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A comparative study**

Mose, Louise S; Pedersen, Susanne S; Jensen, R H; Gram, Bibi

Published in:
Acta Neurologica Scandinavica

DOI:
10.1111/ane.13111

Publication date:
2019

Document version:
Accepted manuscript

Citation for published version (APA):
Mose, L. S., Pedersen, S. S., Jensen, R. H., & Gram, B. (2019). Personality traits in migraine and medication-overuse headache: A comparative study. *Acta Neurologica Scandinavica*, 140(2), 116-122.
<https://doi.org/10.1111/ane.13111>

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Article type : Original Article

Personality traits in migraine and medication-overuse headache: A comparative study

RUNNING TITLE: Personality across headache diagnoses

Mose LS^{1,2}, Pedersen SS^{3,4}, Jensen RH⁵, Gram B²

¹ Department of Neurology, Hospital of South West Jutland, Denmark

² Research Unit of Health Science, Hospital of South West Jutland, Denmark and Department of Regional Health Research, University of Southern Denmark, Odense, Denmark

³ Department of Psychology, University of Southern Denmark, Odense, Denmark

⁴ Department of Cardiology, Odense University Hospital, Odense, Denmark

⁵ Danish Headache Centre, Department of Neurology, Rigshospitalet-Glostrup, University of Copenhagen, Denmark

Corresponding author:

Louise Schlosser Mose, MHS, PhD fellow, (ORCID:0000-0002-6898-4611)

Department of Neurology, Hospital of South West Jutland, Denmark and Research Unit of Health Science, Hospital of South West Jutland, Denmark and Department of Regional Health Research, University of Southern Denmark, Odense, Denmark

E-Mail: Louise.schlosser@rsyd.dk, Phone: +45 60178780

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/ane.13111

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ACKNOWLEDGEMENTS

The authors especially would like to thank the Neurology Department and Headache Clinic at Hospital South West Jutland, Denmark for the collaboration at including patients, and lastly the patients for their goodwill in participating.

SOURCES OF FUNDING STATEMENT

The study was financially supported with grants from TrygFonden, Carola Jørgensen Foundation and the Danish patient organization Migræne og Hovedpineforeningen.

CONFLICT OF INTEREST STATEMENT

L. Mose, S.S. Pedersen and B. Gram have declared no conflict of interests. R.H. Jensen has received honoraria for lectures and patient leaflets from MSD, Berlin-Chemise Maharini, ATI, and Pfizer; participated in medical advisory boards for ATI and Electro core and conducted clinical trials for Eli-Lilly and ATI and has also received research funding from Tryg-Foundation.

ABSTRACT

Objectives: Medication-overuse headache (MOH) is recognized as a biobehavioural disorder, warranting that both biological and psychological factors are targeted throughout treatment. A psychological factor of importance may be personality that could be used to tailor treatment if differences are found across headache diagnoses. The objectives were: (1) To investigate if migraine patients and patients with MOH differed on personality traits, (2) To investigate if the two headache groups differed from a Danish normative sample, with respect to personality traits.

Materials & Methods: The NEO-Five-Factor-Inventory was completed and an age-matched cohort of episodic migraine patients (n=94) and MOH patients (n=94) was included. Multivariate regression models and sex-stratified comparisons were made on patients' raw scores from five personality traits; neuroticism, extraversion, openness, agreeableness and conscientiousness. The headache groups were also compared to personality traits from a Danish normative sample (n=1032).

Results: MOH females obtained significantly lower scores on extraversion (24.4±4.3 vs. 27.1±7.2, p<0.01), openness (23.7±3.9 vs. 26.2±6.4, p<0.01) and conscientiousness (28.9±3.7 vs. 34.6±5.8, p>0.01) as compared to female migraineurs. Males showed no differences. Compared to the normative sample, both headache groups showed a lower score on extraversion (p<0.01). Furthermore, MOH patients had statistically significant lower scores on conscientiousness while the migraine patients had a higher score.

Conclusion: Results suggests some personality trait differences between migraine and MOH patients. Especially, females showed different personality traits, where the MOH females appeared more introvert and less socially orientated. If confirmed in larger studies, this information could be used in personalized treatment in clinical practice.

Keywords: Psychological profiles, NEO-Five-Factor-Inventory, Migraine, Medication-overuse headache.

