

Research Submission

Childhood Maltreatment and Migraine (Part III). Association With Comorbid Pain Conditions

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Objective.—To evaluate in a headache clinic population the relationship of childhood maltreatment on the prevalence of pain conditions comorbid with migraine.

Background.—Childhood maltreatment is highly prevalent and has been frequently associated with recurrent headache. The relationship of maltreatment and pain has, however, been a subject of some debate.

Methods.—Cross-sectional data on self-reported physician-diagnosed pain conditions were electronically collected from persons with migraine (diagnosed according to International Classification of Headache Disorders-2), seeking treatment in headache clinics at 11 centers across the US and Canada. These included irritable bowel syndrome (IBS), chronic fatigue syndrome (CFS), fibromyalgia (FM), interstitial cystitis (IC), arthritis, endometriosis, and uterine fibroids. Other information included demographics, migraine characteristics (frequency, headache-related disability), remote and current depression (The Patient Health Questionnaire-9), and remote and current anxiety (The Beck Anxiety Inventory). Patients also completed the Childhood Trauma Questionnaire regarding sexual, emotional, and physical abuse, and emotional and physical neglect under the age of 18 years old. Statistical analyses accounted for the survey design and appropriate procedures in SAS such as *surveymeans*, *surveyfreq*, and *surveylogistic* were applied to the weighted data.

Results.—A total of 1348 migraineurs (88% women) were included in this study (mean age 41 years). Based on physician diagnosis or validated criteria, 31% had IBS, 16% had CFS, and 10% had FM. Diagnosis of IC was reported by 6.5%, arthritis by 25%, and in women, endometriosis was reported by 15% and uterine fibroids by 14%. At least 1 comorbid pain condition was reported by 61%, 2 conditions by 18%, and 3 or more by 13%. Childhood maltreatment was reported by 58% of the patients. Emotional abuse was associated with increased prevalence of IBS, CFS, arthritis, and physical neglect with arthritis. In women, physical abuse was associated with endometriosis and physical neglect with uterine fibroids. Emotional abuse, and physical abuse and neglect ($P < .0001$ for all) were also associated with increased total number of comorbid conditions. In ordinal logistic regression models, adjusted for sociodemographics and current depression (prevalence 28%) and anxiety (prevalence 56%), emotional abuse (odds ratios [OR] = 1.69, 95% confidence intervals [CI]: 1.224-2.33) and physical neglect

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(OR = 1.73, 95% CI: 1.22-2.46) were independently associated with an increased number of pain conditions. The cohort of women, similarly, had associations of emotional abuse (OR = 1.94, 95% CI: 1.40-2.72) and physical neglect (OR = 1.90, 95% CI: 1.34-2.68) with an increased number of pain comorbidities.

Conclusion.—The association of childhood maltreatment and pain was stronger in those reporting multiple pain conditions and multiple maltreatment types. This finding suggests that in migraineurs childhood maltreatment may be a risk factor for development of comorbid pain disorders.

Key words: comorbid pain, migraine, childhood maltreatment

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Childhood maltreatment is prevalent, particularly in clinic populations, and has been associated with a wide range of adult psychiatric and physical disorders.¹⁻⁵ Many studies have focused on the relationship of abuse with depression and anxiety, 2 conditions strongly associated with painful conditions,⁶ including migraine.⁷ Although there are scant data on migraine per se, both population- and clinic-based studies have demonstrated an association of childhood abuse and recurrent headache.⁸⁻¹¹ However, the relationship of childhood maltreatment and chronic pain conditions remains a subject of considerable debate.^{1,12,13}

