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Association of headache with childhood adversity and mental disorder: cross-national study

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Background
Community studies about the association of headache with both childhood family adversities and depression/anxiety disorders are limited.

Aims
To assess the independent and joint associations of childhood family adversities and early-onset depression and anxiety disorders with risks of adult-onset headache.

Method
Data were pooled from cross-sectional community surveys conducted in ten Latin and North American, European and Asian countries (n=18,303) by using standardised instruments. Headache and a range of childhood family adversities were assessed by self-report.

Results
The number of childhood family adversities was associated with adult-onset headache after adjusting for gender, age, country and early-onset depression/anxiety disorder status (for one adversity, hazard ratio (HR)=1.22–1.6; for two adversities, HR=1.19–1.67; for three or more adversities, HR=1.37–1.95). Early and current onset of depression/anxiety disorders were independently associated (HR=1.42–1.89) with adult-onset headache after controlling for number of childhood family adversities.

Conclusions
The findings call for a broad developmental perspective concerning risk factors for development of headache.

Declaration of interest
None. Funding detailed in Acknowledgements.
was not made if the respondent indicated that the episode of depression or anxiety symptoms was due to physical illness or injury or use of medication, drugs or alcohol.

This paper includes anxiety disorders (generalised anxiety disorder, panic disorder and/or agoraphobia, post-traumatic stress disorder and social phobia) and major depressive episode, which occurred in the previous 12 months and before age 21 years. Depression and anxiety disorders were aggregated into a single category, on the basis of prior findings from the WMH surveys that anxiety disorders and major depression have independent associations of a comparable magnitude with headache and with other chronic physical conditions.

Headache

Severe headache was ascertained as part of a chronic physical disorder checklist, of the kind commonly used in national health surveys. Respondents were asked whether they had ever had frequent or severe headache in the previous 12 months. Prior research has demonstrated reasonable correspondence between self-reported chronic conditions (e.g. diabetes, heart disease and headache) and records of general practitioners, but lifetime history of severe headache is subject to recall bias. Although we assessed whether recall bias associated with current depression or anxiety disorder influenced the association of childhood family adversities with adult onset of frequent or severe headaches, the problem of retrospective recall may admittedly remain.

Childhood family adversities

The following kinds of childhood family adversities were included in the present study: physical abuse, sexual abuse, neglect, parental death, parental divorce, other parental loss, parental mental disorder, parental substance misuse, parental criminal behaviour, family violence and family economic adversity. Those respondents who met the criteria specified for a given adversity before the age of 18 years were coded as having experienced childhood family adversity (online Appendix DS1).

Training and field procedures

Experienced CIDI trainers in the USA trained bilingual supervisors in each country. The WHO translation protocol was used to translate instruments and training materials. Some surveys were carried out in bilingual form (Belgium). Other surveys were carried out exclusively in the country’s official language. Persons who could not speak these languages were excluded. Quality control protocols, described in more detail elsewhere, were standardised across countries to check on interviewer accuracy and to specify data cleaning and coding procedures. The institutional review board of the organisation that coordinated the survey in each country approved and monitored compliance with procedures for obtaining informed consent and protecting participants.

Statistical analysis

The association of childhood family adversities and early-onset mental disorders with adult-onset frequent or severe headache was studied with discrete-time survival analyses, using retrospectively reported age at onset of headache (reported in whole years). The start of the period at risk of adult-onset headache was set at age 21 years. Persons who reported that frequent or severe headache developed before age 21 were excluded.

Cox proportional hazards models were constructed to estimate risk of adult-onset headache as a function of number and type of childhood family adversities and early-onset depression/anxiety disorder status while adjusting for potential confounders (gender, current age and smoking). Country was included in the analyses as a stratifying variable, which allowed each country to have a unique hazard function. This was necessary because of large differences in prevalence rates of childhood family adversities, mental disorders and chronic physical disorders between countries, and to allow for the slight differences in measurement of childhood family adversities among countries (e.g. data from European countries did not include childhood neglect or parental divorce).

In the Cox proportional hazard regression analyses, time to age at onset of headache from age 20 was the dependent variable. Persons who had not developed headache were censored at their current age. The associations are expressed as hazard ratios measuring relative risk. Childhood family adversities were analysed in four categories of number of adversities (none, 1, 2, 3+), with no adversities as the reference group. Childhood family adversities and early-onset mental disorders were included in the models both separately and simultaneously.