INTRODUCTION

Medication-overuse headache (MOH) is a disorder where frequent use of pain medication leads to an unhealthy circular process of persistent headache and increased medication intake¹. This results in severe disability affecting all aspects of life². MOH is considered a biobehavioral disorder, with both biological and psychological factors contributing to the onset. Hence, targeting both factors in treatment is essential and key to effective treatment³⁻⁵. Nevertheless, factors affecting the behavioral part of treatment remain unexplored and there is no consensus on which behavioral and psychological factors must be taken into consideration when planning treatment. Personality might be one psychological factor that influences the onset and maintenance of headaches. Personality is conceptualized as characteristic patterns of behaviors, thoughts and feelings across situations and time⁶.

Associations between personality and headache have received considerable interest in the literature over time^{7, 8}. Comparative studies of different headache diagnoses and personality traits have shown that patients with chronic headache and medication overuse are more likely to be socially introverted as compared to patients with episodic headaches^{9, 10}. According to a review from Silberstein and colleagues⁸, migraine patients often have a higher level of neuroticism and vulnerability to negative affect, as compared to non-migraineurs. A high neuroticism score predisposes to depression and anxiety¹¹, which is clinically interesting, because MOH patients are diagnosed with depression more frequently than migraineurs¹².

Studies suggest that MOH represents a spectrum of addictive behaviors^{13, 14} and some have shown a relation to characteristics of obsessive-compulsive personality disorder^{15, 16}. If MOH exemplifies a dependency-like behavior, personality traits should differ as compared to migraine patients. However, other studies discuss the drug addictive behavior as a consequence of coping with an aggravated headache¹⁷. Either way, knowledge of personality could be valuable for planning treatment.

The objectives of the current study were (1) To investigate if patients diagnosed with migraine and patients with MOH differed on personality characteristics, as measured with the NEO-Five-Factor-Inventory (NEO-FFI-3) personality questionnaire, (2) To compare the two groups of headache patients to a Danish normative sample of adults with regard to personality traits.

We hypothesized that MOH patients would show a significant lower score on the personality trait extraversion indicating e.g. less social orientation. Additionally, we hypothesized that both headache groups would report a lower score on extraversion, indicating a more introvert and socially retracted personality. Since both headache groups are at risk of developing depression and anxiety, we hypothesized that headache patients would have higher scores on the neuroticism trait when compared to a Danish normative sample.

MATERIALS & METHODS

Study design

The study was conducted as a single-center survey concerning personality traits measured by the NEO-FFI-3. Diagnosed episodic migraine patients and MOH patients seen at the Headache Clinic at University Hospital of Southern Denmark, Esbjerg, Denmark, between October 2015 and June 2017, were invited to participate.

According to the Helsinki Declaration, all patients prior to inclusion received both oral and written information before signing a written informed consent. Information about the study was given by the nurses or neurologists at routine consultations at the headache Clinic. The Regional Committees on Health Research Ethics for Southern Denmark approved the study (ID S-20140114). Permission was also obtained from the Danish Data Protection Agency (2008-58-0035).

Study populations

Two types of patients were included; migraine patients and MOH patients. Migraine patients were eligible for participation if they were proficient in the Danish language, aged between 18-65 years, diagnosed with episodic migraine or episodic migraine with occurrence of tension-type headache according to the criteria of ICHD-III (Beta)¹⁸ and did not meet the exclusion criteria of chronic migraine and MOH based on ICHD criteria (Beta).

MOH patients were eligible for inclusion if they were diagnosed based on the ICHD-III (Beta) criteria for MOH¹⁸, were aged 18-65 years and had proficient Danish language skills. With the risk of ambiguity in the personality data, patients with

comorbidity of untreated depression, anxiety or personality disorders in both groups were excluded. Also, patients with comorbidity of whiplash, arthritis or back/neck pain requiring daily analgesic treatment were excluded in both groups. After inclusion, migraine and MOH patients were matched on age (± 3 years).

Collection of data for the Danish normative manual was performed by the psychological publisher. The normative Danish sample consisted of a total of 5000 males and 5000 females aged >18 years. They were all invited by letter to fill out the personality questionnaire. The invited individuals had been randomly sampled from the Danish Civil Registration System based on the unique 10-digit Central Person Register numbers (CRP-number)¹⁹. The Danish normative sample represents a total of 1032 individuals (453 females and 579 males). Of those, 283 were single and 749 were cohabiting²⁰.

