Migraine Headache in Patients With Tourette Syndrome

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Background: Tourette syndrome (TS) is recognized as one of the most common childhood movement disorders, characterized by motor and phonic tics often associated with neurobehavioral comorbidities, such as obsessive-compulsive disorder. Neurotransmitter dysregulation, particularly involving the serotonin system, has been implicated in the pathogenesis of TS, obsessive-compulsive disorder, and migraine headache.

Objectives: To investigate the possible association between migraine headache and TS and to report preliminary findings of family history of migraine headache in patients with TS.

Methods: Subjects diagnosed as having TS at the Baylor College of Medicine Parkinson’s Disease Center and Movement Disorders Clinic were administered a migraine headache questionnaire based on the migraine criteria established by the Headache Classification Committee of the International Headache Society.

Results: Of 100 patients with TS, 25 (25.0%) satisfied the diagnostic criteria for migraine headache, significantly greater than the estimated 10% to 13% in the general adult population (P<.001) and the estimated 2% to 10% in the general pediatric population (P<.04). There was no significant (P=.44) difference in the presence of comorbid obsessive-compulsive traits in the TS migraine and TS nonmigraine sample groups. Furthermore, our TS group with migraines was not more likely to have features of obsessive-compulsive disorder compared with attention-deficit/hyperactivity disorder. Of patients with TS, 56.0% reported a family history of migraines, 44.0% of whom were first-degree relatives.

Conclusions: The frequency of migraine headache in a clinic sample of TS subjects was nearly 4-fold more than the frequency of migraines reported in the general population. Contrary to previous reports, the co-occurrence of migraines and TS in our sample group may possibly be attributed to another TS comorbidity, other than obsessive-compulsive traits.

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Graine headache.\(^{20,21}\) However, to our knowledge, the occurrence of migraine headache in TS patients, or their family members who may have a high incidence of OCD, has not been well studied. This study determines the prevalence of migraines in our sample of TS subjects and in their first-degree family members, and explores whether the TS comorbid features of attention-deficit/hyperactivity disorder and OCD correlate with the occurrence of migraines.

### METHODS

One hundred one subjects diagnosed as having TS according to the TS Classification Study Group criteria\(^{22}\) were included in the study. All subjects were diagnosed at the Baylor College of Medicine’s Department of Neurology. A written consent form, approved by the Institutional Review Board for Human Research for the Baylor College of Medicine, was reviewed and signed by all subjects or their legal guardians. Questionnaires were designed based on the diagnostic criteria for migraine headache, established by the Headache Classification Committee of the International Headache Society.\(^{21}\) The questionnaires were administered to all new or follow-up consecutive patients seen during the study period at the Baylor College of Medicine’s Department of Neurology. All questionnaires were completed through either a personal interview in the clinic or telephone contact. Data collected included the following information: (1) demographic data; (2) age at onset of TS symptoms; (3) occurrence of comorbidities, such as attention deficit with or without hyperactivity and obsessive-compulsive traits based on Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, criteria\(^{24}\); (4) age at onset of migraine headache; (5) the presence of aura with migraine; (6) family history of migraine headache; and (7) other information. To ensure data accuracy and reliability, all but one patient was interviewed again through repeated administration of the questionnaire by telephone. Each subject’s medical record was also reviewed for accuracy of age of onset of TS symptoms and presence of comorbid attention-deficit or obsessive-compulsive traits. All data analysis was performed on 100 verified subjects.

Nonparametric analyses were performed using the \(\chi^2\) exact test based on the Goodman and Kruskal (\(\alpha < .05\)) statistic, comparing the variables of TS patients with migraine headache, family history of migraine headache, and obsessive-compulsive and attention-deficit traits. A univariate analysis of variance was also used to compare the age at onset of TS symptoms between both sex and TS migraine and nonmigraine groups. All analyses are performed using SPSS version 10 (SPSS Inc, Chicago, Ill).

### RESULTS

One hundred TS patients (78 males), whose mean age was 20.2±14.2 (range, 7–69) years, were included in this study. Of the 100 patients with TS, 25 satisfied the diagnostic criteria for migraine headache based on International Headache Society criteria. Sixteen percent of pediatric and 39% of adult patients with TS had migraines, significantly greater than the 6% (range, 2%-10%) reported in otherwise healthy children\(^{10-13}\) (\(\chi^2=0.03, P<.04\)) and the 11% (range, 10%-13%) reported in the general adult population\(^{14,15}\) (\(\chi^2=0.11, P<.001\)), respectively (Table 1). Of the 25 TS patients with migraine, 12 (48%) reported migraine with aura.

Also, of the 25 TS patients with migraine, 6 (24%) were females and 19 (76%) were males; this difference did not reach statistical significance (\(P>.99\)). The mean age at onset of migraine headache between sexes was also not significantly different (\(P=.91\)). Of the 25 subjects with migraine, 24 (96%) also had comorbid obsessive-compulsive traits. However, our TS patients with migraines did not have a significantly greater comorbidity of obsessive-compulsive traits or attention deficit compared with the TS group without migraine (\(P=.44\) and \(P>.99\), respectively). Fifty-six percent of patients with TS had a family member with migraine, 44% of whom were first-degree relatives; 46.0% of a non–first-degree relative reported migraines.