In our earlier multicenter clinic survey of women with migraine, those with a history of childhood abuse reported more severe headaches, more depression, and more somatic symptoms.¹⁴ Many of the somatic symptoms were pain-related (limb, joints, abdominal, headache, back, chest, and genital) and some symptom combinations suggested common syndromic disorders (irritable bowel, chronic fatigue, and fibromyalgia [FM]) that are recognized as comorbid with migraine.¹⁵ We found the abuse-somatic symptom association was stronger in the cohort with major depression, yet depression did not fully mediate the relationship. A smaller retrospective chart review study of migraine patients identified distinct groups based on cluster analysis of comorbid pain conditions.¹⁶ Those with the constellation defined by depression, anxiety, and FM also reported more sexual, physical and, in particular, emotional abuse than the cluster with no comorbidity, despite similar demographic profiles. In this current migraine clinic cohort, we report in Part I that 58% have reported some type of childhood maltreatment, and that each type of abuse (sexual, physical, emotional)

and neglect (physical and emotional) was strongly associated with depression and anxiety.¹⁷ Childhood emotional abuse was most prevalent, and it was associated with chronic headache frequency and transformed migraine, even when controlling for depression and anxiety. The literature suggests that chronic daily headache and transformed migraine are associated with other painful conditions.¹⁸

Our objectives in this paper were to assess in a clinic-based population with migraine the relationships of different types of childhood abuse and neglect to comorbid pain conditions. Because childhood maltreatment is also associated with depression and anxiety, which in turn are associated with pain, the influence of these psychiatric conditions on the relationship between maltreatment and migraine comorbidities was examined.

METHODS

Patient Selection and Data Collection.—This multicenter study was conducted by the members of the Women's Issues Section research consortium of the American Headache Society. The recruitment of the cross-sectional survey of headache clinic patients occurred between February 2006 and June 2008 at 11 outpatient headache centers, after each center separately obtained approval from the Institutional Review Boards (IRB). Participants included adult men and women with primary headache disorder as defined by the International Classification of Headache Disorders (ICHD)-2 criteria,¹⁹ who were able to complete an electronic questionnaire. Full details of inclusion/exclusion criteria, and data collection are included in Part I of this study.¹⁷

Measures.—*Childhood Abuse and Neglect.*—In this study, maltreatment exposure occurring in childhood

was assessed using the Childhood Trauma Questionnaire (CTQ).^{20,21} This questionnaire is a 28-item self-reported quantitative measure that provides brief, reliable, and valid screening for history of childhood abuse (physical, sexual, and emotional) and neglect (physical and emotional). Details on the CTQ measure, prevalence of childhood abuse and neglect, correlation between the different categories of abuse and neglect, and the relationship with depression and anxiety in this study population are discussed in Part I of this article.¹⁷

Comorbid Conditions.—Self-reported physician-diagnosed history of comorbid pain conditions such as irritable bowel syndrome (IBS), chronic fatigue syndrome (CFS), FM, interstitial cystitis (IC), arthritis, (in women: endometriosis [EM], uterine fibroids, and pelvic pain and cramps during or between menstrual periods) was recorded on the survey. Additionally for IBS, CFS, and FM a positive screen with the validated instrument was also considered as presence of the condition. Validated questions defined by the Rome II criteria (Rome Foundation, Inc., McLean, VA, USA) for the diagnosis of IBS were used.^{22,23} Criteria established by the U.S. Centers for Disease Control and Prevention (CDC, Atlanta, GA, USA) were used for a likely diagnosis of CFS. The American College of Rheumatology (ACR) criteria²⁴ for the diagnosis of FM was used in this study, including a history of widespread pain plus pain at 11 of the 18 tender point sites as recorded by the examining physician at the end of the survey. In women, EM was based on self-reported physician diagnosis. For the purpose of final analyses respondents were classified as “cases with comorbidities” based on self-reported physician diagnoses, or validated criteria for the comorbidity, or both.

Depression.—The Patient Health Questionnaire (PHQ-9) is a self-reported diagnostic and severity measure for current depression (in the prior 2 weeks) using criteria from the Diagnostic and Statistical Manual of Mental Disorders (DSM) IV.²⁵ In this study, participants with PHQ-9 score >10 were considered positive for current depression.

Anxiety.—The Beck Anxiety Inventory (BAI) was in this study to assess the severity of patient anxiety. The questionnaire consists of both physi-

ological and cognitive components of anxiety addressed in the 21 items describing subjective, somatic, or panic-related symptoms.²⁶ In this study, participants with BAI score ≥ 8 were considered positive for current anxiety.

