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Migraine and the development of additional psychiatric and pain disorders in the transition from adolescence to adulthood

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Abstract

Introduction: The transition from childhood to adolescence and from adolescence to adulthood are vulnerable phases in life. In these phases, late or insufficient treatment of diseases may lead to chronification and favor development of additional disorders. In adolescents, migraine often has a highly negative impact on school performance and everyday life. The hypothesis of the present study was that adolescents with migraine have a higher risk for developing additional disorders such as psychiatric disorders or other pain syndromes in the course of the disease.

Materials and methods: In this study, we analyzed health insurance data of 56,597 German adolescents at the age of 15 years in the year 2006. By using the International Classification of Diseases (ICD 10), we determined a group with migraine diagnosis in the year 2006 and a control group without any headache diagnosis in 2006. We then compared both groups regarding the development of additional disorders (based on the ICD 10) during the following 10 years (2007 to 2016).

Results: Adolescents with migraine had a 2.1 fold higher risk than persons without migraine diagnosis to develop an additional affective or mood disorder, a 1.8 fold higher risk to obtain neurotic, stress-related and somatoform disorders, a 1.8 fold higher risk to subsequently suffer from behavioral syndromes, a 1.6 higher risk to get back pain and a 1.5 fold higher risk for irritable bowel syndrome during the next 10 years.

Conclusion: Adolescents with migraine are at risk for developing additional disorders later. Considering and addressing the patient's risks and potential medical and psychosocial problems might improve the long-term outcome significantly.

Keywords

Headache, migraine, comorbidities, adolescents

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Introduction

Headache is a major health problem due to its high impact on quality of life and impairment of social life, school and work (1). No matter what ethnicity, sex, age or social background, headache is a disorder known worldwide. The worldwide prevalence of current headache disorders in adults is around 46% (2), the prevalence in children is approximately 58% (3). Migraine is among the 10 most disabling diseases worldwide (3,4) with an approximate prevalence of

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11% in adults (2) and 10% in adolescents (5). The transition from adolescence to young adulthood is a sensitive developmental period with many challenges regarding independency, choice of profession, partnerships etc. (6). The possibly resulting higher stress level negatively contributes to migraine (5).

Several studies investigated the co-occurrence of primary headache and other medical conditions (7–11). Milde-Busch et al. reported a co-occurrence of psychopathological symptoms (e.g. emotional symptoms and hyperactivity) in adolescents with headache (9). Those patients presented three times more with psychopathological symptoms. The authors discussed that the co-occurrence of psychopathological symptoms might vary with the type of headache. This might be a relevant aspect for future studies (9). Wang et al. described that 47% of adolescents with chronic daily headache presented with at least one psychiatric comorbidity, mostly major depression and panic disorder (10). A publication of Pavone et al. showed that children with primary headaches, especially with migraine, often had an association with asthma, allergic disorders, sleep disorders and behavioral disorders (11). Regarding the specificity of risk factors for headaches and the correlation between headaches in adolescents and other medical conditions or symptoms, Lehmann et al. reported a higher association in adolescents with headaches and the concurrent existence of other medical complaints and symptoms such as additional abdominal or musculoskeletal pain or psychological symptoms (7). A study from 2014 by Blaschek et al. investigated the association between shoulder/neck pain in adolescents with migraine and tension type headache (TTH) and could display a significant association between those conditions. This study highlighted the importance of the impact of muscular pain for patients with TTH but, as a new finding, also for patients with migraine (8). These previous studies therefore reveal a co-occurrence of other medical conditions in patients with headache, but neglect the aspect of chronological order or suspected causation. Breslau et al. however described that migraine increases the risk of depression and vice versa in adults (12).

The aim of this study was to investigate if adolescents diagnosed with migraine have a significantly higher risk for developing psychiatric comorbidities and pain syndromes during a 10 year time span compared to persons without any headache diagnosis. All diagnoses were based on ICD 10. The comorbidities, previously described in the literature and evaluated in this study are mood disorders, neurotic, stress-related and somatoform disorders, behavioral syndromes associated with physiological disturbances and physical factors, irritable bowel syndrome and back pain (7–11).

Materials and methods

Data acquisition

The dataset of a German general health insurance company (BARMER) covering the period of 2006 to 2016 was analyzed in this secondary data analysis. The BARMER is one of the German statutory insurance companies, serving around 11% of the German population. In Germany, all physicians have to code their diagnoses according to the International Classification of Diseases version 10 (ICD-10). For the present retrospective cohort study, we included all BARMER insured persons who were aged 15 years in 2006 and were continuously insured with the BARMER between 2006 and 2016 (i.e. between their 15th and their 25th year of age), resulting in a cohort of n = 56,597.

