The objective of the present study was to estimate the prevalence and relative risk of symptoms suggestive of childhood periodic syndrome in migraine, migraine subtypes, and tension-type headache, relative to control subjects. The target population was all children (age 5-12 years) enrolled in public elementary schools in one Brazilian city (n = 2173). Consent was obtained for 1994 children; analyzable data were available for 1906 children, for a final sample of 1113 children with migraine, tension-type headache, or no headache. Parents were interviewed using validated questionnaires. Headache diagnosis was assigned according to the International Classification of Headache Disorders, 2nd edition. Relative risk of symptoms was drawn by headache categories relative to controls. For episodic migraine, the relative risk of all symptoms except nocturnal enuresis was significantly increased: motion sickness, recurrent limb pain, recurrent abdominal pain, and parasomnias, such as sleep talking, somnambulism, and bruxism. For tension-type headache, only nocturnal enuresis and motion sickness were not more common than in controls. In multivariate analyses, any interictal symptom was independently associated with any headache (P < 0.001), migraine headaches (P < 0.001), and tension-type headaches (P < 0.01). These findings indicate that interictal symptoms suggestive of childhood periodic syndromes are common in the population, and are associated with migraine and specific migraine subtypes, but also with tension-type headache. © 2010 by Elsevier Inc. All rights reserved.


Introduction

Under the denomination of childhood periodic syndromes, several recurrent, transient, and otherwise unexplained symptoms and signs have been described as being precursors of migraine: vomiting, abdominal pain, fever, parasomnias, motion sickness, benign paroxysmal torticollis, pseudoangina, Tourette syndrome, hyperactivity, and benign paroxysmal vertigo of childhood [1-12]. Evidence linking some of these symptoms to migraine is robust, but for others the association has been described almost anecdotally.

The International Classification of Headache Disorders, 2nd edition, defines the diagnostic criteria for abdominal migraine and for cyclical vomiting as precursors of migraine, but does not mention other potential childhood periodic syndromes [13]. Furthermore, childhood periodic syndromes are categorized as migraine subtypes, empirically assuming that no link with other headaches (e.g., tension-type headaches) exists.

The paucity of large studies with representative population samples on the subject is a barrier to an evidence-based characterization of the childhood periodic syndromes. Accordingly, the aim of the present study was to assess the prevalence of several symptoms suggestive of childhood periodic syndromes in preadolescent children identified from the general population, including the prevalence and relative risk of these symptoms in migraine overall, migraine subtypes (including probable migraine and chronic migraine), and tension-type headache, relative to controls.

Methods

The present study was conducted as part of a large ongoing population study aiming to investigate the mental health of children and adolescents in Brazil (Attention-Brazil Project). The target sample was all children from 5 to 12 years registered in the public school system of one city (Santa Cruz, Brazil).
dias Palmeiras, SP, Brazil). Direct interviews were made with the parents, and the children were examined in February 2009.

**Geographic Characterization and Target Sample**

According to the demographic census (2008 data), the region of study covers an area with 32,862 inhabitants; of these, 30,387 (92.4%) are in the urban area. Life expectancy is 73.7 years [14]. The target sample consisted of all children from 5 to 12 years, living in urban or rural areas, registered in any of the five public elementary school of the city (n = 2173). Parental consent was obtained for 1994 subjects (91.0%), and analyzable data (complete demographic and headache information) were available for 1906 subjects (87% of target sample and 95% of respondents). Of this final sample, 907 were girls (47.6%) and 999 were boys (52.4%). For the present report, the analyses were restricted to children with complete information available, and with migraine, tension-type headache, or no headache (excluding children with other headache diagnoses and non-classified headaches), for a final sample of 1113 children.

**Headache Assessment**

The standardized questionnaire consisted of 97 questions, divided in modules assessing different domains. The headache module of the questionnaire consisted of 10 questions, assessing the distinguishing features required for headache diagnosis, such as headache characteristics (laterality, quality, severity, aggravation by exercises), frequency of pain, nausea, photophobia, phonophobia, duration of the episodes, and consumption of analgesics. Further, behaviors related to pain were also addressed. The questionnaire and the subsequent headache diagnosis followed the diagnostic criteria for primary headaches of the International Classification of Headache Disorders, 2nd edition [13]. Questions focused on the most severe type of headache experienced by the children.

**Assessment of Interictal Symptoms**

A specific module was developed to assess the presence of other symptoms, not associated with headaches. This module included validated questions for the diagnosis of learning disabilities (within the scope of a separate ongoing study), as well as questions about motion sickness (does your child complain about feeling sick or feel sick when in a car ride?), recurrent limb pain (does your child complain about pain in the legs or arms not associated with a trauma?), recurrent abdominal pain (does your child often complain about pain in the belly?), and the following parasomnias: sleep talking (does your child talk while sleeping?), somnambulism (does your child sometimes sit up and/or walk while sleeping?), bruxism (does your child clench the teeth while sleeping?), and nocturnal enuresis (does your child sometimes urinate while sleeping?).