To account for the possibility of differential recall of childhood family adversities among those with a current depressive or anxiety disorder, we performed an additional analysis that adjusted for current (12-month) depression or anxiety disorder. We also performed an additional analysis adjusting for educational attainment. Because the inclusion of education in the models made virtually no difference in results, we report results unadjusted for education (detailed information on education was not collected in France, so to have reported all results adjusted for education would also have meant excluding France from analysis). We screened for interaction of childhood family adversities with early-onset depression/anxiety disorder in predicting headache onset, but the interaction was non-significant so only main effects are reported in this paper.

Ninety-five per cent confidence intervals were calculated for all hazard ratios. Statistical significance level was set at 0.05 for a two-sided test. The analyses were performed using the SURVIVAL procedure in SUDAAN (version 9.0.1, SAS–Windows) statistical software to account for the complex sample design. In all multivariate models, a complete-case approach was used, but the WMH survey used multiple imputation methods to impute missing values for the childhood family adversities. The survival analyses employed sample weights to adjust for differences in probability of selection. The unadjusted cumulative percentage with adult onset of frequent or severe headache by age for persons with v. without early-onset depression/anxiety disorder, and for persons with 0, 1 or 2+ childhood family adversities were graphed with product-limit (Kaplan–Meier) life-table estimates developed using SAS PROC LIFETEST (version 9.1.3, Windows).

Results

Overall, 11.3% of the population had headache and 9.1% had early-onset depression/anxiety disorder. Childhood family adversities were common (43.2%) (Table 1). The prevalence of frequent or severe headache varied; the lowest rate was in Japan (5.9%) and the highest rate was in Colombia (17.5%). Early-onset mental disorder was most common in the USA (17.3%) and least common in Japan (2.2%). Childhood family adversities were most common in Colombia (64.5%) and least common in Spain (28.5%). Among the different types of childhood family adversities, parental death during childhood was generally the most common form (12.9% of the study population experienced this adversity in childhood).
In the proportional hazard analyses of the association of number of childhood family adversities with headache, a linear relationship was found. That is, those with three or more types of childhood family adversities were at higher risk of adult-onset headache than those with one or two adversities (Table 2, model A). This was true for the analysis controlling for depression/anxiety disorders present in the previous year (Table 2, model B) as well as for the analysis controlling for onset of depression/anxiety disorders before age 21 (Table 2, model C). Early-onset depression/anxiety disorders were also associated with increased risk of adult-onset headache after controlling for the number of childhood family adversities. Female gender and higher age were associated with increased risk of adult-onset headache in all models.

When each childhood adversity was considered independently in separate models controlling for gender and age (with stratification by country), we found that sexual abuse, physical abuse, parental mental and substance use disorders, criminal behaviour in family, parental mental disorder and substance use disorder.

<table>
<thead>
<tr>
<th>Country</th>
<th>Sample size</th>
<th>Age, years Mean (s.d.)</th>
<th>Headache %</th>
<th>Any childhood family adversities %</th>
<th>Early onset of any depression/anxiety disorders %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Belgium</td>
<td>916</td>
<td>48.8 (16.81)</td>
<td>9.5</td>
<td>32.9</td>
<td>5.2</td>
</tr>
<tr>
<td>Colombia</td>
<td>1790</td>
<td>39.2 (12.25)</td>
<td>17.5</td>
<td>64.5</td>
<td>9.0</td>
</tr>
<tr>
<td>France</td>
<td>1172</td>
<td>48.3 (16.74)</td>
<td>11.9</td>
<td>39.8</td>
<td>10.0</td>
</tr>
<tr>
<td>Germany</td>
<td>1150</td>
<td>49.1 (17.65)</td>
<td>9.9</td>
<td>31.2</td>
<td>4.6</td>
</tr>
<tr>
<td>Italy</td>
<td>1502</td>
<td>48.9 (17.71)</td>
<td>7.5</td>
<td>28.8</td>
<td>4.2</td>
</tr>
<tr>
<td>Japan</td>
<td>820</td>
<td>52.6 (17.79)</td>
<td>5.9</td>
<td>34.1</td>
<td>2.2</td>
</tr>
<tr>
<td>Mexico</td>
<td>1893</td>
<td>37.9 (12.19)</td>
<td>11.0</td>
<td>53.7</td>
<td>5.7</td>
</tr>
<tr>
<td>The Netherlands</td>
<td>945</td>
<td>47.3 (16.04)</td>
<td>9.9</td>
<td>37.5</td>
<td>7.2</td>
</tr>
<tr>
<td>Spain</td>
<td>1817</td>
<td>47.2 (18.07)</td>
<td>8.4</td>
<td>28.5</td>
<td>3.7</td>
</tr>
<tr>
<td>US</td>
<td>4550</td>
<td>47.9 (17.29)</td>
<td>13.1</td>
<td>49.3</td>
<td>17.3</td>
</tr>
<tr>
<td>Total</td>
<td>16555</td>
<td>46.2 (16.9)</td>
<td>11.3</td>
<td>43.2</td>
<td>9.1</td>
</tr>
</tbody>
</table>

