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Review Article

Migraine in the Pediatric Population—Evolving Concepts

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Studying the prevalence of headaches at age extremes is of important clinical relevance. Pediatric studies inform us about determinants of incident disease; studies of elderly populations inform us about the long-term consequences of headaches, as well as about determinants of headache remission. As with other subspecialties of headache research, research on pediatric headache is an evolving field. However, although substantial advances have been achieved in understanding headaches in adolescents, knowledge of early childhood headaches is not as advanced conceptually. This review provides a theoretical framework for our current understanding, then summarize the results of a large, ongoing, epidemiological study in pre-adolescent children.

It is clear that both in adolescents and in pre-adolescents, migraine is frequent. Diagnostic criteria for migraine and chronic migraine are certainly over-restrictive for young children. Migraine often lasts less than 1 hour in young children. A vulnerable population at risk of migraine progression also exists, likely reflecting increased biological predisposition, but also early life exposures. Indeed, it seems that even prenatal exposures of certain substances may increase the risk of migraine progression. Of relevance is the frequency of headaches within a family. Finally, migraine seems to be associated with behavioral hyperactivity, but is not comorbid with attention-deficit disorder and hyperactivity.

Key words: pediatric population, migraine, epidemiology

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The study of migraine in the pediatric population is important for several reasons. First, migraine is relatively common at all pediatric ages, and not just after puberty.[1] Second, the burden of pediatric migraine has been well established as impacting families[2,3] as well as the children.[4-6] Third, the phenotype of migraine, as well as its differential diagnoses, varies as a function of age, and this may pose diagnostic and therapeutic challenges.[7,8] Finally, studying the prevalence of headaches at age extremes is of relevance. Pediatric studies inform us about determinants of incident disease; elderly studies provide data about the long-term consequences of headaches, as well as provide information about determinants of headache remission. For several neurological disorders (eg, Parkinson's disease and Alzheimer's disease), early onset cases often have the highest level of biological, or genetic, risk as well as a more refractory outcome.[9,10] For migraine headaches the situation is likely similar and early onset of disease probably reflects increased biological predisposition or increased susceptibility to specific environmental risk factors.[11]

Herein, we review selected topics on the subject of pediatric migraines. It is not our objective to

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provide a textbook review of the subject, but to emphasize recent advances and our personal experience in this field of research. We therefore start by reviewing some important changes and new concepts in the field. We follow by describing results of a large ongoing epidemiological study focusing on preadolescent children.

Episodic Migraine at Childhood—Classification Dilemmas.—The diagnosis of migraine headache is often more difficult in early ages than in adults.[12,13] For children below the age of 12, the headache history may be difficult to obtain. Children may not be able to describe the features of the onset of pain, trigger, or associated symptoms. Second, as compared with adults, children with migraine seem to have fewer attacks per month, with a higher number of morning attacks than adults.[14] Their attacks tend to be of shorter duration, less severe and easier to treat. They are often relieved by sleep and are more easily controlled.[15] As children move through adolescence, their migraines begin to resemble migraine in adults.

Considering these particularities, it seems illogical to use the same diagnostic criteria to classify adulthood and childhood migraines. Over the last 3 decades several definitions of pediatric migraine have been proposed (Table 1, modified from the study by Winner et al[16]). In 1962, the Ad Hoc Committee on Classification of Headaches provided a description of migraine but did not specify which features had to be present to make a diagnosis. In 1988, the first Edition of the International Classification for Headache Disorders (ICHD-1) proposed a new set of criteria for migraine headaches based on international expert consensus. The ICHD-1 criteria acknowledged the often shorter duration of headaches for patients under age 15 years (2 to 48 hours) than for those over 15 years (4 to 72 hours).[17]

Nonetheless, the utility of the ICHD-1 for pediatric headache disorders was contested based on the low positive predictive value (from 44% to 66%).[18,19] The utility of unilateral pain was also challenged as a diagnostic criterion.

The ICHD-2 criteria accounted for the new evidence and modified the duration of untreated attacks to be 1 hour,[20] in an attempt to increase the sensitivity of the criteria, without significantly

Table 1.—Definitions of Childhood Migraine

Author/Year	Temporal Pattern	Pain and Associated Features
Vahlquist (1955)	Paroxysmal separated by symptom-free intervals	≥2 of 4: unilateral, nausea, visual aura (or equivalent), positive family history of migraine
Prensky (1976)	Recurrent headaches with symptom-free intervals	≥3 of 6: abdominal pain, nausea, or vomiting, unilateral throbbing, relief after sleep, aura (visual, sensory, motor), positive family history
Deubner (1977)	Periodic	≥2 of 3: unilateral, nausea with or without vomiting, neurologic symptoms (scotomata scintillations, paresthesias)
Congdon and Forsythe (1979)	Periodic	≥3 of 4: aura, nausea, vomiting, positive family history
Kurtz et al (1984)	Recurrent with anorexia or nausea	≥1 of 2: vomiting, specific visual disturbance
ICHD-1 (1988)	At least 5 attacks Headache duration 1-72 hours (in children)	≥2 of 4: unilateral, pulsating quality, moderate to severe pain intensity, exacerbation by routine physical activity ≥1 of 2: photophobia and phonophobia, nausea or vomiting
ICHD-2 (2004)	At least 5 attacks Headache duration 2-48 hours (in children)	≥2 of 4: unilateral, pulsating quality, moderate to severe pain intensity, aggravation by routine physical activity ≥1 of 2: photophobia and phonophobia, nausea or vomiting

ICHD = International Classification for Headache Disorders.

impacting the specificity. Furthermore, although not in the criteria, the following comments are found in the revised classification: (1) migraine headache is often bilateral in young children. An adult pattern of unilateral pain often emerges in late adolescence or early adult life; (2) migraine headache is usually frontotemporal in children; (3) in young children, photophobia and phonophobia may be inferred from behavior.

