ª	3.5±2.7	5.0±2.4ª
HA2	Fear of uncertainty vs. confidence	4.5±1.6 ^a	3.1±1.7	3.2±1.7
HA3	Shyness vs. gregariousness	3.7±2.3ª	2.9±2.2	3.7±1.5 ^a
HA4	Fatigability and asthenia vs. vigour	4.3±2.4ª	2.9±2.4	4.4±1.9 ^a
	Reward dependence	14.6±3.9	13.9±4.1	14.4±3.3
RD1	Sentimentality vs. insensitivity	6.9±2.1ª	5.5±2.2	7.1±1.7 ^a
RD3	Attachment vs. detachment	4.2±2.4 ^a	4.9±2.2	4.8±1.5
RD4	Dependence vs. independence	3.5±1.6	3.4±1.3	2.5±1.7ª
RD2	Persistence	5.1±1.7 ^a	4.7±1.8	4.0±1.5 ^a

Table 3a Comparative analysis of scores of the *temperament* dimensions and subdimensions of the TCI between patients with migraine vs. SC controls

^ap<0.05 vs. Sanchez de Carmona controls* (SC controls) [24]; NMCP = non migraine control pain

Table 3bComparative	analysis of scores o	of the character	dimensions a	nd subdimensions	of the TCI between	n patients with n	igraine vs.
SC controls							

Subscales	Character scales	Migraine patients, mean±SD (<i>n</i> =142)	SC controls, mean±SD (<i>n</i> =269)	NMCP, mean±SD (<i>n</i> =30)
	Self-directedness	29.5±7.8	29.9±10.8	25.4±9.0ª
SD1	Responsibility vs. blaming	5.4±2.1	5.6±2.5	3.6 ± 2.5^{a}
SD2	Purposeful vs. goal-undirected	5.4±2.1	5.6±2.3	5.3±1.5
SD3	Resourcefulness vs. apathy	3.9±1.7	3.6±1.6	2.1±1.5 ^a
SD4	Self-acceptance vs. self-striving	6.2±2.5	6.4±2.9	6.1±2.6
SD5	Congruent second nature	8.6±2.4	8.2±3.2	8.3±2.2
	Cooperativeness	30.3±6.0 ^a	28.22±9.9	25.4±6.6 ^a
C1	Social acceptance vs. intolerance	6.0±1.9 ^a	5.5±2.5	4.6±1.6 ^a
C2	Empathy vs. social disinterest	4.6±1.4	4.4±1.9	4.0±1.5
C3	Helpfulness vs. unhelpfulness	5.6±1.3	5.4±2.0	6.0±1.4
C4	Compassion vs. revengefulness	7.9 ± 2.5^{a}	6.9±3.1	5.4±2.1ª
C5	Pure-hearted vs. self-serving	6.3±1.7 ^a	5.8±2.1	5.3±1.5
	Self-transcendence	16.6±6.2	16.4±6.2	17.0±6.6
ST1	Self-forgetful vs. self-conscious	6.1±2.7	5.9±2.6	6.0±3.0
ST2	Transpersonal identification	4.1±2.2	4.3±2.1	4.9±2.1
ST3	Spiritual acceptance vs. materialism	6.4±3.0	6.1±3.1	6.0±2.8

^ap<0.05 vs. Sanchez de Carmona controls* (SC controls) [24]; NMCP = non migraine control pain

Other analyses

Within the migraine group, comparisons between patients with and without aura revealed no statistically significant differences. Only the SD3 domain scores were higher in patients with aura (p=0.04). We analysed the TCI scores in PWM according to disability and only the subdimension RD3 had higher scores in severe patients.

Reliability of the TCI

In the group of PWM the Cronbach's alpha of the TCI was 0.70, ranging from 0.68 to 0.70. Considering the whole sample (migraine, blood donor, non-migraine pain controls), the Cronbach's alpha of the TCI was 0.75, ranging from 0.74 to 0.75.

Discussion

In this study we have evaluated the personality of PWM using the TCI. This study is remarkable for the use of different control groups. Our migraine patients had higher scores in the HA scale than two different types of healthy controls. Our results are similar to earlier works of Di Piero et al. and Mongini et al. [6, 25] using the TCI and consistent with other studies using other instruments such as the Dimensional Assessment of Personality Pathology [36]. It has been suggested that this scale (Harm Avoidance) indicates a heritable predisposition to form conditioned signals of punishment and frustrative nonreward. That is, such people are easily worried or frightened. In addition, they tend to be sensitive to passive avoidance learning, which is the inhibition of activity in response to such conditioned signals. They tend to readily become inhibited and/or demonstrate shyness [37]. Also, patients are described as careful, insecure and with a high tendency towards anxiety and depression under stressful situations [6, 25].

Deakin and Graeff [38] studied 31 patients using PET and the TPQ. This author observed that HA was associated with activity in the anterior paralimbic circuit, specifically in the right amygdala, the insula, right orbitofrontal cortex and right insula and the left medial prefrontal cortex. It is important to note that this activity pattern is related to the serotoninergic $(5HT_2)$ terminal projections of the dorsal rafe. Using other research strategies, other authors have supported the serotoninergic aetiological link with HA [38–43]. The results of the present study indirectly support serotoninergic involvement in the physiopathology of migraine, as has been shown extensively in the literature [44, 45].