### COMMENT

Our study shows that the frequency of migraine headache in a clinic sample of subjects with TS is 25.0% (39% of adults and 16% of children with TS), which suggests nearly a 4-fold increase over the frequency of migraines reported in a comparable sample group of otherwise healthy individuals\(^{10-13}\) (Table 2). Although these findings are comparable to those of Barabas\(^{8,9}\) and colleagues, who reported a frequency of 27% of migraines in their TS sample, our results must be interpreted cautiously because we used reported control data on the frequency of headaches collected from the general population rather than from a specialty clinic.\(^{10-14}\) Control data from an age-matched group to assess the prevalence of migraines in a sample group with other neurological dis-
orders are being collected. Although other types of headache, including tension, sinus, and medication-related headaches, were reported in our TS sample, the objective of the questionnaire was to diagnose migraine headache.

A primary defect in serotonin metabolism has been proposed for TS and migraine.25,26 Serotonin abnormalities have been suggested in OCD, a hypothesis supported by marked improvement of OCD symptoms with selective serotonin reuptake inhibitors.27 In TS patients, cerebrospinal fluid studies28 have shown reduced levels of 5-hydroxyindoleacetic acid and tryptophan in the basal ganglia, decreased plasma tryptophan levels, and decreased 24-hour serotonin excretion and whole-blood serotonin. However, in contrast to the Barabas et al8 pilot study, our study showed that TS patients with migraines did not have significantly greater obsessive-compulsive features. While 96% of TS patients with migraines had obsessive-compulsive traits, the frequency of these traits in our sample of TS subjects without migraines was also high (88%) (Table 1), indicating that obsessive-compulsive traits are not a predictor of migraine headache. Other biochemical abnormalities have been proposed in TS, including involvement of the cholinergic, dopaminergic, GABAergic, noradrenergic, and opioid systems.29,30 In migraines, mutations in genes involving calcium channels, mitochondrial DNA, dopamine receptors, and prothrombic risk factors have also been detected.31,32

Although genetic linkage analyses have excluded 5-hydroxytryptamine receptor genes in the TS population,19,33 until the TS gene is located, it is unknown whether migraine, TS, obsessive-compulsive traits, and other comorbidities are genetically linked. To our knowledge, our study is the first to support a possible genetic marker for this complex genetic disorder.

Table 2. Comparison of Migraine Studies in TS and Non-TS Populations

<table>
<thead>
<tr>
<th>Source</th>
<th>Sample Size</th>
<th>Prevalence of Migraine, %</th>
<th>Male-Female Ratio</th>
<th>Age at Onset, y</th>
<th>Family History (First-degree Relative), %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present study</td>
<td>100</td>
<td>25</td>
<td>3:1</td>
<td>14.4 ± 7.8</td>
<td>56</td>
</tr>
<tr>
<td>Barabas et al,8 1985</td>
<td>65†</td>
<td>27</td>
<td>NR</td>
<td>14.0 ± 8.9</td>
<td>NR</td>
</tr>
<tr>
<td>Barabas et al,8 1985</td>
<td>60</td>
<td>27</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Mavromichalis et al,29 1999</td>
<td>4000</td>
<td>6.2</td>
<td>1:4</td>
<td>5.0</td>
<td>61</td>
</tr>
<tr>
<td>Aromaa et al,13 1998</td>
<td>968</td>
<td>6.0</td>
<td>NR</td>
<td>4.0†</td>
<td>61</td>
</tr>
<tr>
<td>Metsahonkala et al,35 1997</td>
<td>3580</td>
<td>2.7</td>
<td>NR</td>
<td>8.5†</td>
<td>NR</td>
</tr>
</tbody>
</table>

Abbreviations: NR, not reported; TS, Tourette syndrome.
*Data are given as mean or mean ± SD.
†Five patients were added to the original study of Barabas et al.8
‡Unspecified sex.

However, must be interpreted cautiously, because the reported risk in the general population for migraine headache if one parent is affected is high for the offspring.

A recent review on migraine headache in patients with psychiatric disorders concluded an association between affective disorders, particularly anxiety and depression. Further studies should investigate whether TS subjects with migraines also have an increased prevalence of anxiety, depression, or other psychiatric comorbidities. Furthermore, studies should determine if TS patients with migraine respond more favorably to adjunctive therapy designed to treat TS psychiatric comorbidities, compared with those without psychiatric conditions.

In summary, TS is a spectrum disorder, with varying degrees of severity in individual patients. Because the complexity of the TS gene has yet to be determined, the presence of migraine headache, if present also in family members of patients with TS, may be used as a clinical marker for this complex genetic disorder.

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Author contributions: Study concept and design (Ms Kwak and Dr Jankovic); acquisition of data (Dr Jankovic); analysis and interpretation of data (Mr Vuong and Dr Jankovic); drafting of the manuscript (Ms Kwak and Dr Jankovic); critical revision of the manuscript for important intellectual content (Mr Vuong); statistical expertise (Mr Vuong); study supervision (Ms Kwak and Dr Jankovic).

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