Personality Questionnaire

To assess personality, we used the internationally recognized NEO Personality Inventory Revised questionnaire (NEO-PI-R). It is a hierarchical measure of personality^{11, 21}, which taps into personality from five broad domains; 1) *neuroticism* covering inter alia emotional stability, 2) *extraversion* which includes the interaction with other people, 3) *openness* which includes tendency to be creative and imaginative, 4) *agreeableness* which encompasses traits regarding relationship to others and empathic capability, and 5) *conscientiousness* which covers capacity of behavioral and cognitive control. Originally, NEO-PI-R was designed as a clinical instrument, which enables its use in clinical practice^{11, 22}. Theoretically, NEO-PI-R is based on the Five Factor model of personality (FFM), with these five basic trait domains representing the most common and normal personality traits. Since the 1980's the FFM approach has been used in areas of psychological research with the consensus that it is among the best for mapping basic independent personality dimensions¹¹.

In the current study, we used NEO-FFI-3, which is a brief version of NEO-PI-R. It is developed to provide a concise and reliable measure of the five trait domains, using a 60-item questionnaire. The questionnaire is standardized and validated. Each trait is defined by 12 items that are answered on a 5-point Likert scale ranging from "Strongly disagree" to "Strongly agree"²³. For each of the five traits, a raw score is calculated by adding the 12 items together and the score range is between 0 and 48²⁰.

Statistics

Initially, included migraine and MOH patients were matched on age (± 3 years). Differences in baseline characteristics between groups were tested with Student's *t*

test for numerical outcomes, while the Chi-square test or Fischer exact test was used when comparing categorical outcomes. Baseline characteristics are presented as mean and standard deviation (SD) or as numbers and percentage in brackets (%).

A raw score was calculated for each of the five traits by adding the relevant items together, as indicated in the Danish scoring manual²⁰. To correct for the inter-correlation of the personality traits, multivariate analysis of variance (MANOVA) with the personality traits as dependent variables and age, gender and group as independent variables, were applied. Further, to account for mass significance and type I errors, the Bonferroni correction was applied and all $p < 0.01$ were considered to be statistically significant.

In accordance with the score manual from the psychological publisher, we also conducted unpaired Student's t-test to test for differences in personality traits between groups. These analyses were conducted both with and without sex stratification. These analyses were conducted both with and without sex stratification.

Subsequently, the mean raw score from the MOH and migraine groups, without sex-stratification were compared to a Danish normative sample²⁰. These comparative analyses were conducted to provide knowledge of potential specific headache-related differences. Analyses were carried out using Stata/IC 15.1 (StataCorp LLC, College Station, Texas).

RESULTS

Baseline characteristics

From the total of 229 patients (MOH: $n=98$ and migraine: $n=131$), who completed the NEO-FFI-3 questionnaire, 94 MOH patients and 94 migraine patients were matched on age and included in analyses. Demographic baseline characteristics are presented in table 1. The mean age was 43 years and the MOH group consisted of a proportionally larger number of males: $n=29$ (31%) compared to the migraine group, $n=12$ (13%), ($p < 0.01$). With respect to employment status, a higher percentage of

the MOH group (39%) were unemployed or received sickness benefits when compared to the migraine group (13%), ($p=0.04$).

In the MOH group, eight (8%) patients had either cluster headache (6%) or post traumatic headache (2%) as the primary headache diagnosis. However, with respect to equivalency of the two groups, these patients accounted for a very small group and therefore separate post hoc analyses were not performed on that specific sub-group.

Insert **Table 1 Baseline demographic characteristics of the study population

Personality trait comparisons between migraine and MOH patients

Analyses showed that the migraine group scored statistically significantly higher on openness, agreeableness and conscientiousness when compared to the MOH group ($p<0.01$). No significant differences were observed between groups on the neuroticism and extraversion traits (table 2). Post hoc analyses conducted in accordance to the score manual by unpaired Student's t-test for differences between groups revealed the same picture.