**Analyses**

Sex-specific prevalence estimates of specific symptoms (1-year prevalence) were derived by age and contrasted in migraineurs and controls. To characterize the sample, descriptive statistical analyses were performed (summary tables, means, medians, and standard deviations). To represent the relationship between demographic characteristics and migraine status, cross tabulations were performed. Relative risk and 95% confidence intervals compared specific categories (e.g., specific symptoms) with the reference category.

Adjusted analyses estimated separately any headache, migraine, and tension-type headache, as a function of headache frequency, age, sex, and race. The level of significance adopted was 5%. Statistical analysis was using an SPSS software package (version 15.0 for Windows; SPSS, Chicago IL).

The study was approved by the relevant Institutional Review Board and written informed consents were obtained.

**Results**

**Prevalence of Primary Headaches**

The overall prevalence was 3.76% for migraine, 17.1% for probable migraine, and 0.8% for chronic migraine. Infrequent and frequent episodic tension-type headache occurred in 2.3% and 1.6% of the sample, respectively; probable tension-type headache occurred in 13.5%, and chronic tension-type headache in 0.1% (Fig 1).

**Symptoms Suggestive of Childhood Periodic Syndromes and Migraine**

Of the interictal symptoms investigated, the most prevalent were recurrent abdominal pain (32.9%), sleep talking (26.8%), and recurrent limb pain (23.8%) (Fig 2).

Prevalence and relative risk for interictal symptoms reported by children with migraine (with and without aura), probable migraine, and chronic migraine, as well as in controls subjects, are reported in Table 1. For episodic migraine, the relative risk (RR) of all symptoms except nocturnal enuresis was significantly increased, relative to controls: namely, motion sickness (RR = 2.1, 95% confidence interval 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).

Similar results were observed for probable migraine: all symptoms were present more frequently than in control subjects. For chronic migraine the sample size was small, but motion sickness, recurrent limb pain, recurrent abdominal pain, and somnambulism were significantly more common in this group as well, relative to controls.

Because the RR values for migraine, probable migraine, and chronic migraine (when positive) were similar, the three groups were combined for comparison with the

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**Figure 1.** Prevalence of migraine and tension-type headache, with subtypes, in unselected preadolescent school children (n = 1906). Abbreviations: TTH, tension-type headache; ETTH, episodic tension-type headache; CTTH, chronic tension-type headache.
control group (Fig 3). Except for enuresis, all symptoms were not only significantly more frequent in migraineurs relative to controls, but the magnitude of effect was robust.

**Symptoms Suggestive of Childhood Periodic Syndromes and Tension-Type Headaches**

Prevalence and relative risk for interictal symptoms reported by children with tension-type headache are reported in Table 2. The RR values of all symptoms but nocturnal enuresis and motion sickness were significantly increased, relative to controls. For recurrent abdominal and recurrent limb pain, prevalence was increased more than twofold.

**Multivariate Analyses**

In multivariate analyses, any interictal symptom was independently associated with any headache ($P < 0.001$), migraine headaches ($P < 0.001$), and tension-type headaches ($P < 0.01$). Sex, race, and age (with the caveat that study included only children aged 5-12 years) did not predict associated symptoms.

**Discussion**

Identifying symptoms associated with migraine headaches, or precursors of incident migraine, is of importance. Because the phenotype of migraine changes over time [15], and because at early ages it may be difficult to obtain reliable information on clinical symptoms, interictal symptoms that are associated to migraine may raise suspicion of the disease in the context of diagnostic uncertainty [16]. Furthermore, the specificity of the symptoms is also of interest. If certain symptoms are specific to a disease (e.g., migraine), then clinical relevance is immediate. Alternatively, if symptoms are seen in more than one disease

![Figure 2](image-url)  
*Figure 2. Prevalence of selected interictal symptoms in preadolescent school children (n = 1113).*

<table>
<thead>
<tr>
<th>Interictal Symptom</th>
<th>Prevalence, %</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Motion sickness</td>
<td>18.7%</td>
<td></td>
</tr>
<tr>
<td>Limb pain</td>
<td>23.8%</td>
<td></td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>21.5%</td>
<td></td>
</tr>
<tr>
<td>Sleep talking</td>
<td>16.7%</td>
<td></td>
</tr>
<tr>
<td>Bruxism</td>
<td>8.4%</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 1. Prevalence and relative risk of selected interictal symptoms as a function of headache status and migraine subtype</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Headaches</td>
</tr>
<tr>
<td>--------------</td>
</tr>
<tr>
<td>n</td>
</tr>
<tr>
<td><em>motion sickness</em></td>
</tr>
<tr>
<td>Limb pain</td>
</tr>
<tr>
<td>Abdominal pain</td>
</tr>
<tr>
<td>Sleep talking</td>
</tr>
<tr>
<td>Bruxism</td>
</tr>
<tr>
<td>Somnambulism</td>
</tr>
<tr>
<td>Nocturnal enuresis</td>
</tr>
</tbody>
</table>

Abbreviations:
CI = Confidence interval
RR = Relative risk
(e.g., both migraine and tension-type headache), then this has pathophysiologic relevance.