Nonetheless, as described below, it may be that a sizable proportion of children have attacks resembling migraine but lasting less than 1 hour.

Epidemiology of Episodic Migraine at Childhood.—Studies on the epidemiology of migraine at childhood reflected the evolving issues on classification. Even the most recent studies that adopted the ICHD-1 and ICHD-2 criteria may substantially miss a sizable proportion of migraineurs, if attacks are of short duration.[21] Nonetheless, the epidemiology of migraine is well described in all ages and briefly summarized below.

Studying the incidence of pediatric migraine is challenging. The age of onset may be telescoped (from the real onset to later ages) and therefore biased. Additionally, methods for studying incidence of pain conditions in early ages are incompletely established. The topic has been reviewed elsewhere.[22] Using the reported age of migraine onset from a prevalence study, Stewart et al[23] found that in girls, the incidence of migraine with aura peaked between ages 12 and 13 (14.1/1000 person-years); migraine without aura peaked between ages 14 and 17 (18.9/1000 person-years). In boys, migraine with aura peaked incidence several years earlier, around 5 years of age at 6.6/1000 person-years; the peak for migraine without aura was 10/1000 person-years between 10 and 11 years.

Applying similar study techniques, the same author revisited the topic as part of the American Migraine Prevalence and Prevention study.[24] methods were used to estimate age-specific incidence. The first method (naïve) assumed no systematic bias in the reporting age of onset. The second method used a statistical model to adjust for biases. Finally, a model was constructed based on the 2 methods (Fig. 1). Of note is that the incidence peaked in considerably older ages, between the ages of 20 and 24 years in women (18.2/1000 person-years) and the ages of 15 and 19 years in men (6.2/1000 person-years). Cumulative incidence was 43% in women and 18% in men. Pending confirmation, the data offer interesting insights. If in most individuals with migraine, onset of disease happens later than originally considered, early onset cases become even more unique and special in their ability to provide clues for the pathophysiology of the disease. In other words, if it is common for migraine to start at late teens and early twenties, what are specific genes or exposures that so dramatically expedite the process in some individuals?

The prevalence of headache in children has been investigated in a number of school and population-based studies.[13,25-27] By age 3, headache occurs in 3-8% of children. At age 5, 19.5% have headache and by age 7, 37% to 51.5% have headaches. In 7 to 15 year olds, headache prevalence ranges from 57% to 82%. The prevalence increases from ages 3 to 11 in both boys and girls with higher headache prevalence in 3-5 year old boys than in 3-5 year old girls. Thus, the overall prevalence of headache increases from preschool age children to mid-adolescence.

In the USA, the prevalence of migraine headaches was recently studied in the context of the AMPP study. The 1-year prevalence for migraine in those from 12-17 years of age was 6.3%.[28] The prevalence in boys was 5.0%; in girls it was 7.7%. Table 2 displays the crude and adjusted prevalence ratios (PRs) stratifying by gender. The adjusted prevalence in boys was remarkably stable, ranging from 2.9% to 4.1%. For both genders, the prevalence was significantly higher in Caucasians than African Americans.

Chronic Migraine (CM) and Chronic Daily Headache (CDH).—*Prevalence and Importance.—* Chronic daily headache is not only a worldwide significant problem in adults, but also in children and adolescents.[29-31] Nonetheless, different than in adults, where large population studies are available, few adolescent studies were conducted in representative samples, and the topic is largely understudied in preadolescents (we discuss this topic in further detail later in this paper).[32,33]

Probably the best population study on the topic was conducted in Taiwanese adolescents. Of the 7900

