Neurological Sciences (2020) 41:543–554
https://doi.org/10.1007/s10072-019-04174-x

REVIEW ARTICLE

Personality profile and depression in migraine: a meta-analysis

Federica Garramone[1] · Chiara Baiano[1] · Antonio Russo[2] · Alfonsina D'Iorio[1] · Gioacchino Tedeschi[2] · Luigi Trojano[1] · Gabriella Santangelo[1]

Received: 24 June 2019 / Accepted: 22 November 2019 / Published online: 12 December 2019

Abstract

Background Despite the clinical importance of psychological factors in migraine, the relationship between personality traits, depression, and migraine has been poorly investigated.

Objective To delineate the personality profile distinctive for migraineurs and to explore the relationship between personality traits and depression in migraineurs compared to non-migraineurs.

Methods A systematic literature search was performed up to March 2019 using PsycInfo (PROQUEST), PubMed and Scopus. Sixteen primary studies met inclusion and exclusion criteria and were included in the meta-analysis.

Results The meta-analysis on the personality defined according to Psychobiological model revealed high Harm Avoidance (Hedges'g = 0.31; 95% confidence interval [CI] = 0.01–0.60), Persistence (Hedges'g = 0.37; 95% CI = 0.01to − 0.72) and low self-directedness (Hedges'g = − 0.33; 95% CI = −0.57 to − 0.09) in migraineurs. The meta-analysis on the personality defined according to Three Factor Model revealed high neuroticism (Hedges'g = 0.47; 95% CI = 0.32–0.63) and low extraversion (Hedges'g = − 0.08; 95% CI = − 0.14 to − 0.03) in migraineurs. Meta-regression analysis revealed that neuroticism moderated the relationship between depression and migraine.

Conclusion The findings evidenced that migraine is characterized by specific personality traits. Among them, neuroticism influenced the severity of depression in migraineurs, and, therefore, an early evaluation of the personality traits could allow identifying patients susceptible to develop migraine-associated psychopathological symptoms.

Keywords Depression · Meta-analysis · Migraine · Personality traits

Introduction

Personality is defined as a set of psychological qualities related to feelings, thoughts and behaviours [1]. Many theories of personality structure have been proposed but the most widely known are the Psychobiological Model [2], the Big-Five Model [3] and Eysenck's Three-Factor Model [4]. These models share the idea that personality can be described in terms of several factors but differ from each other in the number and in the formal characteristics of such factors, and in the specific tools needed to assess them. The Psychobiological Model (PM) [2] explored the seven basic personality dimensions of temperament (i.e. novelty seeking, harm avoidance, reward dependence and persistence) and character (i.e. self-directedness, cooperativeness and self-transcendence). The Big-Five Model [3] proposes that five main dimensions characterize personality: extraversion, agreeableness, conscientiousness, neuroticism and openness. The Eysenck's Three-Factor Model (TFM) [4] model was centred on three dimensions: extraversion, neuroticism and psychoticism (for more information, see Supplementary Material 1, A). The three models are the most widely accepted personality theory in the scientific community and are commonly used in the research and study of personality in psychology [5].

Early studies reported that migraineurs' personality is characterized by orderliness, perfectionism, inflexibility and a tendency to react excessively to problems, which, in turn, could lead to attacks of migraine [6]. Later on, studies comparing

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s10072-019-04174-x) contains supplementary material, which is available to authorized users.

✉ Gabriella Santangelo
gabriella.santangelo@unicampania.it

[1] Department of Psychology, University of Campania "Luigi Vanvitelli", Caserta, Italy

[2] Headache Center, Department of Medical, Surgical, Neurological, Metabolic and Aging Sciences, University of Campania "Luigi Vanvitelli", Naples, Italy

personality traits in migraineurs and non-migraineurs reported mixed results. For instance, some studies investigating the personality profile according to the psychobiological model (PM) reported a higher level of harm avoidance in migraineurs [7–10], whereas one study did not observe differences between migraineurs and non-migraineurs [11] and another reported the opposite pattern [12]. Similarly, some studies reported higher levels of Persistence in migraineurs with respect to non-migraineurs [7, 9, 10], but some studies did not observe differences between the two groups [11, 12]. Analogous inconsistencies have been reported for self-directedness, whereas more consistent findings (no difference between migraineurs and non-migraineurs) have been reported for other psychological traits included in the PM [7–12]. When the personality profile was explored by questionnaires assessing the psychological dimensions proposed by the Eysenck's Three-Factor Model (TFM), migraineurs tended to show higher scores than non-migraineurs in neuroticism [13–16], whereas mixed results have been reported about levels of extraversion and psychoticism [13–15]. Finally, only two studies [17, 18] evaluated the personality traits according to the Big-Five Model and found high level of neuroticism, conscientiousness and agreeableness in migraineurs compared to non-migraineurs. Assessing personality traits and psychosomatic mechanisms of migraine patients might allow developing non-pharmacological treatment, to make them less vulnerable to stress and more skilled in coping with pain. Unfortunately, previous findings on the personality traits in migraineurs are heterogeneous and did not reveal a well-established personality profile. On this basis, we performed two separate meta-analyses on primary studies investigating personality traits according to current psychological models in migraineurs and non-migraineurs. We explored the possible influence of demographic and clinical aspects on each personality trait in migraineurs, as suggested in a recent review [19].

Some studies have revealed a significant association between depression and migraine [20] but, until now, no study has explored the possible crucial role of the personality traits in modulating the relationship between depression and migraine. Therefore, we performed a meta-analysis on studies focusing on the depression and personality traits in migraineurs.

Methods

Search strategy and study eligibility criteria

A systematic literature search was performed up to March 2019 using PsycInfo (PROQUEST), PubMed and Scopus entering the following search terms: "personality" or "temperament" or "neurot*" or "psychoticism" or "negative emotionality" or "extraversion" or "introversion" or "openness to experience" or "cognitive rigidity" or "rigidity" or "agreeableness" or "conscientiousness" or "impulsiv*" or "novelty seeking" or "harm avoidance" or "reward dependence" or "persistence" and "Migraine". This search was supplemented by hand searches of reference lists cited in the original and review articles. Two independent observers (F.G., C.B.) evaluated the results and resolved any disagreement by discussion or with recourse to a third arbitrator (G.S.). A primary study was included in the meta-analysis if it (i.) was published in peer-reviewed journal in English from 1980 to 2019, (ii) provided results about comparison on personality traits between patients with a diagnosis of migraine (i.e. migraine without or with aura) according to clinical criteria [21] and individuals without migraine or headache and (iii) reported statistical results (mean, standard deviation, standard difference, p value) about comparisons on personality traits between migraineurs and non-migraineurs. We excluded conference proceedings, letters to the editor, commentaries, theses, studies performed on animals and single cases studies. The data presented in more than one publication were used in their primary version (first publication). When two or more studies included patients from the same sample, we selected the primary study with the highest number of patients.