a. Childhood family adversities included neglect, physical abuse, sexual abuse, parental death, parental divorce, other loss of parent during childhood, family economic adversity, violence in family, criminal behaviour in family, parental mental disorder and substance use disorder.

b. Assessed early-onset (before age 21 years) disorders include major depressive episode, generalised anxiety disorder, post-traumatic stress disorder, social phobia, panic disorder and agoraphobia.

We assessed the interaction of early-onset depression/anxiety disorders and having one or more childhood family adversities, adjusting for gender and age with stratification by country. The interaction of childhood adversity and early-onset depression/anxiety disorders was non-significant (results not shown), so there was no evidence of a synergistic effect of childhood adversity and early-onset mental disorder on risks of adult-onset headache.

Figure 1 shows the cumulative percentage by age for adult-onset headache among respondents with early-onset depression/anxiety disorders v. those without. Both curves were steeper for early adulthood as more than half of adult-onset headaches occurred between ages 21 and 40. The rate of increase and cumulative occurrence of headache were greater for those with early-onset depression/anxiety disorders than those without. As shown in Fig. 2, increase in the number of childhood family adversities was also associated with increase in the cumulative occurrence of headache. The rate of increase was similar initially for those with any number of adversities, but for those who had had more childhood family adversities it increased at a higher rate from age 30 onwards. Thus, as the respondents aged, the presence of multiple childhood family adversities was associated with a greater likelihood of headache onset.
Childhood family adversities are independently associated with adult-onset frequent or severe headache. This association was strongest for persons with three or more childhood family adversities in our study. Early-onset mental disorders and family antisocial behaviours showed the most robust associations with risk of adult-onset headache. Parental death, divorce, and economic adversity were not significantly related. This is different from a previous case–control study, which found significant associations between migraine and parental divorce and chronic financial difficulties in the family after adjustment for education, self-reported general physical health, and depression. Sexual abuse and physical abuse have been the most frequently studied childhood family adversities in relation to adult headache disorders. Our study confirmed previous research showing an association between childhood abuse and headache. Additionally, the association remained significant when early-onset mental disorders were included in the analysis. This is in keeping with studies showing that headache was associated with childhood family adversities after controlling for depression and mental disorders in general.

### Limitations

Our study has several significant limitations relevant to interpretation of its results. Although we used age-at-onset data for childhood family adversities and adult-onset headache to assess temporal ordering, the cross-sectional methodology used imposed a significant shortcoming. Since lifetime history of frequent or severe headache and of childhood family adversities were both ascertained by retrospective self-report, there were multiple opportunities for recall bias to affect both in a similar fashion, thereby introducing spurious correlation. We sought to control this potential bias by carrying out an analysis which controlled for current depression and anxiety disorder. This analysis yielded similar results to analyses which did not control for current mental disorder. None the less, the potential for recall bias to influence the results reported here cannot be excluded, especially for childhood family adversities. Although a

### Discussion

#### Types of association

Because of evidence of clustering of childhood adversities in previous studies of the association between such adversities and mental disorders, we assessed a broad range of childhood family adversities in our study. Early-onset mental disorders and childhood family adversities were independently associated with adult-onset frequent or severe headache. This association was strongest for persons with three or more childhood family adversities. This finding is the first of its kind to show in a large cross-national community sample that the association between childhood family adversities and adult onset of headache is independent of mental disorders. Although mental disorder was still independently associated with headache, distinct associations of both types of predictors with headache have not been demonstrated in previous studies.

In our analyses that decomposed the association of specific childhood family adversities with headache risks, not all the childhood family adversities were found to predict increased risk. Sexual and physical abuse, parental mental and substance disorders and family antisocial behaviours showed the most robust associations with risk of adult-onset headache. Parental death, divorce, and economic adversity were not significantly related. This is different from a previous case–control study, which found significant associations between migraine and parental divorce and chronic financial difficulties in the family after adjustment for education, self-reported general physical health, and depression.