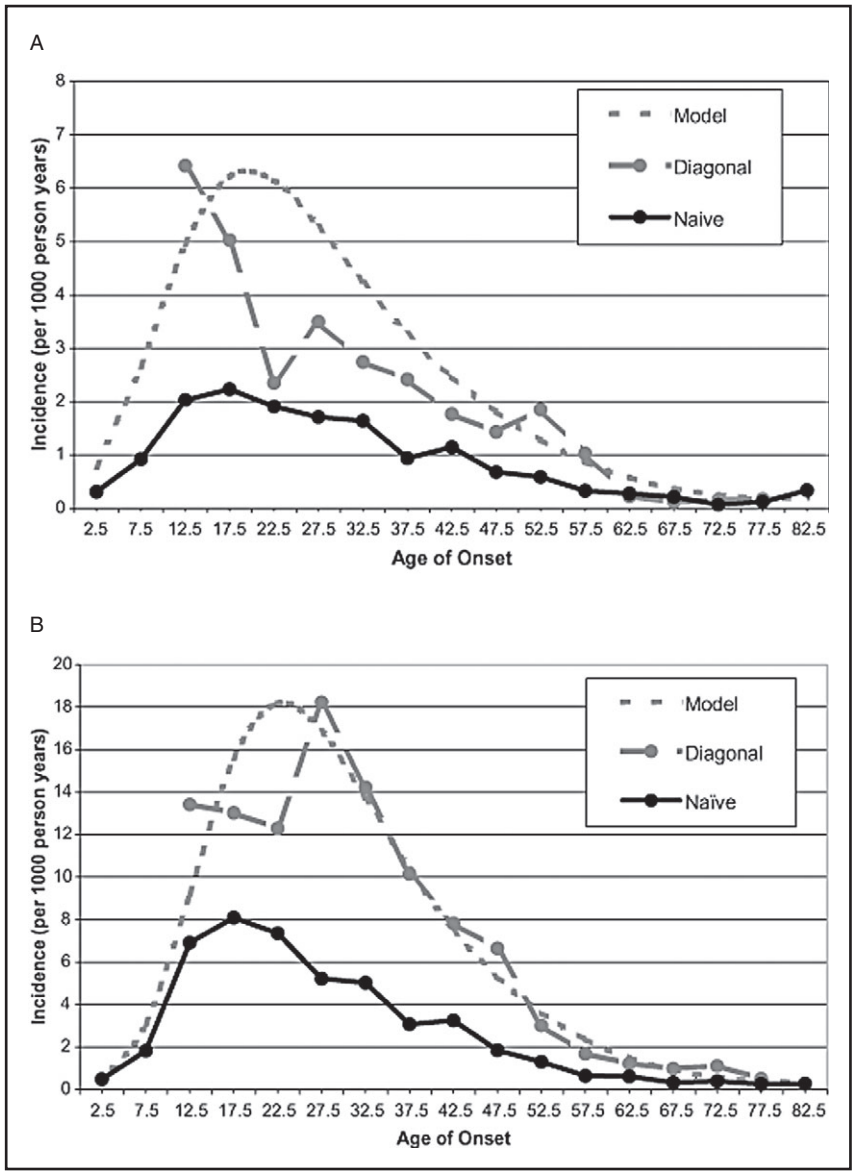

Fig 1.—(A) Male 5-year age-specific migraine incidence for the naive, diagonal, and model-based estimates. (B) Female 5-year age-specific migraine incidence for the naive, diagonal, and model-based estimates (based on reference 24).

participants, 1.5% fulfilled the criteria for primary CDH in the past year. Girls had a higher prevalence (2.4%) than boys (0.8%). Most had chronic tension-type headache (TTH) (65.6%) and a minority fulfilled criteria for CM (6.6%). Only 20% overused medications.[34] A caveat is that the authors used the restrictive definition of CM proposed by ICHD-2, which likely contributed to a substantial underestimate of the true prevalence of this form of CDH.[34-36]

This last caveat (under-diagnosing CM) should not be underemphasized. If the criteria for episodic migraine is too restrictive in young children, and the diagnosis of CM requires a pre-specified number of migraine days per month, the prevalence of CM is being underestimated not once, but twice. Of further interest are the recent follow-up findings of the Taiwan cohort. After 8 years of follow up, CDH was predicted by headache with migraine features. Early onset of CDH predicted refractory outcomes.[37] These findings concur with results of our own group conducted in a tertiary care setting. Early onset of episodic migraine predicted CDH; shorter time of evolution from epi-

Table 2.—Sex-Specific Migraine Prevalence and Prevalence Ratios in Adolescents

	Adjusted Prevalence (%)	
	Male	Female
Race		
White	5.1	7.5
Black	2.6	4.4
Age (years)		
12	3.4	3.2
13	3.6	4.4
14	4.0	4.6
15	3.9	6.0
16	2.9	6.2
17	4.1	9.8
18	3.9	7.8
19	3.2	6.3
Household income		
Under $22,500	5.8	8.1
$22,500-$39,999	3.5	5.9
$40,000-$59,999	3.1	6.2
$60,000-$89,999	3.4	4.8
$90,000 and over	2.8	4.4

Results from the AMPP study, adjusted by age, gender, and sociodemographic features.

sodic to CM predicted refractoriness to treatment.[11] Accordingly, in adolescents as in adults, CM seems to be prevalent, underestimated, and the final result of episodic migraine chronification.