Insert **Table 2 Coefficients from MANOVA with personality traits as dependent variables and age, gender and group as independent variables

Personality trait comparison between migraine and MOH patients, stratified by sex

Table 3 presents the results from the comparative analyses, when the groups are stratified by sex. Sex differences were observed in the personality trait extraversion, showing that the group of MOH females had a significantly lower score compared to the migraine females (24.4 ± 4.3 units vs. 27.1 ± 7.2 units, $p<0.01$). This was not the case for males, where no differences between groups were found (all p values >0.05). A similar pattern was identified for the trait openness, where the MOH females obtained a lower score, compared to the migraine females (23.7 ± 3.9 units vs. 26.2 ± 6.4 units, $p<0.01$), but no differences were detected between males. The trait conscientiousness showed significant differences for females (-5.7 ± 0.8 units (95% CI, $-7.3;-4.0$, $p>0.01$)) but not for males (-4.3 ± 1.7 units (95% CI, $-7.8;-0.8$, $p=0.02$)), and the traits neuroticism and agreeableness showed no statistically significant differences between groups regardless of sex.

****Insert Table 3** Comparison of personality traits of migraine and MOH patients, stratified by sex

Personality trait comparison of headache patients and a Danish normative sample

Comparative results from the analysis of the two headache groups (MOH: n=94, migraine: n=94) against a Danish normative sample (n=1032) are shown in in Figure 1.

****Insert Figure 1** Comparison of headache patients to a Danish normative sample

The MOH group had a significantly higher score on neuroticism when compared to the normative sample ($p < 0.01$), whereas no differences were found between the normative sample and the migraine group ($p = 0.18$). Both headache groups had significantly lower extraversion scores, when compared to the normative sample ($p < 0.01$). Regarding the traits openness and agreeableness, the MOH group had a lower score compared to the normative sample ($p < 0.01$ for both traits), while there were no differences between the migraine group and the normative sample with regard to these traits. Both headache groups were significantly different from the normative sample with respect to conscientiousness; the MOH group had a significantly lower score ($p < 0.01$), whereas the migraine group had a significantly higher score than the normative sample ($p < 0.01$).

DISCUSSION

The main findings of this study were that MOH and migraine patients showed differences in several personality traits as measured with the NEO-FFI-3. MOH females scored lower on extraversion, openness and conscientiousness, as compared to the migraine females. The male MOH patients did not differ significantly from the males with migraine on any of the personality traits. Compared to the Danish normative sample, the MOH group had a significantly higher score on

neuroticism, while they had a significantly lower score on the four other traits. The migraine group differed only significantly from the normative sample, with a lower score on extraversion and a higher score on conscientiousness.

A lower score on extraversion indicates that the individual has a more introvert and reserved personality type. As MOH is known to have a considerable negative impact on social activities², this could be a reason for the lower extraversion score among the females. Furthermore, both headache groups had a significantly lower score on extraversion when compared to the normative sample. We believe that the low extraversion score is a reflection of headache disablement, which causes headache patients in general to be less socially active than the general population.

High openness encompasses the tendency to be imaginative and creative.

Compared to the normative population, only the MOH group scored lower on openness, whereas the migraine group and normative sample were similar. An explanation for this could be that the MOH group is being less open-minded with respect to new ideas, probably due to the lack of resources from the high headache burden. Taken together, the low extraversion and openness scores draw a picture of the MOH group as more socially retracted and conservative, which might reflect their everyday living. One could assume that the chronic headache which the MOH group experiences causes disabilities which makes everyday living difficult. Lauwerier and colleagues point to the fact that MOH patients use medication to retain everyday functioning²⁴. In that manner, our results might have shown some of the consequences which the headache has caused.

Conscientiousness covers elements of cognitive and behavioral control. The low score for females in the MOH group could illustrate a connection to the behavior of uncontrolled medication consumption. However, it is not possible to determine cause

of effect in this study and whether patients' personality profiles play a role in the development of MOH. Interestingly, the MOH patients also had a significantly lower score on the conscientiousness trait when compared to the normative sample, whereas the migraine group had a significantly higher score. Lack of cognitive and behavioral strategies for coping properly with headache could probably be part of the underlying reasons for developing MOH. This would explain the low conscientiousness score in the MOH group. In contrast, the high score obtained in the migraine group could reflect an increased need for controlling headache attacks. Diener and Limmroth have debated that patients using acute migraine medication as prophylactic find themselves at the forefront of the headache attacks²⁵. This pattern could symbolize one way of having control, however, it also underlines a potential risk of developing MOH.