Two groups were defined to evaluate differences regarding psychiatric and pain disorders (see Figure 1; for description of used ICD 10 diagnoses see Supplemental Materials 1):

Group 1 (migraine group = exposed group): Patients with a diagnosis of migraine (G43.-) in 2006 and at least three further G43.- diagnoses but no G44.- or R51 diagnoses between 2006 and 2016) and without any of the analyzed comorbidities (see below) in the index year 2006 (n = 431). We claimed four instances of diagnosis of migraine during the 10 year observation period to guarantee a sufficiently accurate diagnosis. If the diagnosis of migraine was made only one to three times we suspected a false diagnosis as migraine typically does not totally disappear.

Group 2 (control group): Patients without any headache diagnosis (G43.x, G44.x, R51 corresponding to migraine, tension-type headache, unspecific headache, and other headache disorders) and without any of the analyzed comorbidities in the index year of 2006 (n = 22,368).

For all analyses, ICD-10 codes were used. The database was searched for the following comorbidity outcomes in the years 2007 to 2016:

1. Mood disorders (F30-39)
2. Neurotic, stress-related and somatoform disorders (F40-48)
3. Behavioral syndromes associated with physiological disturbances and physical factors (F50-59)
4. Back pain (M54.-)
5. Irritable bowel syndrome (K58.-)

Statistical analysis

The occurrence of any of the five listed psychiatric and pain syndromes in the two groups in the ten subsequent years (2007–2016) was analyzed with SAS Enterprise

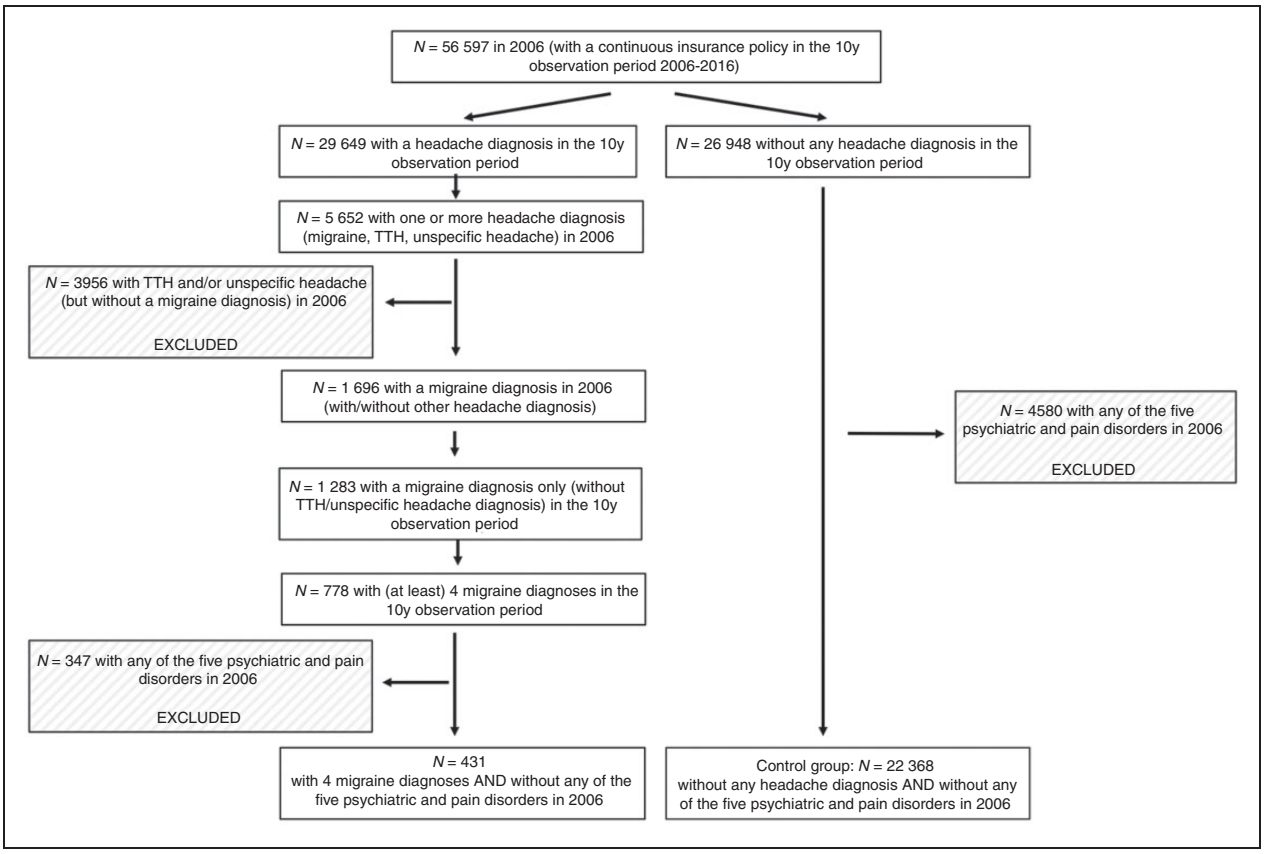

Figure 1. Flow Chart of the study population (N=number of adolescents).