Differences from Adults.—Substantial differences between the distribution of CDH subtypes and specific phenotypes exist between adolescents and adults. In the tertiary care, CM corresponds to a lower proportion of the CDHs in adolescents than in adults (68.8% vs 87.4%, $P < .001$), while new daily persistent headaches (21.1% vs 10.8%, $P < .001$) and chronic TTH (10.1% vs 0.9%, $P < .0001$) are more common in adolescents than in adults.[38]

Furthermore, while most adult individuals with the phenotype of CM overused analgesics, in adolescents this was not the case (28.2% vs 62.5%, $P < .001$). In fact, excluding medication overuse (pure CM); CM was relatively more common in adolescents than in adults (40.5% vs 24.9%, $P < .001$). This issue is of particular importance. It may be speculated that those with special biological vulnerability for frequent pain would develop CDH early and without the needs of particular risk factors; those with intermediate predisposition would develop the disease (CDH) later, in the presence of specific risk factors such as medication overuse, obesity, stressful life events, etc. Those without predisposition would not develop CDH even when exposed to risk factors for migraine progression. They would persist with episodic migraine and could eventually remit.[39]

Finally, adolescents with CM have more migraine attacks than adults. It is well established that during the process of migraine progression, as attack frequency increases, the number of migraine features diminish during the transformation period. Accordingly, it is natural that adolescents with CDH have more migraine days compared with adults, as demonstrated by a study conducted in the specialty care.[40]

THE ATTENTION BRAZIL PROJECT—CRITICAL COMMENT AND ADVANCES IN UNDERSTANDING

An important gap in our understanding of headaches in young children is due to the lack of representative studies. The Attention Brazil Project (ABP) is a large ongoing population study aiming to investigate mental health and development of preadolescent children in Brazil.[41] The project consists of 2 phases. In Phase 1 (pilot phase, completed), the target sample population consisted of all children aged from 5 to 12 years registered in the public school system of a city representative, by demographics, of the Brazilian population. Over 2000 children participated in the study. Mothers were directly interviewed using standardized and validated questionnaires (total of 238 questions), and detailed information was obtained on overall health, learning conditions (eg, attention-deficit hyperactivity disorder [ADHD]), socioeconomic conditions, parental overall health, particular exposures during pregnancy and others. Headaches were assessed according to the ICHD-2. Direct interviews were also conducted with teachers, as per the DSM-IV, in order to investigate impact of disorders, with a specific emphasis on attention and overall activity.

Accordingly, the ABP offers a unique opportunity to study headaches in a pre-adolescent represen-

tative sample carefully and accurately described and investigated. Key points are summarized below:

Prevalence and Frequency of Primary Headaches in young Children.—In the ABP, headaches were analyzed in 2 different ways. First, we strictly followed the ICHD-2 criteria. Children were stratified as a function of headache frequency as having low-frequency episodic headaches (<5 days per month), intermediate-frequency episodic headaches (5-9 days per month), high frequency episodic headaches (10-14 days per month), and CDH (15 or more days).[42]

In this population (5-11 years of age), prevalence of migraine with or without aura was 3.8%, specifically 3.9% in boys and 3.6% in girls (non-significant difference). Prevalence was 3.2% in white children and 4.7% in afro-descendent children. Prevalence in girls was very similar by race (3.6% and 3.5%, respectively), but in boys, prevalence was significantly increased in afro-descendents (5.8% vs 2.9%, relative risk [RR] = 1.99, 95% confidence interval [CI] = 1.1-3.7). Prevalence increased with age. Using the age of 6 as the reference (2.6%), prevalence was numerically increased in all subsequent ages, and significantly increased at the age of 10 or older (5.5%, RR = 2.13, 95% CI = 1.02-4.44).

We were surprised that the prevalence of probable migraine (PM, migraine missing 1 required criterion) was an impressive 17.1%. The vast majority of cases of PM failed to receive a migraine diagnosis based on missing the duration criteria (had experienced headaches lasting less than 1 hour—76%). The second reason for a PM diagnosis was due to missing the associated symptoms criteria (having only one of photophobia or phonophobia and no nausea or vomiting). Based on these findings, we concluded that a sizable proportion of young children have migraine-like attacks of very short duration (<1 hour). If the attacks are frequent, they may trigger medical consultations. Whether the duration of pediatric migraine may be this short, or if this is an artifact based on the fact that the quality of information from young children is compromised, is still unclear. Nonetheless, similar findings have been reported by other groups.[43,44] Providers should be aware of this particular point.

Prevalence of CDH in the ABP study was high (1.68%). Prevalence was higher in girls than in boys (2.09% vs 1.33%), although differences were not significant (PR = 1.6, 95% CI = 0.7-3.4).

As mentioned above, we also assessed the proportion of children that, although still presenting episodic headaches, had high frequency of days with headache. We found that the overall prevalence of children with 10-14 days of headache per month was 2.52%. Prevalence was numerically but not significantly increased in girls than in boys (2.8% and 2.3%). Accordingly, the proportion of children with 10 or more days of headache per month in the population is important (4.2%).