Statistical Analysis.—All statistical analyses in this study were performed using SAS version 9.1 (SAS Institute, Inc., Cary, NC, USA) and described in detail in Part I.¹⁷ An ordinal logistic regression models (CLOGIT) was used to examine the relationship between comorbid pain conditions and childhood abuse and neglect. In this model the dependent variable was number of comorbid conditions defined as 0, 1, 2, ≥ 3 conditions. In a separate model restricted to women, the dependent variable was defined as 0, 1, 2, 3, ≥ 4 conditions. Both models were adjusted for age, race, education, household income, and current depression and anxiety. Adjusted odds ratios (ORs) and 95% confidence intervals (CI) were used to measure the strength of the relationships, and the significance of the ORs was examined using Wald's χ^2 test statistic.

RESULTS

A total of 1348 patients who received a diagnosis of migraine completed the surveys. The ICHD-2 diagnosis and characteristics of the study population are presented in Table 1. Additional characteristics of the study population are available in Table 1 of Part I and II of this study. In brief, a diagnosis of migraine with aura was recorded in 40% of the participants. The majority of the participants were women (88%) and the average age of the participants in this study was 41 years. Thirty-four percent of all participants reported chronic migraine (frequency ≥ 15 days/month). Three-quarters of the chronic headache sufferers reported a transformation from episodic to chronic headache (26% of total study population). Prevalence of current depression was 28% and anxiety was 56%. Frequencies of self-reported physician diagnoses of comorbid pain conditions ranged from 25% for arthritis to 5% for CFS. Additional diagnosis based on validated criteria was also reported for conditions of IBS, FM, and CFS (Table 1). Thirty-one percent ($n = 411$) of the study population had IBS based on physician diagnosis or validated criteria,

Table 1.—Characteristics and Prevalence of Comorbid Pain Conditions in the Study Population

	n (%)†
International Headache Society Diagnosis (ICHD-II)	
Migraine (1.0)	1348 (100)
Migraine with aura (1.2)	543 (40)
Migraine without aura (1.1)	805 (60)
Gender	
Male : female	161 (12) : 1187 (88)
Age, years (mean ± SE)	41 ± 0.4
Headache frequency, days (mean ± SE)	14 ± 0.7
Chronic (≥15 days/month)	458 (34)
Transformed migraine	356 (26)
Current depression	381 (28)
Current anxiety	761 (56)
Irritable bowel syndrome	
Self-reported physician diagnosis	315 (23)
Rome II criteria	176 (13)
Either self-report or Rome II based or both	411 (31)
Fibromyalgia	
Self-report	130 (10)
ACR criteria	
Widespread pain	263 (19)
Tender points	90 (7)
Both	44 (3)
Either self-report or ACR-based or both	133 (10)
Chronic fatigue syndrome	
Self-reported physician diagnosis	65 (5)
CDC criteria	178 (13)
Either self-report or CDC based or both	219 (16)
Interstitial cystitis‡	85 (6.5)
Arthritis‡	338 (25)
Endometriosis‡§	177 (15)
Leiomyoma uteri (Fibroids)‡§	163 (14)

†Values may not add to the total due to missing or unavailable information (see *Methods*).

‡Self-reported physician diagnosis.

§In women sub-population (n = 1187).

ACR = American College of Rheumatology; ICHD = International Classification of Headache Disorder.

16% (n = 219) had CFS, and 10% (n = 133) had FM. Childhood trauma, either abuse or neglect, was reported by 58% of the study population (n = 781). Physical abuse was reported by 21%, sexual abuse by 25%, emotional abuse by 38%, physical neglect by 22%, and emotional neglect by 38% of the study population.