Data extraction and coding

Data extracted and coded from the primary articles included (i) characteristics of the publication (e.g. authors, journal status, year of publication, journal) and (ii) characteristics of the sample (e.g. total sample size, gender, duration and frequency of headache, subjective pain rating). To perform a meta-regression where depression was the outcome and personality trait was the moderator, we selected primary studies which provided mean score of depression questionnaire and mean score of personality traits in patients with migraine. We defined as outcomes seven dimensions put forward by PM, including both temperament (i.e. novelty seeking, harm avoidance, reward dependence and persistence) and character (i.e. self-directedness, cooperativeness and self-transcendence) and three dimensions included in the TFM (i.e. neuroticism, psychoticism and extraversion). When a study evaluated personality traits by questionnaires not specifically developed on the basis of the PM or TFM, we decided to use the dimensions considered theoretically associated to each personality model.

Statistical analyses

We synthesized study data using meta-analytic methods (ProMeta 3; Intenovi, 2015). Meta-analytic method was used to synthesize study data: we computed the effect sizes (ES) from data reported in the primary studies (e.g. means and standard deviations; p values) using Hedges' g unbiased approach (like the Cohen d statistic). Negative values of the

Hedges' g indicated that migraineurs had lower scores than non-migraineurs on each outcome. Conventionally, values of Hedges' $g < 0.20$ indicate small effects, values of about 0.50 moderate effects, and values of about 0.80 large effects. For each ES, 95% confidence interval, variance, standard error and statistical significance were computed. Moreover, ES across studies were pooled for obtaining an overall effect size with the inverse-variance method. We used the random-effects model since it is a conservative approach useful to account for different sources of variation among studies and to generalize the meta-analytic finding beyond the studies included here. Q and I^2 statistics index were computed to assess the heterogeneity among the studies. A significant Q value indicates a lack of homogeneity of findings among studies; the proportion of observed variance that reflects real differences in ES was estimated by I^2. A value of 25, 50 and 75% was considered as low, moderate and high, respectively. Sensitivity analyses were performed to check the stability of study findings, computing how the overall ES would change removing one study at a time. To explore the publication bias, we applied the funnel plot, a scatter plot of the ES estimated from individual studies against a measure of their precision (e.g. their standard errors). To evaluate the funnel plot more reliably, we employed the Egger's regression method, which to statistically test the asymmetry of the funnel plot, with non-significant results indicative of absence of publication bias. Moreover, we applied the trim and fill procedure, an iterative non-parametric statistical technique, which evaluates the effect of potential data censoring on the result of the meta-analyses. In this method, the absence of publication bias is indicated by zero trimmed studies, or in the presence of trimmed studies, by a trivial difference between the observed and the estimated ES. To further explain heterogeneity across studies and to explore the possible influence of demographic (age at evaluation, gender, years of schooling) and clinical variables (i.e. duration and frequency of headache, subjective pain rating) on each outcome, we performed several meta-regressions. Meta-regressions were also performed to evaluate which personality trait moderate the severity of depression in migraine. The references for methodological procedures were reported in Supplementary Material 1, C. Statistical analyses were conducted with the meta-analytic software ProMeta 3.0.

Results

Study selection

Figure 1 shows the flow diagram based on PRISMA statement. The initial search identified 3777 articles; after removing duplicates, we obtained 2611 articles. After full-text assessment, 181 studies were considered eligible. According to inclusion and exclusion criteria, we included eight studies [7–12, 22, 23] in the meta-analysis on the personality defined

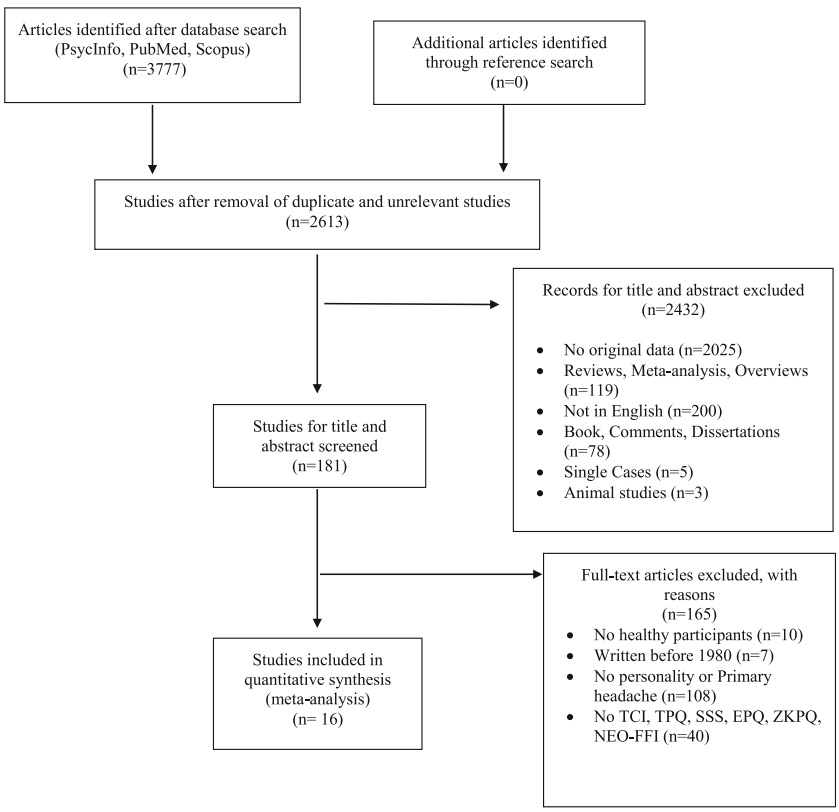

Fig. 1 Flowchart of the selection process of the primary studies (PRISMA)