Medical Needs in Children with Migraine and CDH.—Most children with migraine seen in the ABP had consulted a medical doctor because of their headaches, and proportion was higher among children with CM (93.7%) than in migraine (75.6%) or probable migraine (58.5%). Figure 2 displays the number of days using any acute treatment in the past month as a function of headache frequency, among children with migraine subtypes. Of interest is the fact that, for all subtypes, most children used acute medication for at least 1 day, and 42.7% of the children with migraine used acute medication on 2-4 days highlighting that, even in the young non-referred population, the burden of headaches is not negligible.[42]

Prenatal Exposures and Risk of CDH.—As mentioned, increased vulnerability of pediatric subpopulations to certain diseases may reflect a combination of stronger biological predisposition, pre-natal exposures, or early life exposures/comorbidities.[45] Among the prenatal exposures, tabagism and exposure to alcohol are of interest. Nicotine targets specific neurotransmitter receptors in the fetal brain, eliciting abnormalities of cell proliferation and differentiation, leading to shortfalls in the number of cells and eventually to altered synaptic activity.[46] For alcohol, alterations in fetal biometric measurements were reported in those with consistent exposure during pregnancy.[47]

In the ABP, we specifically asked about active or passive exposure to nicotine during pregnancy, as well as alcohol consumption.[48] Odds of CDH were significantly higher when maternal tabagism was reported.

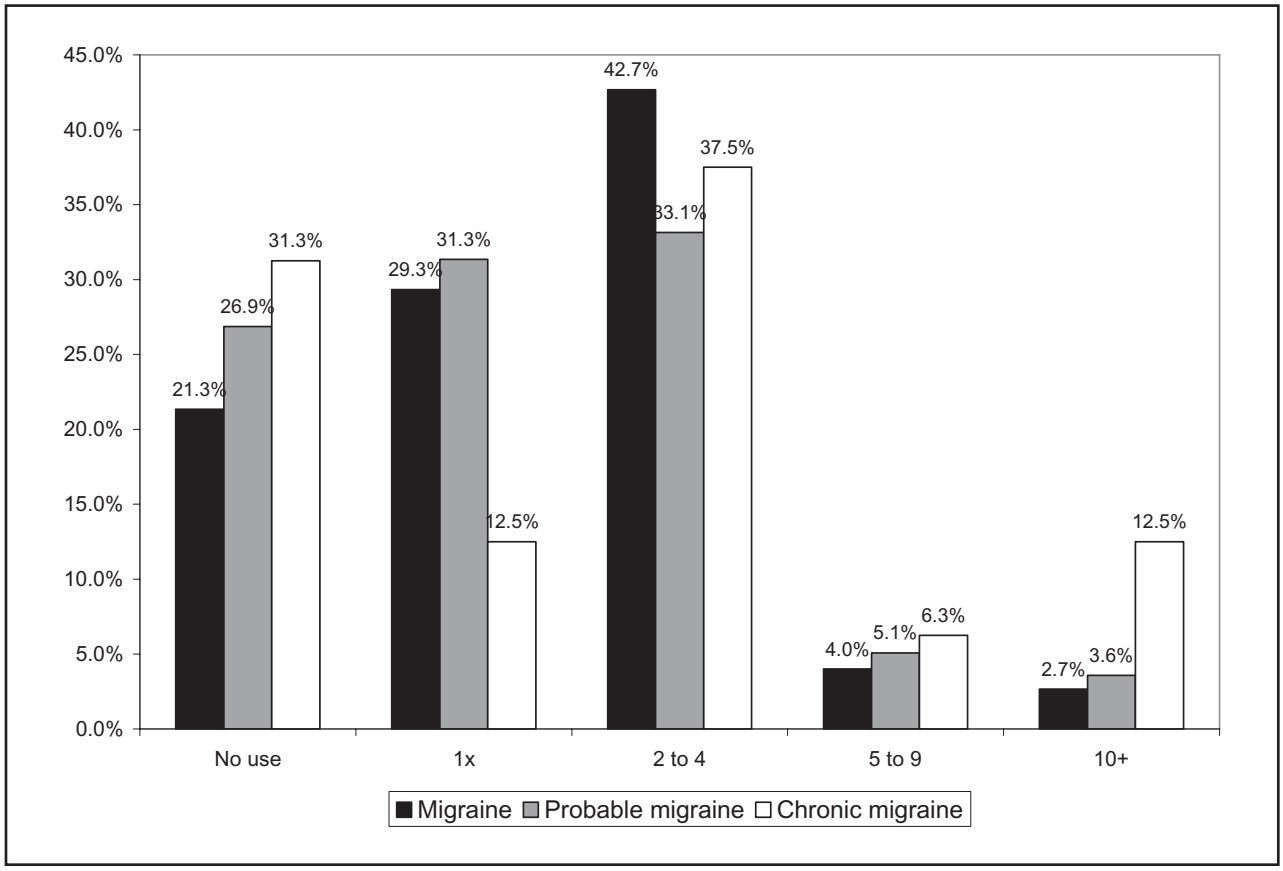

Fig 2.—Frequency of use of acute medication as a function of the migraine subtype (over 1 month).

When active, and passive, smoking were reported, odds ratio (OR) of CDH were 2.29 (95% CI = 1.6 vs 3.6); for active tabagism, OR = 4.2 (95% CI = 2.1-8.5). Alcohol use more than doubled the chance of CDH (24% vs 11%, OR = 2.3, 95% CI = 1.2-4.7). The risk remained significantly elevated after adjusting for family income, parental headache status, and medical care during pregnancy, hypertension during pregnancy, and use of illegal drugs (Table 3).