We did not detect any between group differences with respect to the traits neuroticism and agreeableness. A high neuroticism score refers to the tendency to experience negative emotions and potentially develop depression and stress. As both migraine and MOH patients are known to have increased risk of depression and anxiety, this finding is surprising and interesting. It is also contrary to the findings of previous studies linking a high neuroticism score to headache²⁶⁻³⁰. An explanation for our finding could be the fact that all patients with comorbidity of untreated depression and anxiety were excluded. In that manner, we were unable to show between group differences, however, compared to the normative sample, the MOH group still showed a significantly higher score on neuroticism. This may strengthen the assumption that severely affected headache patients have a tendency to experience more negative emotions and to be stressed. This is in line with a previous study comparing chronic headache patients to healthy controls²⁹. For the agreeableness score, only the MOH group had a significantly lower score than the normative sample. This may be seen as the group being more introvert and less socially active, which could be a result of inadequate coping strategies and equivalent resources.

Interestingly, in the current study the results indicated that males and females perceived and responded to pain in different ways. This is in line with a review, describing how psychosocial factors, such as social roles and coping strategies, can

contribute to sex-differences in perception and response to headache and pain³¹.

However, in our study an alternative explanation of sex-differences could also be the reduced sample size of males and likely reduced statistical power to find a difference if present. Our data showed that males were more comparable across headache diagnoses, although this finding should be interpreted with some caution, as the number of males were very low (total n= 41). Therefore, we were unable to rule out the possibility that the lack of comparability across genders might be a result of a type II error.

Strengths and limitations

We chose the brief version of the NEO-PI-R personality questionnaire (NEO-FFI-3), which enabled us to investigate personality and the five dominant traits according to FFM. Had we used the longer and original version of the NEO-PI-R, we would have been able to conduct supplementary in-depth analyses of personality by adding valuable knowledge from the underlying trait facets. However, for pragmatic reasons such as time constraints and burden to patients, we chose to use the brief questionnaire.

We excluded patients with comorbidities of severe untreated depression, anxiety or personality disorders or other pain comorbidities, which we thought might confound the personality data. However, other potential comorbidities, were not accounted for.

Strengths of this study were the inclusion of properly classified patients, the large normative material and the use of a well-documented and validated approach for investigating personality. Furthermore, the NEO-FFI-3 questionnaire was easily accessible to the patients and completion was feasible, which made data collection very cost-effective and implementable in clinical practice.

In conclusion, especially females with MOH appeared more introvert and less socially orientated compared to females with migraine, whereas males were more comparable across diagnostic groups. Both headache groups differed from the Danish normative sample with respect to personality traits. If confirmed in larger studies, this information could be used in personalized treatment planning and management of headache patients in clinical practice.

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Table 1 Baseline demographic characteristics of the study population

	Total (n=188)	Migraine (n=94)	MOH (n=94)
Age (years)	43 ±11	43±11	43±11
Sex			
Males	41 (22)	12 (13)	29 (31)
Females	147 (78)	82 (87)	65 (69)
Civil status			
Single	31 (16)	12 (13)	19 (20)
Cohabiting	157 (84)	82 (87)	75 (80)
Education attainment			
Primary/secondary school	27 (14)	14 (15)	13(14)
Vocational	94 (50)	44 (47)	50 (53)
Bachelor or higher degree	67 (36)	36 (38)	31 (33)
Employment status			
Employed/student	127 (68)	70 (74)	57 (61)
Unemployed/sickness benefits	61 (32)	24 (26)	37 (39)
Primary diagnosis			
Migraine	93 (50)	57 (61)	36 (38)
Migraine + TTH	55 (29)	37 (39)	18 (19)
TTH	32 (17)		32 (35)
Cluster headache	6 (3)		6 (6)
Post traumatic headache	2 (1)		2 (2)

Differences between groups were tested using unpaired t-test and the Chi-square test (Fisher's exact if appropriate). Age is presented as mean ± standard deviation (SD), all other variables as numbers with percentages (%) in brackets. TTH: Tension-type headache.

Table 2 Coefficients from MANOVA with personality traits as dependent variables and age, gender and group as independent variables

	Migraine versus MOH	
	Coefficient (SE)	95 % CI
Neuroticism	-0.53 (1.08)	-2.66;1.60
Extraversion	1.94 (0.90)	0.16;3.72
Openness	2.39 (0.82)*	0.77;4.00
Agreeableness	6.77 (0.94)**	4.90;8.63
Conscientiousness	5.40 (0.75)**	3.92;6.89

MOH is used as reference group. The coefficient shows the change in the migraine group as compared to the MOH group. SE: Standard Error, 95 % CI: 95% confidence intervals, * p<0.01, ** p<0.0001