Table 2 shows the differences in the prevalence of comorbid pain conditions based on the reports of

childhood abuse and neglect. For IBS, FM, and CFS, a self-reported physician diagnosis or validated positive criteria, or both, was considered as presence of the condition. Due to testing of multiple hypotheses, only associations reported in Table 2 with $P < .01$ should be viewed as significant. Persons with childhood physical abuse had a higher prevalence of arthritis ($\chi^2 = 9.93$, $P = .002$). Emotional abuse was associated with a higher prevalence of IBS ($\chi^2 = 16.65$, $P < .001$), FM ($\chi^2 = 18.76$, $P < .001$), CFS ($\chi^2 = 26.27$, $P < .001$), and arthritis ($\chi^2 = 16.04$, $P < .001$). Physical neglect was associated with higher prevalence of IBS ($\chi^2 = 6.90$, $P = .009$), CFS ($\chi^2 = 16.63$, $P < .001$), IC ($\chi^2 = 6.90$, $P = .009$), and arthritis ($\chi^2 = 9.36$, $P = .002$). In women, physical abuse was associated with EM ($\chi^2 = 12.02$, $P = .0015$) and uterine fibroids ($\chi^2 = 11.08$, $P = .001$), emotional abuse with EM ($\chi^2 = 6.449$, $P = .011$), physical neglect with EM ($\chi^2 = 10.93$, $P = .001$), and uterine fibroids ($\chi^2 = 13.11$, $P = .001$). Emotional neglect was associated only with prevalence of uterine fibroids ($\chi^2 = 5.97$, $P = .011$).

In the study population, 61% (n = 827) had at least 1 comorbid pain condition. Eighteen percent (n = 237) had 2, and 13% (n = 171) had 3 or more pain conditions. Table 3 shows the relationship of childhood abuse and neglect with prevalence of comorbid pain conditions based on total number present. Migraineurs reporting emotional abuse or physical neglect had significantly higher number of comorbid pain conditions compared with those without these childhood trauma categories. Similarly, in the subgroup analysis of women that included conditions of EM and uterine fibroids, about 65% (n = 761) had at least 1 comorbid pain condition. Eighteen percent (n = 215) had 2, 7% (n = 83) had 3, and the remaining 7% (n = 83) had 4 or more comorbid conditions. All the 5 childhood trauma categories were significantly associated with increased number of comorbid pain conditions. In ordinal logistic regression models, adjusted for demographic variables and current depression and anxiety, emotional abuse (OR = 1.69, 95% CI: 1.22-2.33, $P = .0013$) and physical neglect (OR = 1.73, 95% CI: 1.22-2.46, $P = .0018$) were independently associated with a higher number of pain conditions. Similarly in the model restricted to women, emotional abuse (OR = 1.94, 95% CI:

Table 2.—Childhood Abuse and Neglect and Association With Comorbid Pain Conditions

Comorbid condition	Childhood abuse and neglect‡														
	Physical abuse			Sexual abuse			Emotional abuse			Physical neglect			Emotional neglect		
	Yes	No		Yes	No		Yes	No		Yes	No		Yes	No	
Irritable bowel syndrome	93 (33)	318 (30)		122 (36)**	289 (29)		188 (37)***§	223 (26)		107 (37)*§	304 (29)		166 (32)	245 (29)	
Fibromyalgia	37 (13)**	96 (9)		52 (15)***	81 (8)		73 (14)***§	60 (7)		43 (15)*§	90 (8)		63 (12)**	70 (8)	
Chronic fatigue syndrome	58 (21)**	161 (15)		76 (22)***	143 (14)		116 (23)***§	103 (12)		70 (24)***§	149 (14)		100 (20)*	119 (14)	
Interstitial cystitis	22 (8)	63 (6)		26 (8)	59 (6)		38 (8)	47 (6)		28 (10)**	57 (5)		34 (7)	51 (6)	
Arthritis	90 (32)*§	248 (23)		101 (30)**	237 (23)		158 (31)***§	180 (21)		93 (32)*§	245 (23)		153 (30)*§	185 (22)	
Endometriosis†	52 (22)*§	125 (13)		60 (19)**	117 (13)		83 (18)**	94 (13)		54 (22)*	123 (13)		70 (16)	107 (14)	
Leiomyoma uteri (Fibroids)†	48 (20)*§	115 (12)		50 (16)	113 (13)		74 (16)**	89 (12)		52 (21)***§	111 (12)		75 (17)**	88 (12)	

* $P < .01$, ** $P < .05$, *** $P < .001$.

Values reported are number (percentage) in each group of childhood trauma. Comorbid conditions based on self-reported physician diagnosis.