Table 3.—Main Effect of Tabagism and Alcohol Use during Pregnancy in Chronic Daily Headaches in Childhood after Adjustments

	Overall	Boys	Girls
Tabagism	2.03 (1.3-3.2)	1.4 (1.1-2.1)	3.1 (1.5-4.2)
Alcohol	1.8 (1.3-3.1)	1.2 (0.2-3.4)	2.7 (1.5-4.1)

Frequency of Headaches in Children as a Function of Frequency of Headaches in the Parents.— Migraine aggregates within families,[49-51] and aggregation increases as a function of disease severity.[52,53] The familial aggregation of the CDH and of episodic headaches of different frequencies has been very poorly studied and this is of importance for several reasons. First, if headache frequency also aggregates in the family, the identification of probands severely affected offers a possibility for screening and early treatment of first degree relatives.[54] Second, because most common CDHs evolve from episodic headaches, investigating if CDHs aggregate not only in the families of individuals with CDH, but also in the families of individuals with high frequency episodic headaches, offers pathophysiological insights.[55]

In the ABP, as compared with negative lifetime family history, any headache history in the mother or in the father increased the RR of episodes (1.6, 95%

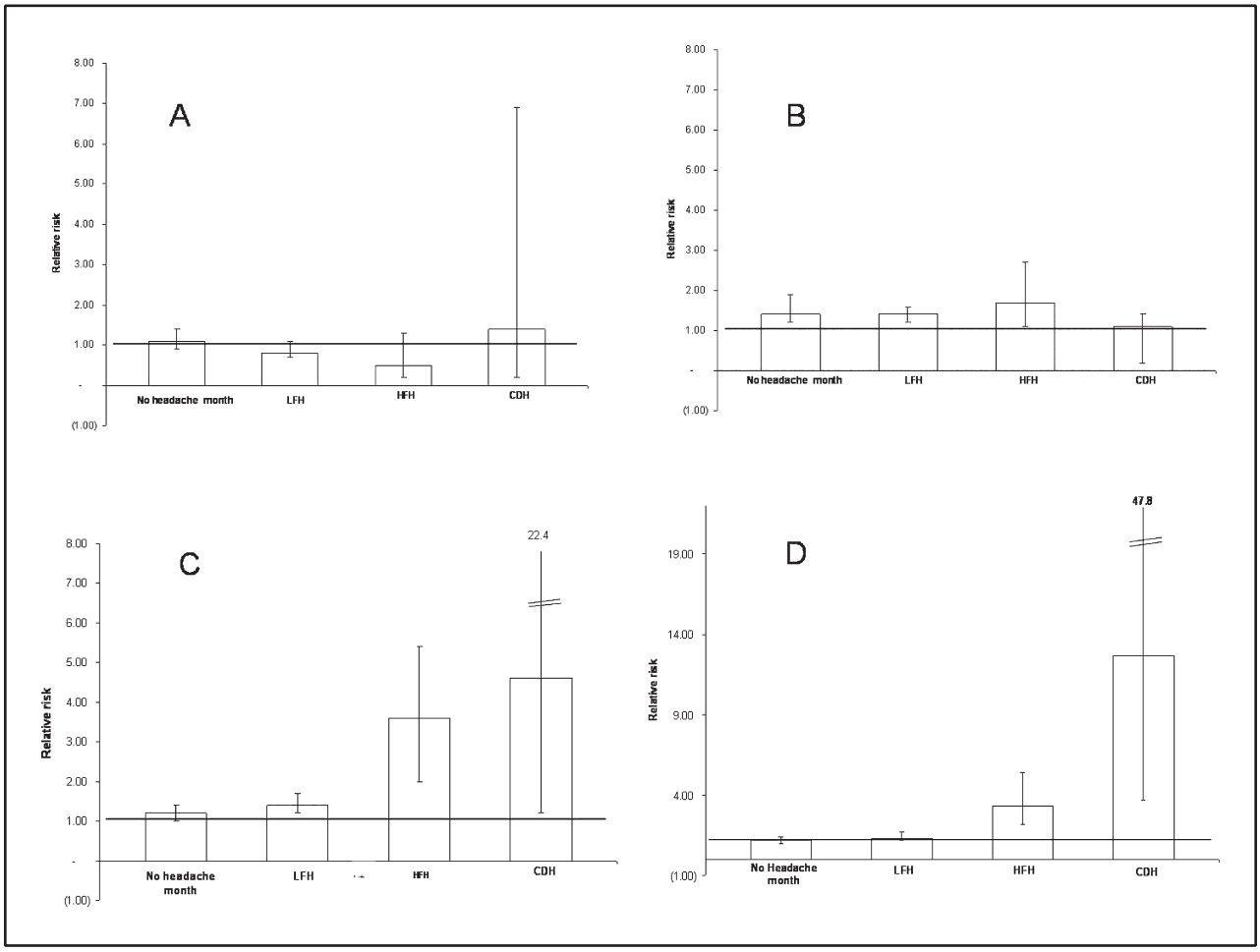

Fig 3.—Adjusted relative risk of headache status in children as a function of headache status in the mother, as compared with no headaches in children or mother. (A) mother with no headaches during past month; (B) mother with low frequency episodic headaches; (C) mother with intermediate or high frequency episodic headaches; (D) mother with chronic daily headaches. CDH = chronic daily headache; HFH = high frequency headaches; LFH = low frequency headaches.