according to PM and 10 studies [13–18, 22–25] in the meta-analysis on personality defined according to TFM. Moreover, we included a study by Karmakar et al. [18] where a self-reported provider diagnosis (SRPD) of migraine was used. As three studies [14, 17, 24] provided mean and standard deviations of migraineurs with and without aura as two separate groups, these were collapsed into one group by calculating the pooled means and standard deviations from statistics provided in each paper. As for the association between personality traits and the type of the migraine, among the eight studies included in the meta-analysis on the personality defined according to PM, four studies specified that the sample included migraineurs without aura [8, 10, 22, 23] whereas the remaining four studies did not specify the type of migraine [7, 9, 11, 12]. Out of 10 studies included in the meta-analysis on the personality defined according to TFM, five included migraineurs without aura [14, 17, 22–24], three included migraineurs with aura [14, 17, 24], whereas the remaining five studies did not specify the type of migraine [14–16, 18, 25]. Characteristics of primary studies included in the meta-analysis are reported in Table 1.

Personality profile according to PM

Novelty seeking The ES (= − 0.16; 95% CI = − 0.40–0.08) was not significant and there was no publication bias. The heterogeneity among the studies was significant and moderate. After removing Wang et al.'s study [22], the ES (= − 0.09; 95% CI = − 0.31–0.13) remained not significant and the heterogeneity became not significant (Table 2; Supplementary Material Figure 2A).

Harm avoidance The ES (= 0.45; 95% CI = 0.07–0.83) was significant and moderate: migraineurs scored higher than non-migraineurs. There was no publication bias, whereas the heterogeneity across the studies was high. After removing Park et al.'s study [8], ES (= 0.31; 95% CI = 0.01–0.60) remained significant and the heterogeneity decreased (Table 2; Supplementary Material Figure 2B).

Reward dependence The ES (= 0.01; 95% CI = −0.15-0.18) was not significant, without publication bias and heterogeneity across the studies (Table 2; Supplementary Material Figure 2C).

Persistence The ES (= 0.25; 95% CI = − 0.11–0.61) was not significant without publication bias. The heterogeneity across the studies was significant and high (I^2 = 78%). After removing Boz et al.'s study [12], the ES (= 0.37; 95% CI = 0.01–0.72) became significant and moderate and the heterogeneity decreased slightly (I^2 = 71%) (Table 2; Supplementary Material Figure 2D).

Self-directedness The ES (= − 0.16; 95% CI = − 0.53–0.21) was not significant, without publication bias, but the heterogeneity was high. After removing Sanchez-Roman et al.'s the study [9], the ES (= − 0.33; 95% CI = −0.57 to − 0.09) became significant and moderate whereas the heterogeneity decreased (Table 2; Supplementary Material Figure 3A).

Cooperativeness The ES (= 0.11; 95% CI = − 0.25–0.48) was not significant. There was no publication bias; the heterogeneity was significant and high. After removing Sanchez-Roman et al.'s the study [9], the ES (= − 0.05; 95% CI = −0.28–0.17) remained not significant and the heterogeneity became not significant (Table 2; Supplementary Material Figure 3B).

Self-transcendence The ES (= − 0.04; 95% CI = − 0.25–0.17) was not significant, without publication bias or the heterogeneity across the studies (Table 2; Supplementary Material Figure 3C).

Comparison between migraineurs with and without aura A subgroup analysis to identify possible differences on personality traits between the two groups was not performed as only 4/8 studies specified the type of migraine.

Personality profile according to TFM

Neuroticism The ES (= 0.56; 95% CI = 0.34–0.78) was significant and moderate: migraineurs scored higher than non-migraineurs. There was no publication bias, whereas the heterogeneity across the studies was high. After removing Brandt et al.'s study [13], the ES (= 0.47; 95% CI = 0.32–0.63) remained significant and moderate but the heterogeneity decreased (Table 3; Supplementary Material Figure 4A).

Psychoticism The ES (= − 0.04; 95% CI = −0.39–0.30) was not significant, without publication bias; the heterogeneity across the studies was significant and high (Table 3; Supplementary Material Figure 4B).

Extraversion The ES (= − 0.08; 95% CI = −0.14 to − 0.03) was significant but very low: migraineurs scored lower than non-migraineurs. No publication bias and heterogeneity across studies were found (Table 3; Supplementary Material Figure 4C).

Lie The ES (= − 0.19; 95% CI = − 0.45–0.07) was not significant, without publication bias. The heterogeneity across the studies was high and significant. After removing Brandt et al.'s study [13], the ES (= − 0–09; 95% CI = −0.33–0.15) remained not significant and the heterogeneity became not significant (Table 3; Supplementary Material Figure 4D).

Table 1 Characteristics of primary studies included in the meta-analysis

migraineurs ($n = 3164$)								Non-migraineurs[a] ($n = 13,767$)	
Authors	Country	No. of subjects	Age (years)	Education (years)	nM	Duration (month)	Classification criteria	Medication	Chronic/ episodic
Mongini et al. [6]	Italy (Turin)	49 migraineurs	NR	NR	0	NR	ICHD-I	NR	Episodic
Park et al. [7]	South Korea (Seoul)	97 migraineurs without aura	45.8 (9.5)	NR	0	NR	ICHD-II	NR	NR
Nylander et al. [10]	Sweden (Umeà)	26 migraineurs	45.1 (18.19)	NR	11	NR	ICHD-I	NR	Mixed sample
Sanchez-Roman et al. [8]	Mexico (Mexico City)	142 migraineurs	36.7 (13)	NR	30	NR	ICHD-II	NR	NR
Abbate- Daga et al. [9]	Italy (Turin)	105 migraineurs without aura	37.7 (11.98)	NR	25	NR	ICHD-II	NR	Chronic
Boz et al. [11]	Turkey (Trabzon)	51 migraineurs	28.2 (0.85)	11.49 (2.46)	17	NR	ICHD-I	NR	NR
Wang et al. [21]	Belgium (Liege)	26 migraineurs without aura	28.8 (6.4)	NR	8	10.5	ICHD-I	No medications	NR
Wang et al. [22]	Belgium (Liege)	22 migraineurs without aura	35.3 (9.6)	NR	4	NR	ICHD-I	NR	NR
Ashina et al. [15]	USA (New York)	43 migraineurs	NR	NR	NR	NR	ICHD-I	NR	Mixed sample
Brandt et al. [12]	Baltimore (MD)	162 migraineurs	22.8 (4.30)	NR	31	NR	ICHD-I	NR	NR
Breslau et al. [13]	Ohio (Cleveland)	59 migraineurs with aura 69 migraineurs without aura	26 for both groups of migraineurs	NR	NR	NR	ICHD-I	NR	NR
Cao et al. [23]	China (Anhui)	15 migraineurs with aura; 57 migraineurs without aura	34.1 (8.2) 32.8 (6.1)	NR	NR	NR	ICHD-I	NR	NR
Ishii et al. [16]	Japan (Tokyo)	24 migraineurs with aura 67 migraineurs without aura	42.4 (10.2) for both groups of migraineurs	NR	20	NR	ICHD-II	NR	NR
Perrozzo et al. [14]	Italy (Turin)	51 migraineurs	35.2 (11.3)	NR	18	NR	ICHD-I	NR	NR
Karmakar et al. [17]	USA (Toledo)	1927 migraineurs	29.25 (1.81)	NR	508	NR	ICHD-I	NR	NR
Wang et al. [21]	Belgium (Liege)	21 migraineurs without aura	28.8 (6.4)	NR	8	10.5	ICHD-I	NR	NR
Wang et al. [22]	Belgium (Liege)	22 migraineurs without aura	35.3 (9.6)	NR	4	NR	ICHD-I	NR	NR
Muscogiuri et al. [24]	Milan (Italy)	124 migraineurs	NR	NR	22	NR	ICHD-III	NR	NR