Guide 7.1. The Chi Square Test was used to evaluate differences between the investigated groups. Relative risks for disorders and their confidence intervals (logarithmic transformation) in the migraine group compared to the control group were calculated.

Ethics approval

The presented study was approved by the Ethics committee at the Ludwig-Maximilians-University Munich (No 17-744 UE). The insurance data was used in an anonymized way only.

Results

56,597 adolescents at the age of 15 years were insured by the BARMER insurance company in 2006. 431 of these adolescents received the consistent diagnosis of migraine by their physicians, had no other headache diagnosis (G44.- and/or R51) and none of the predefined psychiatric and pain disorders in 2006 and therefore met the inclusion criteria for the migraine group. The control group consisted of 22,368 individuals. For detailed information of inclusion and exclusion process see Figure 1.

A high percentage of the adolescents with migraine (88.4%) developed at least one of the evaluated additional disorders in the 10-year follow-up period (Control group: 69.7%). The overall analysis (Table 1) showed that patients with a migraine diagnosis had a 1.3(1.2;1.3) fold higher risk to develop one or more of the evaluated additional disorders compared to persons without a headache diagnosis.

The analysis of the different later additional disorders resulted in the following:

In the course of the disease, patients with migraine had a 2.1(1.8;2.4) fold higher risk to develop an affective or mood disorder (ICD 10 diagnoses F30 - F39), compared to the control group.

Patients diagnosed with migraine developed neurotic, stress-related and somatoform disorders (ICD 10 diagnoses F40 - F48) 1.8(1.6;1.9) fold more often than persons without a migraine and/or any other headache diagnosis.

Furthermore the risk for adolescents diagnosed with migraine for suffering from a subsequent behavioral syndrome associated with physiological disturbances and physical factors (ICD 10 diagnoses F50 - F59) in the course of the disease was 1.8(1.3;2.3) fold higher compared to the control group.

Table 1. Adolescents with migraine developing the evaluated additional disorders over the 10 year follow up compared to the control group.

Type of additional disorder	Migraine (Total N = 431) n (%)	Control group No headache (Total N = 22,368) n (%)	P value	Relative risk (CI)
Any of the evaluated additional disorders	381 (88.4%)	15,585 (69.7%)	<0.001	1.3 (1.2;1.3)
Mood disorders	138 (32.0%)	3,479 (15.6%)	<0.001	2.1 (1.8;2.4)
Neurotic and somatoform disorders	238 (55.2%)	6,973 (31.2%)	<0.001	1.8 (1.6;1.9)
Behavioral syndromes (associated with physiological disturbances)	50 (11.6%)	1,483 (6.6%)	<0.001	1.8 (1.3;2.3)
Back pain	313 (72.6%)	10,245 (45.8%)	<0.001	1.6 (1.5;1.7)
Irritable bowel syndrome	27 (6.3%)	907 (4.1%)	0.022	1.5 (1.1;2.2)

Patients with migraine had a 1.6 (1.5;1.7) fold higher risk to develop back pain (ICD 10 diagnoses M54.-) in comparison to the control group, and a 1.5 (1.1;2.2) fold higher risk of having irritable bowel syndrome (ICD 10 diagnoses K58.-).

The comparison of patients with migraine without aura (ICD G43.0 in 2006 and three further G43.0 diagnoses in the subsequent years 2007 to 2016; n = 28) to patients with migraine with aura (ICD G43.1 in 2006 and three further G43.1 diagnoses in the subsequent years 2007 to 2016; n = 34) showed no significant difference (all p-values >0.05) in developing additional psychiatric and pain disorders, but sample sizes are small due to the possibility of unspecific coding (e.g. ICD G43.9: 75% of all migraine patients in 2006) and due to the possibility of switching categories in the subsequent years (e.g. G43.0 in 2006 and G43.1 in 2008).

Discussion and conclusion

To our knowledge, our study is the first showing that adolescents diagnosed with migraine, compared to adolescents without any headache diagnosis, show a significantly higher risk for developing an additional, co-morbid disorder (psychiatric disorders/pain syndromes) over the next 10 years in their transition into adulthood. This vulnerability of adolescent patients with migraine contributes to the idea that migraine is a brain state with underlying alterations in the activity of multiple brain networks (13). Interestingly, other pain syndromes might also represent a risk for later psychological disorders, e.g. abdominal pain for the development of anxiety disorders as described by Shelby et al. (14). The question if migraine as a brain state constitutes a specific risk factor for additional psychological disorders or if chronic pain non-specifically leads to a higher vulnerability for later disorders is not yet answered.