In our study PWM and NMCP had higher scores in the HA dimension compared with both healthy controls. This observation is interesting because both groups of patients have chronic pain, being a feature with a high tendency to develop avoidance to situations associated with real or imaginary damage [6, 25]. This type of personality is reflected in patients as worries, fear and fatigue [6, 25]. PWM had higher scores in the HA2 subdimension compared with the NCMP. This observation is remarkable and we believe that the higher scores in PWM are related to the nature of pain, being more paroxistic, difficult to predict, and even with the control of some triggers. On the other hand the higher scores of HA in patients with acquired pain, such as radiculopathies, neuropathies and osteoarthritis, raise the possibility of developing this personality profile in acquired conditions also, and not only genetically related, as some authors have suggested [46]. In keeping with our results, Pud et al. [47] showed a correlation between high scores of HA with pain threshold (latency to pain onset), pain magnitude (VAS), and pain tolerance (time to withdrawal) using the cold pressor test in healthy patients. The involvement of serotonin in chronic pain [48-51] is consistent with the proposed physiopathological mechanisms of HA in the central nervous system [23].

Regarding temperament, our study shows that persistence could be a feature of the personality of PWM when compared with the HGHP of the study of SC [24], but not when was compared with the BD, suggesting some rigidity and obsessivity, as Mongini et al. [6] reported previously. In contrast with the study of Nylander et al. [23], we found lower scores in the subdimensions of NS in PWM compared with the two controls. The explanation for the difference in the scores is probably the type of population; Nylander et al. [23] evaluated a family of migraineurs that might not reflect the personality profile of the general population of migraineurs. We consider that the lower scores in NS could be a consistent pattern in patients with chronic pain, being represented as an avoidance personality with less motivation to explore new things, avoiding the possibility of experiment pain. Finally, other dimensions, such as sentimentality and detachment, not previously reported, were associated with PWM in our study and require further investigations.

PWM had higher scores of SD and C than the NMCP but similar scores compared with blood donors. We consider that due to the chronicity of migraine and the nature of the pain, patients have more interest in helping medical societies and are more likely to help other patients, probably implying the use of adaptation resources to confront pain. The elevation of these scales in BD is consistent with people who donate blood in an altruistic way. These observations contrast with previous studies where PWM are more prone to use internal defence mechanisms and avoid social support to resolve their problems [52].

A high score in Harm Avoidance (HA), as found among our PWM, has been related to features of the Cluster C personality disorders in the DSM-IV (fearful, anxious subtype), although it is difficult to support a specific personality disorder in PWM. A potential argument to support the lack of a specific personality disorder is the similar TCI profile of PWM with NMCP, supporting the idea of potential personality features for patients who are confronted with a chronic pain disorder.

As with any study, the present one has limitations. The main limitation is the lack of a standardised interview to rule out psychiatric conditions in order to perform a correlation with the TCI domains. It is possible that harm avoidance could be related with depression and anxiety disorders, especially in PWM, where the comorbidity with psychiatric conditions is high [52-59]. Also, the lack of a standardised interview avoids a potential comparison between some groups of interest such as patients with aura, where the prevalence of psychiatric conditions is reportedly higher [56, 57]. The relationship between migraine and depression is controversial, but both diseases involve mood changes and monoamine alterations [58, 60, 61]. Another relative weakness in our study is the inclusion of a control group of blood donors. This group represents a selected population that might not correctly represent the normal population. Although it is a very selected group, it has some advantages. For example, these patients are screened well to rule out other medical conditions before the donation of blood, and this is a property that fits more with a healthy population. On the other hand, the age of this group is close to the age of patients with migraine, allowing valid comparisons. According our study, BD could be people with more energy (HA 4), with a tendency to help other people (C3) and more optimistic (HA1). Finally, the main strength of this study was the inclusion of two healthy control groups and a group of patients with chronic pain other than migraine, showing consistently higher scores of HA in PWM.

The comparison between NMCP and the two control groups was very consistent. Regarding the temperament scales, NMCP had higher scores on HA and lower scores of NS. In the character scales NMCP had consistently low scores in SD and C scales. Svrakic et al. [62] have pointed out that low scores of SD and C could be associated with personality disorders. Specifically, the combination of high scores of HA and low scores of NS has been associated with cluster C avoidant personality, which has been associated with anxiety and depression [62]. In summary, this analysis supports a possible personality profile in NMCP, as we mentioned before, and validates our methodology.

Taken as a whole, we have corroborated that HA scales are elevated in PWM, in keeping with the proposed serotoninergic mechanism of migraine. We have demonstrated that patients with other types of pain can share the same profile, raising the possibility of this personality profile developing in acquired conditions and not only by genetic mechanisms. The potential correlation of this instrument with different physiopathological pathways in the central nervous system allows the possibility to approach different neurological conditions in order to evaluate mechanisms of disease.

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