migraineurs ($n = 3164$)	Non-migraineurs[a] ($n = 13,767$)				Personality Model	Tools	Personality dimensions
Authors	No. of subjects	Age (years)	Education (Years)	nM			
Mongini et al. [6]	47	NR	NR	0	PM	TCI	Novelty seeking, harm avoidance, reward dependence, persistence, self-directedness, cooperativeness, self-transcendence
Park et al. [7]	100	48.3 (9.0)	NR	–	PM	TPQ	Harm avoidance
Nylander et al. [10]	87	44.7 (17.56)	NR	–	PM	TCI	Novelty seeking, harm avoidance, reward dependence, persistence, self-directedness, cooperativeness, self-transcendence
Sanchez-Roman et al. [8]	30 (NMCP)	NR	NR	24	PM	TCI	Novelty seeking, harm avoidance, reward dependence, persistence, self-directedness, cooperativeness, self-transcendence

Table 1 (continued)

Abbate- Daga et al. [9]	79	35.9 (10.57)	NR	17	PM	TCI	Novelty seeking, harm avoidance, reward dependence, persistence, self-directedness, cooperativeness, self-transcendence
Boz et al. [11]	82	25.8 (6.26)	11.62 (2.02)	28	PM	TCI	Novelty seeking, harm avoidance, reward dependence, persistence, self-directedness, cooperativeness, self-transcendence
Wang et al. [21]	30	27.5 (9.9)	NR	10	PM	SSS	Sensation seeking
Wang et al. [22]	26	32.0 (12.3)	NR	11	PM	SSS	Sensation seeking
Ashina et al. [15]	324	NR	NR	NR	TFM	EPQ	Neuroticism
Brandt et al. [12]	162	22.7 (4.28)	NR	31	TFM	EPQ	Neuroticism; extraversion; psychoticism
Breslau et al. [13]	879	26	NR	NR	TFM	EPQ	Neuroticism; extraversion; psychoticism
Cao et al. [23]	58	29.6 (8.3)	NR	NR	TFM	ZKPQ	Neuroticism-anxiety; sociability
Ishii et al. [16]	119	40.7 (10.4)	NR	31	TFM	NEO-FFI	Neuroticism; extraversion
Perrozzo et al. [14]	45	38.6 (11.1)	NR	21	TFM	EPQ/R	Emotional liability; Intra/extratensive; Antisociality and maladjustment
Karmakar et al. [17]	11,566	29.31 (1.87)	NR	5761	TFM	Mini-IPIP	Neuroticism; extraversion
Wang et al. [21]	30	27.5 (9.9)	NR	10	TFM	ZKPQ	Neuroticism-anxiety; sociability
Wang et al. [22]	26	32.0 (12.3)	NR	11	TFM	ZKPQ	Neuroticism-anxiety; sociability
Muscogiuri et al. [24]	77	NR	NR	14	TFM	PID-5	Anxiousness

nM number of males, *NR* not reported, *TCI* Temperament and Character Inventory, *TPQ* Tridimensional Personality Questionnaire, *SSS* Zuckerman's Sensation Seeking Scale, *PM* Psychobiological Model, *TFM* Eysenck's Three-Factor Model, *EPQ* Eysenck Personality Questionnaire, *ZKPQ* Zuckerman-Kuhlman's Personality Questionnaire, *NEO-FFI* NEO Five-Factor Inventory, *EPQ/R* Eysenck Personality Questionnaire revised, *mini-IPIP* mini International Personality Item Pool, *PID-5* Personality Inventory for DSM-5, *ICHD-I* International Classification of Headache Disorders, first edition, *ICHD-II* International Classification of Headache Disorders, 2nd edition, *ICHD-III* International Classification of Headache Disorders, 3rd edition

[a] People who did not suffer from any form of headache or migraine

Table 2 Summary of meta-analytic results of the following personality domains: novelty seeking, harm avoidance, reward dependence, perseverance/persistence, self-directedness, cooperativeness, self-transcendence