CI = 1.3-1.8), and of CDHs (6.6, 1.4-28.4) in the children.[56] Frequency of headaches in the mother predicted frequency of headaches in the children; when mother had a low headache frequency, children had an increased chance of experiencing low or intermediate headache frequency (RR = 1.4, 1.2-1.6) but not CDHs. When the mother had CDH, the risk of CDH was increased almost 13-fold. The risk of infrequent headaches, however, did not rise accordingly. In multivariate models, frequency of headaches in the children were independently predicted by frequency of headaches in the mother after adjustments, suggesting that headache frequency (not only headache status) aggregates in the family (Fig. 3).[56]

Headaches and Symptoms of Childhood Periodic Syndrome.—The concept that in some children migraine evolves from being acephalgic into a condition where headache develops is well accepted since the first pivotal descriptions in 1933.[57] Over time, several other manifestations were suggested as being associated with migraine, including "growing pains",[58,59] parasomnias,[26] motion sickness,[60] benign paroxysmal torticollis,[61] pseudoangina,[62] Tourette syndrome,[63] hyperactivity,[64] and benign paroxysmal vertigo of childhood.[65] However, while evidence linking some of these symptoms to migraine is robust, for others, association has been described almost anecdotally.

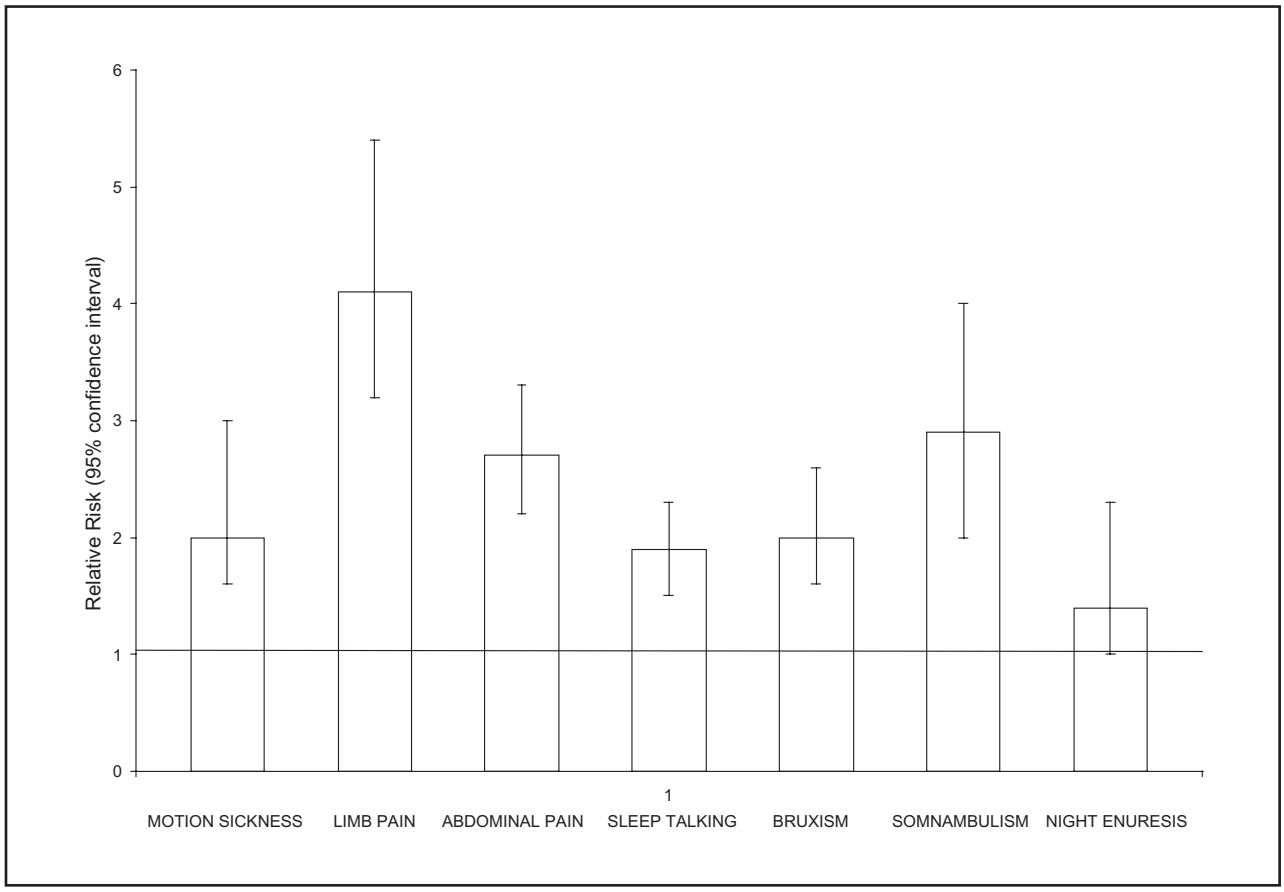

Fig 4.—Relative risk of selected symptoms in children with migraine, relative to controls.