Table 3 Comparison of personality traits of migraine and MOH patients, stratified by sex

	Comparison of females				Comparison of males			
	MOH (n=65) Mean (SD)	Migraine (n=82) Mean (SD)	Between group difference Mean (SE)	95% CI	MOH (n=29) Mean (SD)	Migraine (n=12) Mean (SD)	Between group difference Mean (SE)	95% CI
Neuroticism	23.8 (4.6)	22.5 (8.7)	1.4 (1.2)	-1.0;3.7	20.7 (5.5)	22.7 (11.7)	-2.0 (2.7)	-7.4;3.4
Extraversion	24.4 (4.3)	27.1 (7.2)	-2.6 (1.0)*	-4.6;-0.6	25.9 (4.1)	24.6 (8.3)	1.3 (1.9)	-2.6;5.2
Openness	23.7 (3.9)	26.2 (6.4)	-2.5 (0.9)*	-4.2;-0.7	23.4 (4.1)	25.7 (7.8)	-2.3 (1.9)	-6.0;1.5
Agreeableness	23.4 (5.0)	31.4 (7.4)	-8.1 (1.1)	-10.2;-5.9	25.4 (4.9)	27.0(5.9)	-1.6 (1.8)	-5.2;2.0
Conscientiousness	28.9 (3.7)	34.6 (5.8)	-5.7 (0.8)**	-7.3;-4.0	28.1 (2.4)	32.4 (8.5)	-4.3 (1.7)	-7.8;-0.8

SD: Standard Deviation, SE: Standard Error; 95 % CI: 95% confidence intervals,

Data are presented as mean (SD) and differences between groups are presented as mean (SE) with 95% CI based on unpaired t-test. Significant change:*
p<0.01, ** p< 0.0001.

Figure 1 Comparison of headache patients to a Danish normative sample

Data are presented as means of the raw scores of each of the five personality traits.
*: Significantly different from the normative sample ($p < 0.01$)

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This study was approved by the Regional Committees on Health Research Ethics for Southern Denmark (ID S-20140114). Permission was obtained from the Danish Data Protection Agency (2008-58-0035).

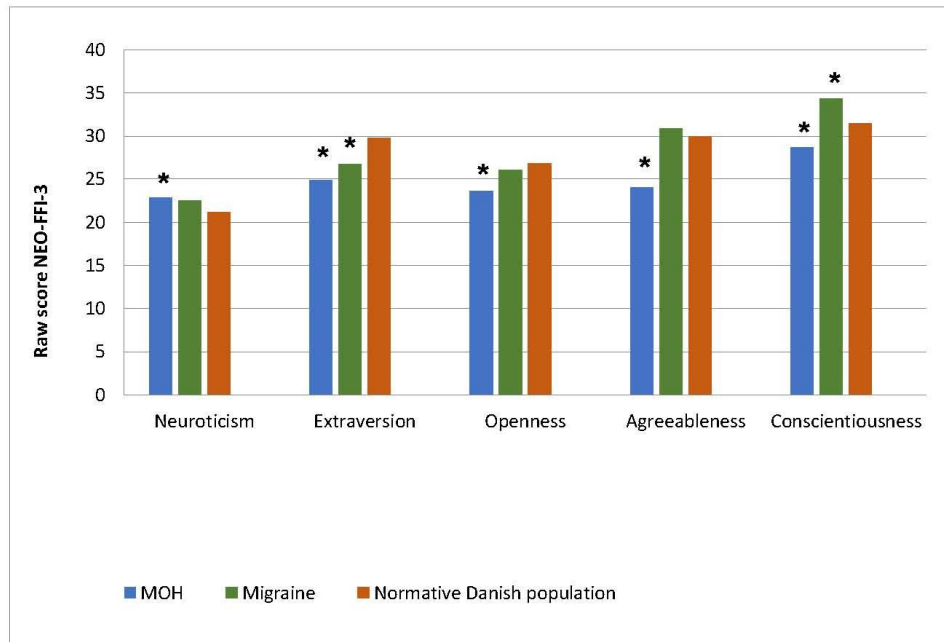
DATA AVAILABILITY STATEMENT

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

AUTHORS' CONTRIBUTIONS

LSM and BG conceived the idea for this article. LSM was project leader. LSM performed the data analyses and data interpretations. LSM, BG, SSP, and RHJ contributed with inputs to this article. The article was drafted by LSM and all authors reviewed and approved the final manuscript.

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