	K	Number of participants	Migraineurs	Non-migraineurs	Pooled effect size Hedges'*g* (*P* value)	(95% confidence intervals)		Homogeneity statistics			Egger's *t* test for publication bias	Trim and fill
						LL	UL	Q (df)	P	I^2		
Novelty Seeking	7	797	416	381	− 0.16 (0.197)	− 0.40	0.08	14.67 (6)	*0.023*	59.10	− 1.53 (0.188)	0
Sensitivity analysis after removing Wang et al. [21]	6	749	394	355	− 0.09 (0.445)	− 0.31	0.13	9.57 (5)	0.088	47.74	− 0.71 (0.517)	0
Harm avoidance	6	895	470	425	0.45 (*0.022*)	0.07	0.83	34.87 (5)	*< 0.001*	85.66	− 1.58 (0.189)	0
Sensitivity analysis after removing Park et al. [7]	5	698	373	325	0.31 (*0.041*)	0.01	0.60	12.36 (4)	*0.015*	67.63	− 0.84 (0.462)	0
Reward dependence	5	698	373	325	0.01 (0.856)	− 0.15	0.18	2.82 (4)	0.588	0.00	0.80 (0.480)	0
Perseverance/persistence	5	698	373	325	0.25 (0.173)	− 0.11	0.61	18.66 (4)	*0.001*	78.56	− 0.00 (0.997)	0
Sensitivity analysis after removing Boz et al. [11]	4	565	322	243	0.37 (*0.042*)	0.01	0.72	10.46 (3)	*0.015*	71.32	− 0.17 (0.882)	0
Self-directedness	5	698	373	325	− 0.16 (0.398)	− 0.53	0.21	19.94 (4)	*0.001*	79.94	0.86 (0.453)	0
Sensitivity analysis after removing Sanchez-Roman et al. [8]	4	526	231	295	− 0.33 (*0.007*)	− 0.57	−0.09	5.17 (3)	0.160	42.00	0.59 (0.612)	0
Cooperativeness	5	698	373	325	0.11 (0.538)	− 0.25	0.48	19.24 (4)	*0.001*	79.20	0.69 (0.541)	0
Sensitivity analysis after removing Sanchez-Roman et al. [8]	4	526	231	295	− 0.05 (0.637)	− 0.28	0.17	4.59 (3)	0.205	34.59	0.21 (0.851)	0
Self-transcendence	5	698	373	325	− 0.04 (0.731)	− 0.25	0.17	6.62 (4)	0.157	39.61	2.78 (0.069)	0

Statistically significant values are reported in italics. Q and I^2 indicate heterogeneity statistics

K number of studies, *LL* lower limit, *UL* upper limit, *df* degrees of freedom

Table 3 Summary of meta-analytic results of the following personality domains: Neuroticism, Psychoticism, Extraversion, Lie

	K	Number of participants	Migraineurs	Non-migraineurs	Pooled effect size Hedges'g (*P* value)	(95% confidence intervals)		Homogeneity statistics			Egger's *t* test for publication bias	Trim and fill
						LL	UL	Q (df)	*P*	I^2		
Neuroticism	10	15,927	2641	13,286	0.56 (*< 0.001*)	0.34	0.78	78.19 (9)	*< 0.001*	88.49	1.16 (0.280)	0
Sensitivity analysis after removing Brandt et al. [12]	9	15,603	2479	13,124	0.47 (*< 0.001*)	0.32	0.63	26.07 (7)	*< 0.001*	69.31	0.80 (0.450)	0
Psychoticism	3	1427	341	1086	− 0.04 (0.806)	− 0.39	0.30	11.58 (2)	*0.003*	82.72	0.03 (0.983)	0
Extraversion	8	15,359	2474	12,885	− 0.08 (*0.004*)	− 0.14	− 0.03	7.31 (7)	0.398	4.19	−2.16 (0.074)	0
Lie	4	1794	384	1410	− 0.19 (0.145)	− 0.45	0.07	11.53 (3)	*0.009*	73.98	1.17 (0.361)	1
Sensitivity analysis after removing Brandt et al. [12]	3	1470	222	1248	− 0.09 (0.478)	− 0.33	0.15	4.18 (2)	0.124	52.15	1.71 (0.337)	0

Q and I^2 indicate heterogeneity statistics. Statistically significant values are reported in italics

K number of studies, *LL* lower limit, *UL* upper limit, *df* degrees of freedom

Comparison between migraineurs with and without aura A subgroup analysis on five studies [14, 17, 22–24] revealed no difference between the two groups on neuroticism (Q = 0.14, df = 1, $p = 0.710$) and extraversion (Q = 0.17, df = 1, $p = 0.682$) (Supplementary Material Figure 5).

Moderator analysis

Age moderated the level of neuroticism: higher levels were found in younger than in older migraineurs (B = − 0.04, $p = 0.038$). Sex had no significant effect on each trait. We could not assess the possible effect of education, frequency and duration of attacks; pain intensity on the relationship between personality traits and migraine since there were not at least 10 samples to 1 covariate as suggested by Borenstein et al. [26].

Personality traits as moderators of depression in migraineurs

Studies that provided mean score of depression and mean score of personality traits in patients with migraine were reported in Table 4. Among the personality traits, only neuroticism moderated the severity of depressive symptomatology (B = 10.46, $p = 0.034$). Other personality traits did not influence the severity of the depression.

Discussion

Personality profile associated with migraine

The present meta-analytic study focused on personality traits associated with migraine. When personality was conceptualized according to PM, we found a higher level of both harm avoidance and persistence and a lower level of self-directedness in migraineurs with respect to non-migraineurs. No significant difference was found between migraineurs and non-migraineurs on the remaining dimensions of temperament and character. When we took into account the TFM, a higher level of neuroticism and a lower level of extraversion were significantly related to migraine. Only neuroticism moderated the severity of depressive symptomatology in migraineurs. A higher level of harm avoidance seems thus to be a distinctive personality trait of migraineurs [7–10]. Since in PM harm avoidance is characterized by behavioural inhibition, excessive fear/worry, our findings suggested that migraineurs are prone to have a pessimistic apprehension in anticipation of future problems and to show passive avoidant behaviours such as fear of uncertainty and rapid fatigability [2]. Only two studies did not report any difference between migraineurs and non-migraineurs on this personality trait, but