In the ABP we found that for episodic migraine, the RR of all symptoms except nocturnal enuresis was significantly increased, relative to controls. They included motion sickness (RR = 2.1, 95% CI = 1.4-3.1); recurrent limb pain (RR = 5.2, 95% CI = 3.7-7.2), recurrent abdominal pain (RR = 2.7, 95% CI = 2.2-3.3) and parasomnias, such as sleep talking (RR = 2.3, 95% CI = 1.7-3.0), somnambulism (RR = 3.4, 95% CI = 2.2-5.1), and bruxism (RR = 2.4, 95% CI = 1.7-3.3) (Fig. 4). Similar findings were seen for PM and CM. For TTH, the magnitude of effect was clearly inferior to what was seen with migraine headaches, only nocturnal enuresis and motion sickness were not more common in TTH than in controls. In multivariate analyses, any interictal symptom was independently associated with any headache ($P < .001$), migraine headaches ($P < .001$), and TTHs ($P < .01$).[66]

In our opinion, the most relevant component of our findings was not that interictal symptoms suggestive of childhood periodic syndromes are common in the population and associated with migraine and specific migraine subtypes, but that they could also be associated with TTH. It is important to replicate the study.

Headaches and ADHD.—Attention-deficit hyperactivity disorder is a condition characterized by pervasive and impairing symptoms of inattention, hyperactivity, and impulsivity.[67,68] According to a meta-analysis, its worldwide-pooled prevalence is 5.3%.[69] In the USA, over 8% of the children from 8 to 15 years have ADHD.[70] The condition been with a broad range of negative outcomes for affected (Table 4).[71]

The prevalence of ADHD in children with headaches has not been established. This is of importance,

Table 4.—Prevalence of ADHD, Hyperactivity-Impulsivity, and Inattention as a Function of Headache Diagnosis

		ADHD Overall			
	Total	n	%	95% CI of Prevalence	RR (95% CI)
No headache	345	23	6.7	4.1-9.3%	Reference
Migraine overall	427	31	7.3	4.8-9.7%	1.1 (0.6-1.8)
Migraine with or without aura	118	11	9.3	4.1-14.5%	1.4 (0.7-2.7)
Chronic migraine	14	1	7.1	0-20.6%	1.1 (0.1-7.4)
Probable migraine	309	20	6.5	3.7-9.2%	1.0 (0.5-1.7)

ADHD = attention-deficit hyperactivity disorder.

as both conditions are frequent in children. Because headaches have been controversially suggested as impacting learning,[72] and ADHD is an important cause of learning disability,[73] studying the association of both conditions is of clinical and educational importance.

As part of the ABP, ADHD was assessed according to DSM-IV criteria by the MTA-SNAP-IV scale[74] and mental health status was assessed with the validated Brazilian version of the Child Behavior Checklist (CBCL/6-18).[75] Prevalence of ADHD was 6.1%. As contrasted to controls, prevalence of ADHD was not significantly different by headache category. For hyperactivity-impulsive symptoms, prevalence was 8.1% in controls; it was significantly higher in with or without aura (23.7%, RR = 2.6, 95% CI = 1.6-4.2), and probable migraine (18.4%, RR = 2.1, 95% CI = 1.4-3.2). Prevalences were also significantly increased in frequent ETTH (16.5%) and probable TTH (13.6%). Concerning inattention as a symptom, no differences were seen as a function of headache status. In multivariate analyses, ADHD or inattention symptoms were not predicted by headache subtypes or headache frequency. Hyperactivity-impulsivity symptoms were significantly associated with any headache ($P < .01$), TTH ($P < .01$), or migraine ($P < .001$).

Accordingly, the conclusion of the study was that migraine and TTH are not comorbid to ADHD overall, but are comorbid to hyperactive-impulsive behavior.

The mechanisms of the comorbidity between headache disorders and behavioral hyperactivity-impulsivity are still to be fully elucidated. Hyperactivity is conceptualized as a condition where tonic norepinephrine and dopamine fire rates are low. Other neurotransmitters of importance include GABA and serotonin.[76,77] Hypoactivity in areas that inhibit specific behaviors seem to be of importance in this condition and, in some aspects, hyperactivity (and ADHD overall) may be considered a disease where lack of inhibition is pivotal. Migraine has long been considered a disorder characterized by cortical hypoexcitability,[78,79] but current theories (similarly to behavioral hyperactivity) consider it as a disorder resulting from lack of inhibition.[80,81] Accordingly, although affecting different areas, both disorders share the concept that modulatory inhibitory systems in the brain are malfunctioning.

CONCLUSION

Herein, we critically discussed relevant topics relative to migraine in childhood. It is clear that in both adolescents and in preadolescents, migraine is frequent. Diagnostic criteria for migraine and CM are certainly over-restrictive for young children. A vulnerable population at risk of migraine progression also exists, likely reflecting increased biological predisposition, but also early life exposures. Indeed, it seems that even prenatal exposures of certain substances may increase the risk of migraine progression. Of relevance is also the fact that frequency of headaches aggregate in the family. Finally, migraine seems to be associated with behavioral hyperactivity, but is not comorbid with ADHD.

STATEMENT OF AUTHORSHIP

Category 1

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