†In women sub-population ($n = 1187$).‡Based on Childhood Trauma Questionnaire cutoff scores for low to extreme trauma compared with none or minimal trauma (physical abuse ≥ 8 , sexual abuse ≥ 6 , emotional abuse ≥ 9 , physical neglect ≥ 8 , emotional neglect ≥ 10).§Significant after Bonferroni correction for multiple hypotheses testing ($P < .01$).

Table 3.—Childhood Abuse and Neglect and Association With Comorbid Pain Conditions

Total pain conditions	Childhood abuse and neglect†									
	Physical abuse		Sexual abuse		Emotional abuse		Physical neglect		Emotional neglect	
	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
≥3	63 (23)	108 (10)	70 (21)	101 (10)	104 (21)	67 (8)	70 (24)	101 (9)	92 (18)	79 (9)
2	51 (18)	186 (17)	57 (17)	180 (18)	142 (17)	95 (19)	50 (17)	187 (17)	84 (16)	153 (18)
1	68 (25)	351 (33)	111 (33)	308 (31)	156 (31)	263 (31)	85 (29)	334 (31)	157 (31)	262 (31)
0	96 (34)	425 (40)	100 (30)	421 (42)	152 (30)	369 (44)	86 (29)	435 (41)	178 (35)	343 (41)
χ^2, P value‡	34.07, <0.001		33.06, <0.001		55.69, <0.0001		46.25, <0.001		22.079, <0.001	

Values reported are number (percentage) in each group of childhood trauma. Comorbid conditions based on self-reported physician diagnosis or validated criteria (for irritable bowel syndrome, fibromyalgia, and chronic fatigue syndrome).

†Based on Childhood Trauma Questionnaire cutoff scores for low to extreme trauma compared with none or minimal trauma (physical abuse ≥ 8 , sexual abuse ≥ 6 , emotional abuse ≥ 9 , physical neglect ≥ 8 , emotional neglect ≥ 10).

‡From chi-square analysis (d.f. = 3).

1.39-2.71, $P = .0002$) and physical neglect (OR = 1.893, 95% CI: 1.34-2.68, $P = .0006$) were independently associated with higher number of comorbid pain conditions.

There was a weak but significant direct positive correlation ($r = 0.22, P < .001$) between the number of maltreatment types and the number of pain conditions. We had reported in Part II that emotional and physical abuse were associated with frequency >15 days per month and with transformation from episodic to chronic migraine. In this analysis, we found that those participants who reported ≥ 4 pain comorbidities were more likely to be diagnosed transformed migraine as compared with those who had 3 or fewer comorbidities ($\chi^2 = 4.64, P = .03$). As compared with those participants who had no comorbidities, the participants with pain conditions were significantly more likely to be diagnosed with chronic headaches ($P = .003, \chi^2 = 9.060$) and were significantly more likely to be diagnosed with continuous daily headaches ($P < .001, \chi^2 = 26.21$).

DISCUSSION

In this study on childhood maltreatment and adult pain, there are several novel findings. In specialty clinic patients with ICHD-2 criteria-based, physician-diagnosed migraine, both comorbid pain conditions and childhood maltreatment history were

common, reported by over half of those surveyed. Migraineurs reporting childhood emotional abuse or physical neglect had significantly higher number of comorbid pain conditions compared with those without a history of maltreatment. The associations of maltreatment and pain were independent of depression and anxiety, both of which are highly prevalent in this population.

Our findings of an abuse-pain relationship are in keeping with those from a number of studies similarly based on retrospective interviews with patients in specialty pain practices.²⁷ The possibility of selection-bias in clinic-based studies is well recognized, but several population-based samples have also found abuse-pain associations. A community sample of 3381 women, for example, found that chronic pain was significantly associated with physical but not sexual abuse.²⁸ A second smaller ($n = 649$) community-based study in men and women found a relationship between self-reports of abuse and adult pain conditions, but for sexual and not physical abuse.²⁹ In a study of sexual abuse using a random sample of students (486 men and 510 women) in Norway it was found that severity of abuse was linearly associated with pain complaints, including genital, abdominal, muscular, and head pain.³⁰ Data from a nationally representative US sample ($n = 1727$) found that those who experienced physical

and sexual abuse in childhood reported more pain.⁶ A prospective study of 422 women from the general population in Sweden found that among persons who were pain free at baseline, those reporting a history of childhood physical or sexual abuse were more likely to report pain and/or functional difficulties on follow-up evaluation than those without abuse histories.³¹ In that study there was no clear relationship between abuse and worsening pain or disability for those already reporting pain at baseline. None of these studies measured neglect or emotional abuse and neglect, and all used self-reports. There was no consistency between studies as to interview tools to measure either abuse or pain.