Accordingly, the present study was designed to test for the association of headache status and interictal symptoms. Although evidence for the association is more robust for migraine, apparently no reports relate these symptoms to migraine subtypes (e.g., full migraine, probable migraine, and chronic migraine). The association with tension-type headache was also tested, to assess the specificity of the expected association (e.g., migraine only, or not). Three relevant findings deserve particular mention and discussion.

First, as expected, several interictal symptoms that have been reported as potentially associated with migraine emerged as significantly associated. In this regard, the present data are confirmatory to findings from several other studies [17-19]. Of interest is that the International Classification of Headache Disorders, 2nd edition, recognizes only three childhood periodic syndromes (cyclical vomiting, abdominal migraine, and benign paroxysmal vertigo of childhood) [13]. Nonetheless, parasomnias have also been associated with pediatric migraine diagnosis [20], although others have not found differences in the prevalence of parasomnias in migraine vs tension-type headache [21].

Second, association was observed for the three tested migraine subtypes, and frequency of headaches did not influence the association. Others have demonstrated that the comorbidity profiles of probable migraine [22,23] and of chronic migraine [24,25] are similar to episodic migraine, but with different magnitude. The similarities between interictal symptoms in migraine and probable migraine are not surprising, because the difference between both is largely artificial (only one symptom of difference). For chronic migraine, the similarities may indeed reflect a bias. The present study asked about interictal symptoms, and children with chronic migraine have a lower interictal pool because they have more headache days and fewer headache-free days. The finding should therefore be interpreted with caution. The relevant message is that the relationship was identified over the spectrum of migraine subtypes. Future studies should focus on the relationship of these symptoms with later development of episodic vs chronic migraine.

Finally, children with tension-type headache were also more likely to present the same interictal symptoms, in contrast to controls, in both crude and adjusted analyses. To our knowledge, similar findings have not been published. The tension-type headache group represents pure tension-type headache because, as described in the Methods section, this group had qualifying tension-type

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Table 2. Prevalence and relative risk of selected interictal symptoms in children with tension-type headaches, relative to controls

<table>
<thead>
<tr>
<th>Symptom</th>
<th>n</th>
<th>Prevalence (%)</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Motion sickness</td>
<td>51</td>
<td>16.6</td>
<td>1.0 (0.7-1.4)</td>
</tr>
<tr>
<td>Limb pain</td>
<td>97</td>
<td>31.6</td>
<td>2.6 (1.9-3.3)</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>144</td>
<td>46.9</td>
<td>2.0 (1.6-2.5)</td>
</tr>
<tr>
<td>Sleep talking</td>
<td>104</td>
<td>33.9</td>
<td>1.4 (1.1-1.8)</td>
</tr>
<tr>
<td>Bruxism</td>
<td>80</td>
<td>26.1</td>
<td>1.4 (1.0-1.8)</td>
</tr>
<tr>
<td>Somnambulism</td>
<td>63</td>
<td>20.5</td>
<td>1.9 (1.3-2.7)</td>
</tr>
<tr>
<td>Nocturnal enuresis</td>
<td>31</td>
<td>10.1</td>
<td>1.1 (0.7-1.8)</td>
</tr>
</tbody>
</table>

Abbreviations:
CI = Confidence interval
RR = Relative risk
headache but not migraines (only the most severe headache type of headaches was classified, according to a well accepted and validated algorithm) [26,27]. It may be that these symptoms are not associated with any headache syndrome, but rather with trigeminal pain. Alternatively, it may be that migraine and tension-type headaches represent different portions of the intensity spectrum of a similar condition; thus, for migraine increased predisposition would translate into a more robust phenotype that is either trigeminal (e.g., migraine) or extra-trigeminal (e.g., abdominal pain), whereas tension-type headache would represent a milder phenotype [28,29]. A similar rationale has been used to discuss the spectrum of episodic vs chronic daily headaches [30].

Several limitations of the present study deserve comment. First, the assessment was of the presence of interictal symptoms, not of specific syndromes. This is largely an inherent limitation of conducting population studies in small children. The present data, however, are in agreement with clinic-based studies. Second, the questions used were broad, and may be seen as of little specificity. This potential limitation of the study questionnaire (which was constructed in the absence of any validated instrument for the assessment of childhood periodic syndromes) is largely neutralized by the presence of a control group. Third, the prevalence of the tension-type headache was likely underestimated, because only the most severe type of headache presented by patients was classified. Again, this choice is justifiable, because young children may not be capable of providing information on more than one type of headache, and will likely focus on the most severe or frequent forms. This inherent limitation is also a strength of the present study, to the extent that probable migraine is not misclassified as tension-type headache [31].

Interictal symptoms suggestive of periodic syndromes are common in the population, and are associated not only with migraine and specific migraine subtypes, but also with tension-type headache. The magnitude of the association varies as a function of symptoms and seems to be highest for motion sickness, somnambulism, and limb pain.

References

[27] Lipton RB, Diamond S, Reed M, Diamond ML, Stewart WF. Migraine diagnosis and treatment: results from the American Migraine Study II. Headache 2001;41:638-45.