For clinical care, the result of our study implicates that the risk profile and vulnerability of young patients with migraine regarding later additional disorders have to be considered in the initial medical assessment and during the clinical course of the disease.

Possible shared mechanisms in neurochemical and metabolic pathways in the central nervous system (CNS) support the idea of a correlation and bidirectional influence between migraine and psychiatric disorders (15,16). A review of Dresler et al. showed that genetic susceptibility for a dysfunction in the 5HT-Serotonin and D2- Dopamine receptor gene as well as an imbalance of serotonin neurotransmitters are shared pathways in the CNS metabolism that can lead to depressive or pain (migraine/headache) syndromes. Additionally, an imbalance between pro-inflammatory and anti-inflammatory cytokines in the hypothalamic-pituitary adrenal (HPA) axis with a resulting abnormal increased level of pro-inflammatory cytokines states a possible link between depression and migraine (16). Those aspects could be part of an explanation to bidirectional dependence of the onset of primary headache and mood disorders and vice versa (15). The complexity of interlinkage between primary headaches and psychopathological disorders regarding central nervous system mechanisms implies that there are multiple causes and potential constellations of reciprocal influence.

Limitations

The first limitation of the presented study is that the retrospective evaluation of epidemiological data based on the ICD-diagnoses of treating physicians might be error-prone as diagnosis depends on the physician's experience and the patient's description of symptoms. Furthermore, we cannot relate the severity of the migraine to the seen co-morbidity since there is no code for that in the ICD 10. Therefore, we only

included patients with the diagnosis of migraine in at least three physician's visits. Other headache types, like TTH or unspecific headaches were excluded as to our clinical experience these diagnoses seem to be less stable and more error-prone in adolescence.

Moreover, the analyzed data was obtained from only one big insurance company. Therefore, data might not be completely comparable to all patients with statuary health insurance in Germany. Nevertheless, the chosen insurance company comprises 11% of German policyholders all over the country and therefore probably presents a good average of patients and physicians.

Another limitation is that retrospective data was analyzed and might contain mistakes e.g. psychiatric disorders before the starting year (2006), which by chance were not diagnosed in the index year. Future prospective studies with standardized diagnostic criteria and patients' examination by experienced neurologists and psychiatrists are needed to confirm the higher risk for developing psychiatric disorders in patients with primary headache.

Another reflection, and maybe limitation, might be that patients with migraine might visit physicians more frequently and therefore have a higher chance to be detected as psychiatrically ill.

The next limitation is that we selected only five categories of psychiatric and pain disorders as potential additional disorders in patients with primary headaches. The reason was that these investigated five disorders represent previously described common comorbidities in patients with migraine and TTH (7–11). Future studies might include additional disorders especially other psychosomatic and pain syndromes but also vascular disorders as stroke and cardiac ischemia.

Conclusion

Migraine is one of the most frequent diseases with a high impact on the quality of life and the everyday life functioning of affected patients. Therefore, migraine also influences the financial, social and health system. In our study, we showed that adolescents with migraine have a 1.3 fold higher risk to develop later additional psychiatric or pain disorders compared to adolescents without any headache diagnosis. This elevated risk for additional disorders might multiply the negative impact of migraine on the individual's well-being and on the burden for the society. Thus, not only reducing the frequency and intensity of migraine attacks but also early assessment of risks for additional disorders is essential in the care of these patients. Especially the transition from childhood to adulthood seems to be a vulnerable phase for this aspect and requires an increased awareness.

Clinical implications

- 88% of adolescent patients with migraine develop an additional psychiatric or pain disorder in the next ten years.
- Patients with migraine have a 1.3 fold higher risk to develop at least one additional disorder compared to the sample without primary headache.
- The most frequent later additional disorders in adolescents with migraine are affective or mood disorders (ICD 10 diagnoses F30 – F39).
- The development of neurotic, stress-related and somatoform disorders (ICD 10 diagnoses F40 - F48) as additional disorders is 1.8 fold more often in patients with migraine than in the sample without primary headache.
- As the risk in adolescents with migraine for developing additional psychiatric disorders later in life is augmented compared to adolescents without headache, adequate care and early recognition of psychological symptoms in the transition from adolescence to adulthood is important.

Declaration of conflicting interests

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Supplemental Materials 1: Used ICD 10 diagnoses.

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