The reliance on self-reports of exposure to childhood abuse has called into question the validity of studies reporting abuse–pain associations. Several studies have supported the reliability of retrospective reports of abuse.^{32,33} Two population-based studies, however, which defined abuse by documentation in court records, did not find a significant association between childhood maltreatment and adult pain complaints.^{29,34} Since most abuse is unreported, reliance on court records may introduce bias and underestimate the abuse–pain relationship. Of note, both of these studies found that analysis of the cohorts based on self-report data demonstrated a significant association of abuse and pain. This raises the possibility that remembrance, perception, and interpretation of persons regarding their abusive experiences may be important with regards to experiencing and reporting chronic pain in adulthood.²⁷ Current psychiatric symptoms is one factor that may cause persons to view childhood in a negative light. In this context, the role of depression at the time of participation on the perception and reporting of both past experiences and pain has been considered by several investigators,^{6,28,29} including our research team.

In our study we controlled for both depression and anxiety, yet the relationship of emotional abuse and physical neglect to painful conditions remained significant. Three recent population-based studies likewise found that the childhood abuse–adult pain relationship was not fully mediated by current depression.^{6,28,29} This suggests that although depression is strongly associated with, and may be a sequela

of, childhood maltreatment, emotional abuse and physical neglect each independently contributes to enhanced pain experience.⁶ A biopsychosocial pathway,³⁵ by which overactivity of neuronal pathways of fear and pain result in cognitive, behavioral, and neurobiological changes, has been invoked to explain the putative link between abuse-related psychosocial stress and pain disorders.²⁸ Hypocortisolism has, for example, been described in response to acute stress in healthy adults with a history of childhood maltreatment,³⁶ as well as in persons with chronic pain.³⁷ Research also suggests that genetic and epigenetic modifications in the hypothalamic-pituitary-adrenal system and serotonin system influence the outcome of early life stress.³⁸ In one recent study, for example, childhood abuse appeared to exert life-long effects by altering DNA and reducing levels of glucocorticoid receptors in the brain, which are important for stress response.³⁹ Timing and type of abuse may be important determinants of the stress response.⁴⁰ Few studies have even examined prevalence of emotional abuse, which only recently has been recognized as a distinct entity.⁴¹ Emotional maltreatment, which often reflects a poor family environment, may have more dire consequences than other types of abuse, which occurs as an isolated incident. Neglect, which is similarly difficult to measure, has also received scant attention from self-report and parent-report studies, even though it is the category of child maltreatment most frequently recorded by child protection agencies.¹ Prevalence of both emotional abuse and neglect were at least fourfold greater in our clinic-based sample than has been estimated from large US population-based, self-report studies.¹

A strength of our study is the evaluation and diagnosis by headache specialists according to ICHD-2 criteria. We also used validated tools to measure abuse and neglect, and current depression and anxiety. Although diagnoses of comorbidities relied on patient-reported physician diagnoses (has a doctor ever told you that you have . . . ?) we used symptom-based criteria as well, when available.²²⁻²⁴ Our sample size was large enough to allow us to adjust the logistic regression models for possible confounders including age, race, education, household income, depression, and anxiety. Limitations of this

study are inherent in the design (clinic-based, retrospective, self-reports of abuse and comorbidities) as we have described in the preceding paragraphs. Our findings suggest that for persons presenting for migraine treatment, childhood maltreatment may be an important risk factor for development of comorbid pain disorders. Since migraine onset preceded onset of the comorbid pain conditions in our population (unpublished data), treatment strategies such as cognitive behavioral therapy may be particularly well suited in these cases.^{42,43}

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