Sexual abuse and physical abuse have been the most frequently studied childhood family adversities in relation to adult headache disorders. Our study confirmed previous research showing an association between childhood abuse and headache. Additionally, the association remained significant when early-onset mental disorders were included in the analysis. This is in keeping with studies showing that headache was associated with childhood family adversities after controlling for depression and mental disorders in general.

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**Table 3** Hazard ratios for the association of specific childhood adversity as independent predictor of adult onset of frequent or severe headache

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Hazard ratios</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Childhood family adversities</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sexual abuse</td>
<td>1.73***</td>
<td>1.38–2.17</td>
</tr>
<tr>
<td>Physical abuse</td>
<td>1.64***</td>
<td>1.44–1.88</td>
</tr>
<tr>
<td>Parental mental disorder</td>
<td>1.52***</td>
<td>1.25–1.83</td>
</tr>
<tr>
<td>Family violence</td>
<td>1.51***</td>
<td>1.30–1.76</td>
</tr>
<tr>
<td>Criminal behaviour in family</td>
<td>1.44**</td>
<td>1.10–1.18</td>
</tr>
<tr>
<td>Parental substance use disorder</td>
<td>1.42***</td>
<td>1.18–1.71</td>
</tr>
<tr>
<td>Other loss of parent during childhood</td>
<td>1.29*</td>
<td>1.06–1.58</td>
</tr>
<tr>
<td>Neglectc</td>
<td>1.21*</td>
<td>1.02–1.43</td>
</tr>
<tr>
<td>Economic adversity</td>
<td>1.21</td>
<td>0.98–1.48</td>
</tr>
<tr>
<td>Parental death</td>
<td>1.10</td>
<td>0.93–1.31</td>
</tr>
<tr>
<td>Parental divorcec</td>
<td>1.01</td>
<td>0.84–1.22</td>
</tr>
<tr>
<td>Depression/anxiety disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Panic/agoraphobia</td>
<td>1.76***</td>
<td>1.37–2.25</td>
</tr>
<tr>
<td>Major depressive episode</td>
<td>1.68***</td>
<td>1.40–2.03</td>
</tr>
<tr>
<td>Generalised anxiety disorder</td>
<td>1.65***</td>
<td>1.32–2.06</td>
</tr>
<tr>
<td>Post-traumatic stress disorder</td>
<td>1.65**</td>
<td>1.19–2.30</td>
</tr>
<tr>
<td>Social phobia</td>
<td>1.61***</td>
<td>1.35–1.91</td>
</tr>
</tbody>
</table>

---

**Fig. 1** Kaplan–Meier curve for adult-onset headache by age for persons with none, one, and two or more childhood family adversities.

**Fig. 2** Kaplan–Meier curve for the cumulative percentage of frequent or severe headache by age for persons with none, one, and two or more childhood family adversities.
comprehensive review indicates that adult retrospective reports of adverse childhood experiences have a worthwhile place in research, substantial false negatives and measurement errors remain possible.19,20 Prospective research that encompasses corroborative tools of assessment of childhood adversities is needed to address this methodological weakness of our study. We also have not tackled the potentially different meaning and impact of childhood adversity across the participating countries. Parental divorce, for example, may exert dissimilar impact on individuals who grow up in countries with different social and religious attitudes towards broken families. Likewise, the impact of family economic adversity or parental death may vary according to the quality of social service available in a country. These and other cultural differences need to be examined in future country-specific analyses that take social context into account. Regarding the assessment of headache, it was based on a question about history of frequent or severe headache, so that information about the subtypes, chronicity and frequency of attacks of headache was lacking. Consequently, our findings may not be readily compared with research that focused on specific types of headache, especially migraine, which may differ from other kinds of chronic headache in etiology and the association with depression and childhood family adversities.1,20

A broad developmental perspective

Recognising the limitations of this research, our results suggest that childhood family adversities may predispose individuals to adult-onset headache via mechanisms in addition to Axis I psychopathology. Prior research has found that inadequate coping style and maladaptive personality factors are observed among people who have experienced childhood family adversities.21–23 Neuroimaging studies indicate that the brain areas activated during distress caused by social adversities such as exclusion are also activated during physical pain.24 However, it should be noted that our analyses did not identify interaction or synergistic effects of the number of childhood family adversities with the presence of early-onset depression/anxiety disorder.

In summary, this research found that the association of risk of developing headache was independently associated with both number of childhood family adversities and the presence of early-onset depression/anxiety disorder. Although the aetiology of headache remains poorly understood, these results suggest that a broad developmental perspective concerning risk factors for development of severe or frequent headache may be needed to understand how life stressors influence risk in combination with depression and anxiety disorders.