Table 4 Characteristics of primary studies that provided mean score of depression and personality traits in patients with migraine

		migraineurs ($n = 2459$)						Personality model	Personality questionnaire	Personality dimensions	Depression questionnaire
Authors	Country	No. of subjects	Age (years)	Education (years)	n M	Duration (month)	Classification criteria				
Abbate- Daga et al. [9]	Italy (Turin)	105 migraineurs without aura	37.7 (11.98)	NR	25	NR	ICHD-II	PM	TCI	Novelty seeking, harm avoidance, reward dependence, persistence, self-directedness, cooperativeness, self-transcendence	BDI
Boz et al. [11]	Turkey (Trabzon)	51 migraineurs	28.2 (0.85)	11.49 (2.46)	17	NR	ICHD-I	PM	TCI	Novelty seeking, harm avoidance, reward dependence, persistence, self-directedness, cooperativeness, self-transcendence	BDI
Wang et al. [21]	Belgium (Liege)	26 migraineurs without aura	28.8 (6.4)	NR	8	10.5	ICHD-I	PM	SSS	Sensation seeking	PVP
Wang et al. [22]	Belgium (Liege)	22 migraineurs without aura	35.3 (9.6)	NR	4	NR	ICHD-I	PM	SSS	Sensation seeking	PVP
Ashina et al. [15]	USA (New York)	43 migraineurs	NR	NR	NR	NR	ICHD-I	TFM	EPQ	Neuroticism	MDI
Cao et al. [23]	China (Anhui)	15 migraineurs with aura; 57 migraineurs without aura	34.1 (8.2) 32.8 (6.1)	NR	NR	NR	ICHD-I	TFM	ZKPQ	Neuroticism-anxiety, sociability	PVP
Perozzo et al. [14]	Italy (Turin)	51 migraineurs	35.2 (11.3)	NR	18	NR	ICHD-I	TFM	EPQ/R	Emotional liability; Intra/extratensive; antisociality and maladjustment	BDI
Karmakar et al. [17]	USA (Toledo)	1927 migraineurs	29.25 (1.81)	NR	508	NR	ICHD-I	TFM	mini-IPIP	Neuroticism; extraversion	CES-D

M males, *NR* Not reported, *TCI* Temperament and Character Inventory, *TPQ* Tridimensional Personality Questionnaire, *SSS* Zuckerman's Sensation Seeking Scale, *PM* Psychobiological Model, *TFM* Eysenck's Three- Factor Model, *EPQ* Eysenck Personality Questionnaire, *ZKPQ* Zuckerman-Kuhlman's Personality Questionnaire, *NEO-FFI* NEO Five-Factor Inventory, *EPQ/R* Eysenck Personality Questionnaire revised, *mini-IPIP* mini International Personality Item Pool, *BDI* Beck Depression Inventory, *PVP* Plutchik-van Praag's Depression Inventory; *MDI* Major Depression Inventory; *CES-D* Center for Epidemiologic Studies-Depression Scale, *ICHD-I* International Classification of Headache Disorders, first edition, *ICHD-II* International Classification of Headache Disorders, 2nd edition, *ICHD-III* International Classification of Headache Disorders, 3rd edition

the features of their sample might have biased these reports. Boz et al. [12] enrolled a sample of migraineurs smaller and older ($n = 51$; age = 28.24) than the sample of non-migraineurs ($n = 82$; age 25.84), whereas Nylander et al. [11] explored the personality traits in a small sample of 26 individuals belonging to the same family with a dominant autosomal inheritance pattern for migraine. On this basis, we would conclude that high level of harm avoidance is a very consistent finding in the migraineurs. The present meta-analysis cannot address neurobiological issues, but the finding of a consistent association between high level of harm avoidance and migraine might suggest that both conditions share common neurobiological mechanisms. In particular, it has been suggested that both harm avoidance and migraine might depend on a dysfunction of serotonergic transmission [8]. Indeed, high brain serotonin levels and lower 5-HT4 receptor binding within neocortex were found in migraineurs between attacks, whereas low serotonin levels occur typically during a migraine attack [27, 28]. Moreover, high level of harm avoidance seems to be associated with altered serotoninergic activity in dorsal raphe nuclei [29]. High level of persistence was another personality feature consistently associated with migraine [7, 9, 10]. According to PM, high levels of persistence characterize eager, ambitious, determined, resolute individuals who tend to persevere despite frustration and fatigue; this trait expresses the tendency to maintain unrewarded behaviours and correlate with high rigidity and obsessiveness [2]. From this perspective, migraineurs might be characterized by a tendency to be vulnerable to stress and a higher risk of developing depressive and anxiety symptoms when exposed to stressful events [30]. Moreover, this trait seems to influence the clinical course of migraine, as it might favour progression of episodic migraine to the chronic form, and/or the tendency to develop overuse of symptomatic medications [31, 32]. On neurobiological grounds, persistence has been related to altered glutamatergic systems [2], which have been involved in migraine pathophysiology [33]. The present meta-analysis would thus encourage future studies addressing the possible links between persistence and migraine. Among modifiable traits (characters) included in PM, only self-directedness differed in migraineurs and non-migraineurs and was lower in migraineurs. This finding, together with the high level of persistence, would confirm that patients suffering from migraine have poor coping skills and are vulnerable to stress. In the only study reporting conflicting results, Sanchez-Roman et al. [9] compared migraineurs with non-migraine individuals affected by chronic pain conditions, a sample characterized by very low levels of self-directedness [34]. Moreover, two studies [11, 12] did not find differences in self-directedness between migraineurs and control individuals, but, as specified above, the results of these papers could be biased by sample-related factors. Moreover, it is worth mentioning that Boz et al. [12] did observe a specific significant difference in one single subscale of the self-directedness character. Low levels of self-directedness and high levels of harm avoidance have been associated with altered serotonergic activity [35], an issue deserving to be investigated. Our meta-analysis of studies on the personality profile according to TFM revealed a higher level of neuroticism and a lower level of extraversion in migraineurs with respect to non-migraineurs. The strong relationship between migraine and high levels of neuroticism is in keeping with the finding of high level of harm avoidance described above, as the two personality traits overlap at least partially [36]. This finding would confirm that migraineurs might be less able to endure migraine pain, and, possibly, less able to cope with that pain [37]. Moreover, we found that high level of neuroticism was associated with more severe depressive symptoms supporting that the neuroticism is related to the tendency to experience negative emotions [3] and could be a predictor of development of depressive symptoms in migraineurs. Therefore, these findings suggested the clinical relevance of an early evaluation of personality profile in patients even early phase of disease to identify patients with maladaptive coping abilities and therefore more at risk for depression [38]. Our moderator analysis showed that age moderated the degree of association between neuroticism and migraine: younger subjects tend to have higher level of neuroticism than older ones. This finding confirmed the idea of cross-sectional age differences in this personality trait [39]. Extraversion is thought to be related to the desire of being with others as opposed to being alone and pursuing solitary activities [4]. The observed low level of extraversion might suggest that migraineurs can be prone to experience less positive life events such as fulfilling social interactions and to show a maladaptive response to stress and a general feeling of malaise, which is one of the most common trigger for migraine attacks [40]. As five studies investigated the TFM personality traits specifically associated with MwA [14, 17, 24] or MwoA [14, 17, 22, 23], we could perform a subgroup analysis. Our findings did not show differences on neuroticism and extraversion personality traits between the two groups. However, this finding should be considered cautiously due to the few studies comparing MwA and MwoA patients on the personality profile [14, 17, 22–24] and needs to be addressed in future studies.