Acknowledgements

The surveys discussed in this article were carried out in conjunction with the World Health Organization’s World Mental Health (WMH) Survey Initiative. The WHO commissioned the WMH staff for assistance with instrumentation, fieldwork, and data analysis. These activities were supported by the US National Institute of Mental Health (R01-MH70884), the John D. and Catherine T. MacArthur Foundation, the Pfizer Foundation, the US Public Health Service (R13-MH06649, R01-MH63964 and R01-DA016558), the Fogarty International Center (FIRCA R01-TW00481), the Pan American Health Organization, Eli Lilly & Co, Ortho-McNeil Pharmaceutical Inc, GlaxoSmithKline, and Bristol-Myers Squibb. A complete list of WMH publications can be found at www.hcp.med.harvard.edu/wmhv. The Colombian National Study of Mental Health is supported by the Ministry of Social Protection. The ESPIMO project is funded by the European Commission (Contracts QLG5-1999-0734; SANCO 200014123, the Piedmont Region (Italy), Fondo de Investigación Sanitaria, Instituto de Salud Carlos III, Spain (PIF 00009208), Ministerio de Ciencia y Tecnología, Spain (SAF 2002-15836-C02-01), Department of Salud, Generalitat de Catalunya, Spain (ICERB 0260/0046, RETICS R062-KID), other local agencies, and by an unrestricted educational grant from GlaxoSmithKline. The World Mental Health Japan Survey is supported by the Grant for Research on Psychiatric and Neurological Diseases and Mental Health (H13-SHOGA-023, H14-TOKUBETSU-026, H16-KOKORO-013) from the Japan Ministry of Health, Labour and Welfare. The Mexican National Comorbidity Survey is supported by the National Institute of Psychiatry Ramón de la Fuente (INPRIMED2X 42B63) and by the National Council on Science and Technology (CONACyT) G30544-H, with supplemental support from the Pan American Health Organization. The US National Comorbidity Survey Replication is supported by the National Institute of Mental Health (DA164229) with supplemental support from the National Institute of Drug Abuse, the Substance Abuse and Mental Health Services Administration, the Robert Wood Johnson Foundation (Grant 044730), and the John W. Alden Trust.

References


Look into my eyes

Peter Byrne

When Freud abandoned hypnosis as a means of accessing the unconscious in 1909, he forgot to tell the motion picture industry. The evil mesmerist became the regular villain of one-reelers of early cinema. Hypnosis signified loss of control, its dark powers preying upon the innocent. It could be performed by ‘foreigners’ such as Dr Fu Manchu (in over 15 films), but most hypnotists were well-heeled professionals. Any dramatic impact of the unmasking of these charlatans was heightened by giving them trusted medical status. The crossover with psychiatry was established early: Dr Mabuse from Dr Mabuse the Gambler (1922, six remakes) is credited as cinema’s first psychoanalyst. Hypnotists stole and defrauded (The Magician, 1926), but ‘taking advantage of the ladies’ was their central activity, beginning with Under the Hypnotist’s Influence (1897). Cabinet of Dr Caligari (Germany, 1919; pictured) was at once a horror show and Nazi metaphor – the director spiked it with verbatim quotes from Mein Kampf. The Nazis’ detestation of both this film (banned as ‘degenerate art’) and psychiatry are documented elsewhere. In the decade ending 1939, three-quarters of screen hypnotists were either evil or mad, and mostly both. Though hypnosis helped Fred Astaire’s love life and dancing in Carefree (1938), it framed an innocent woman in Whirlpool (1949) and facilitated low espionage in Masterplan (1955) and The Manchurian Candidate (1962).

Given this popularity and its appearance in children’s animation, Jungle Book (1967) and Robin Hood (1973), hypnosis is probably the most (mis)represented of all ‘psychiatric treatments’ on film. It remains a popular narrative ploy, mostly in thrillers – Dead Again (1991) and the Bourne trilogy (2002–07) – where no smart money is bet on the integrity of the hypnotist. In Stir of Echoes (1999) and countless dissociative identity disorder films, hypnosis is the catalyst for libidinous mayhem. Movie hypnosis is seldom used for good (Inner Sanctum/Calling Dr Death 1943) – as with the television news maxim, ‘if it bleeds, it leads’. Its power is ferocious – in Silence of the Lambs (1991), psychiatrist Hannibal Lecter is able to induce suicide in a detested fellow prisoner whom he cannot see, separated by several layers of bars and glass. Go figure.