Limitations

The present meta-analysis is characterized by some limitations: we could not investigate the possible moderator effect of relevant clinical variables such as duration, drugs, frequency, pain intensity and type (i.e. chronic versus episodic) on the relationship between personality traits and migraine because these clinical aspects were not reported in enough primary studies. Moreover, we could not exclude that personality profile of migraineurs evidenced in the current meta-analysis was

a consequence of the disease since personality profile has never been investigated before the onset of the migraine. Finally, since we included only cross-sectional studies, we could not investigate the causal role of the personality traits on the onset of migraine.

Clinical implications

Despite the abovementioned limitations, our results might have relevant clinical implications. Some personality traits could negatively influence long-term history of migraine and the response to drug treatment [41]. The meta-analytic evidence of a specific personality migraine reinforces the relevance of psychological evaluation to obtain prognostic information and to possibly identify patients at high risk of development of psychopathological disturbances such as depression and anxiety. Assessing personality traits can also help in planning non-pharmacological therapies such as psychoeducational interventions focused on personality traits, i.e. self-directedness and neuroticism. As migraineurs often show vulnerability to psychological distress, and reduced success in personal, social, cognitive and spiritual development because of maladaptive coping styles [38], might follow psychoeducational interventions aimed at enhancing self-directedness and neuroticism to improve their well-being. Finally, specific personality traits, especially neuroticism, could influence the Quality of Life (QoL) [42] and the type of coping strategies used to overcome unexpected troubles and tolerate stressful events. On the basis of these considerations, a well-established personality profile associated with migraine might allow developing psychological interventions to improve the exploitation of adaptive coping strategies and to early identify patients at risk of developing psychopathological disturbances such as depression.

Funding information This research did not receive any specific grant from funding agencies in the public, commercial or not-for-profit sectors.

Compliance with ethical standards

Ethical approval retrospective studies This article does not contain any studies with human participants or animals performed by any of the authors.

Since the study was a meta-analysis based on already available data from published papers, ethical approval is not necessary.

Conflict of interest The authors declare that they have no conflict of interest.

References

1. Cervone D, Pervin LA (2010) Personality: theory and research, 11th edn. Wiley, Danvers
2. Cloninger CR, Svrakic DM, Przybeck TR (1993) A psychobiological model of temperament and character. Arch Gen Psychiatry 50: 975–990. https://doi.org/10.1001/archpsyc.1993.01820240059008
3. Costa PT, McCrae RR (1990) Personality disorders and the five-factor model of personality. J Personal Disord 4:362–371. https://doi.org/10.1521/pedi.1990.4.4.362
4. Eysenck HJ (1991) Dimensions of personality: 16, 5, or 3?–Criteria for a taxonomic paradigm. Pers Individ Differ 12:773–790. https://doi.org/10.1016/0191-8869(91)90144-Z
5. Bucher MA, Suzuki T, Samuel DB (2019) A meta-analytic review of personality traits and their associations with mental health treatment outcomes. Clin Psychol Rev 70:51–63. https://doi.org/10.1016/j.cpr.2019.04.002
6. Wolff HG (1937) Personality features and reactions of subjects with migraine. AMA Arch NeurPsych 37:895–921. https://doi.org/10.1001/archneurpsyc.1937.02260160195019
7. Mongini F, Fassino S, Rota E, Deregibus A, Levi M, Monticone D, Abbate-Daga G (2005) The temperament and character inventory in women with migraine. J Headache Pain 6:247–249. https://doi.org/10.1007/s10194-005-0198-6
8. Park JW, Han SR, Yang DW, Kim YI, Lee KS (2006) Serotonin transporter protein polymorphism and harm avoidance personality in migraine without aura. Headache 46:991–996. https://doi.org/10.1111/j.1526-4610.2006.00439.x
9. Sánchez-Román S, Téllez-Zenteno JF, Zermeño-Phols F, García-Ramos G, Velázquez A, Derry P, Hernández M, Resendiz A, Guevara-López UM (2007) Personality in patients with migraine evaluated with the "temperament and character inventory". J Headache Pain 8:94–104. https://doi.org/10.1007/s10194-007-0352-9
10. Abbate-Daga G, Fassino S, Lo Giudice R, Rainero I, Gramaglia C, Marech L, Amianto F, Gentile S, Pinessi L (2007) Anger, depression and personality dimensions in patients with migraine without aura. Psychother Psychosom 76:122–128. https://doi.org/10.1159/000097971
11. Nylander PO, Schlette P, Brändström S, Nilsson M, Forsgren T, Forsgren L, Adolfsson R (1996) Migraine: temperament and character. J Psychiatr Res 30:359–368. https://doi.org/10.1016/0022-3956(96)00009-X
12. Boz C, Velioglu S, Ozmenoglu M et al (2004) Temperament and character profiles of patients with tension-type headache and migraine. Psychiatry Clin Neurosci 58:536–543. https://doi.org/10.1111/j.1440-1819.2004.01297.x
13. Brandt J, Celentano D, Stewart WF, Linet M, Foistein MF (1990) Personality and emotional disorder in a community sample of migraine headache sufferers. Am J Psychiatry 147:303–308. https://doi.org/10.1176/ajp.147.3.303
14. Breslau N, Andreski P (1995) Migraine, personality, and psychiatric comorbidity. Headache 35:382–386. https://doi.org/10.1111/j.1526-4610.1995.hed3507382.x
15. Perozzo P, Savi L, Castelli L (2005) Anger and emotional distress in patients with migraine and tension-type headache. J Headache Pain 6:392–339. https://doi.org/10.1007/s10194-005-0240-8
16. Ashina S, Bendtsen L, Buse DC, Lyngberg AC, Lipton RB, Jensen R (2017) Neuroticism, depression and pain perception in migraine and tension-type headache. Acta Neurol Scand 136:470–476. https://doi.org/10.1111/ane.12751
17. Ishii M, Shimizu S, Sakairi Y, Nagamine A, Naito Y, Hosaka Y, Naito Y, Kurihara T, Onaya T, Oyamada H, Imagawa A, Shida K, Takahashi J, Oguchi K, Masuda Y, Hara H, Usami S, Kiuchi Y (2012) MAOA, MTHFR, and TNF-b genes polymorphisms and personality traits in the pathogenesis of migraine. Mol Cell Biochem 363:357–366. https://doi.org/10.1007/s11010-011-1188-4
18. Karmakar M, Elhai JD, Amialchuk AA, Tietjen GE (2018) Do personality traits mediate the relationship between childhood abuse

and migraine? An exploration of the relationships in young adults using the add health dataset. Headache 58:243–259. https://doi.org/10.1111/head.13206
19. Davis RE, Smitherman TA, Baskin SM (2013) Personality traits, personality disorders, and migraine: a review. Neurol Sci 34:7–10. https://doi.org/10.1007/s10072-013-1379-8
20. Amiri S, Behnezhad S, Azad E (2019) Migraine headache and depression in adults: a systematic review and meta-analysis. Neuropsychiatr 33:131–140. https://doi.org/10.1007/s40211-018-0299-5
21. International Headache Society (2004) International classification of headache disorders. Cephalalgia 24(suppl 1):1–160
22. Wang W, Wang GP, Ding XL, Wang YH (1999) Personality and response to repeated visual stimulation in migraine and tension-type headaches. Cephalalgia 19:718–724. https://doi.org/10.1046/j.1468-2982.1999.019008718.x
23. Wang W, Wang YH, Fu XM, Sun ZM, Schoenen J (1999) Auditory evoked potentials and multiple personality measures in migraine and post-traumatic headaches. Pain 79:235–242. https://doi.org/10.1016/S0304-3959(98)00168-7
24. Cao M, Zhang S, Wang K, Wang Y, Wang W (2002) Personality traits in migraine and tension-type headaches: a five-factor model study. Psychopathology 35:254–258. https://doi.org/10.1159/000063829
25. Muscogiuri G, Dimaggio L, Giani L, Mariani C, Pantoni L, Lovati C (2018) Personality traits in migraineurs: a case-control study by personality inventory for DSM-5 (PID-5). Neurol Sci 39:129–130. https://doi.org/10.1007/s10072-018-3360-z
26. Borenstein M, Hedges LV, Higgins JPT, Rothstein HR (2009) Introduction to meta-analysis. John Wiley & Sons, Hoboken, NJ
27. Villalon CM, Centurion D, Valdivia LF, de Vries P, Saxena PR (2003) Migraine: pathophysiology, pharmacology, treatment and future trends. Curr Vasc Pharmacol 1:71–84. https://doi.org/10.2174/1570161033386826
28. Deen M, Hansenb HD, Hougaard A (2018) High brain serotonin levels in migraine between attacks: a 5-HT4 receptor binding PET study. Neuroimage Clin 18:97–102. https://doi.org/10.1016/j.nicl.2018.01.016
29. Meylakh N, Henderson LA (2016) Dorsal raphe nucleus and harm avoidance: a resting-state investigation. Cogn Affect Behav Neurosci 16:561–569. https://doi.org/10.3758/s13415-016-0415-6
30. Cloninger CR, Zohar AH, Hirschmann S, Dahan D (2012) The psychological costs and benefits of being highly persistent: personality profiles distinguish mood disorders from anxiety disorders. J Affect Disord 136:758–766. https://doi.org/10.1016/j.jad.2011.09.046
31. Cupini LM, De Murtas M, Costa C et al (2009) Obsessive-compulsive disorder and migraine with medication-overuse headache. Headache 49:1005–1013. https://doi.org/10.1111/j.1526-4610.2009.01457.x
32. Curone M, D'Amico D, Bussone G (2012) Obsessive-compulsive aspects as predictors of poor response to treatments in patients with chronic migraine and medication overuse. Neurol Sci 49:211–213. https://doi.org/10.1007/s10072-012-1070-5
33. Rothrock JF, Mar KR, Yaksh TL, Golbeck A, Moore AC (1995) Cerebrospinal fluid analyses in migraine patients and controls. Cephalalgia 15:479–493. https://doi.org/10.1046/j.1468-2982.1995.1506489.x
34. Gustin SM, Burke LA, Peck CC, Murray GM, Henderson LA (2016) Pain and personality: do individuals with different forms of chronic pain exhibit a mutual personality? Pain Pract 16:486–494. https://doi.org/10.1111/papr.12297
35. Peirson AR, Heuchert JW, Thomala L, Berk M, Plein H, Cloninger CR (1999) Relationship between serotonin and the temperament and character inventory. Psychiatry Res 89:29–37. https://doi.org/10.1016/S0165-1781(99)00079-7
36. Zuckerman M, Cloninger CR (1996) Relationships between Cloninger's, Zuckerman's, and Eysenck's dimensions of personality. Pers Individ Dif 21:283–285. https://doi.org/10.1016/0191-8869(96)00042-6
37. Mattsson P, Ekselius L (2002) Migraine, major depression, panic disorder, and personality traits in women aged 40–74 years: a population-based study. Cephalalgia 22:543–551. https://doi.org/10.1046/j.1468-2982.2002.00407.x
38. Materazzo F, Cathcart S, Pritchard D (2000) Anger, depression, and coping interactions in headache activity and adjustment: a controlled study. J Psychosomat Res:69–75. https://doi.org/10.1016/S0022-3999(00)00144-6
39. Donnellan MB, Lucas RE (2008) Age differences in the big five across the life span: evidence from two national samples. Psychol Aging 3:558–566. https://doi.org/10.1037/a0012897
40. Theeler BJ, Kenney K, Prokhorenko OA, Fideli US, Campbell W, Erickson JC (2009) Headache triggers in the US military. Headache 50:790–794. https://doi.org/10.1111/j.1526-4610.2009.01571.x
41. Luconi R, Bartolini M, Taffi R (2007) Prognostic significance of personality profiles in patients with chronic migraine. Headache 47:1118–1124. https://doi.org/10.1111/j.1526-4610.2007.00807.x
42. Huang IC, Lee JL, Ketheeswaran P, Jones CM, Revicki DA, Wu AW (2017) Does personality affect health-related quality of life? A systematic review. PLoS One 12:e0173806. https://doi.org/10.1371/journal.pone.0173806