Physical and psychological correlates of primary headache in young adulthood: A 26 year longitudinal study

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Objectives: To determine if physical and/or psychological risk factors could differentiate between subtypes of primary headache (migraine, tension-type headache (TTH), and coexisting migraine and TTH (combined)) among members of a longitudinal birth cohort study.

Methods: At age 26, the headache status of members of the Dunedin Multidisciplinary Health and Development Study (DMHDS) was determined using International Headache Society criteria. Headache history and potential physical and psychological correlates of headache were assessed. These factors included perinatal problems and injuries sustained to age 26; and behavioural, personality, and psychiatric disorders assessed between ages 5 to 21.

Results: The 1 year prevalences for migraine, TTH, and combined headache at the age of 26 were 7.2%, 11.1%, and 4.3%, respectively. Migraine was related to maternal headache, anxiety symptoms in childhood, anxiety disorders during adolescence and young adulthood, and the stress reactivity personality trait at the age of 18. TTH was significantly associated with neck or back injury in childhood (before the age of 13). Combined headache was related to maternal headache and anxiety disorder at 18 and 21 only among women with a childhood history of headache. Headache status at the age of 26 was unrelated to a history of perinatal complication, neurological disorder, or mild traumatic head injury.

Conclusions: Migraine and TTH seem to be distinct disorders with different developmental characteristics. Combined headache may also have a distinct aetiology.

Migraine and tension-type headache (TTH) are common clinical disorders associated with significant burden of disease. Despite extensive research and the attempt by the International Headache Society to facilitate headache diagnosis, controversy exists over whether migraine and TTH are discrete entities or sit at the opposite ends of a “pain severity” continuum. Specifically, it remains unclear whether (1) people with migraine are different from those with TTH, and (2) those with both migraine and TTH (previously called interval headache and hereafter referred to as “combined headache”) differ from patients with either “pure” migraine or “pure” TTH. The aim of this study was to determine whether physical and/or psychological risk factors measured between birth and 26 years of age could differentiate between subtypes of headache (migraine, TTH, and combined headache) diagnosed at the age of 26 in a representative birth cohort. The study describes several new aspects of headache epidemiology that may have therapeutic and experimental implications.

Previous research has shown a relation between headache and head or neck injury and between headache and certain personality traits and/or psychiatric disorders. For example, headache after minor head, neck, or back injury can often be indistinguishable from chronic TTH or migraine with or without aura, and is often treated similarly to the primary headache disorders. Further, they typically occur in those with a history of recurrent headache and symptoms may be delayed for months or years after the injury.

Certain personality traits or psychiatric problems are thought to precipitate headaches by increasing the vulnerability to headache. Early clinical researchers described a constellation of traits, including rigidity, ambitiousness, orderliness, hostility, and obsessions, that came to be regarded as typifying a “migraine personality.” The association between personality and headache continues to be investigated, in part because evidence suggests that certain personality traits are related to the development of chronic disorders. If a personality profile can be identified which increases the risk for migraine or TTH, this information may be useful for prevention and treatment planning.

Population based research has found that the likelihood of migraine is significantly greater among those with a history of depressive or anxiety disorders. The relation between psychiatric disorder and TTH or combined headache is less well understood, particularly with regard to the direction of causality. That is, anxiety or depressive disorders may trigger headache attacks, or conversely, they may result from chronic pain. Alternatively, in some cases psychiatric disorder and headache may represent comorbid conditions with similar underlying aetiology.

This longitudinal study investigates the correlations between physical and psychological problems early in life and adult headache disorders. There are methodological advantages to the study of multiple correlates of headache across the lifespan in a representative birth cohort. That is, most previous studies have used subjects referred to neurologists or specialist headache clinics. Because only about 2% of the population seek treatment for headaches, there may be important differences between those who seek treatment and those who do not. By using a longitudinal, prospective design and standardised diagnostic interviews, we also minimised the problems associated with retrospective recall such as forgetting and distortion.

Abbreviations: TTH, tension-type headache; RBPC, revised behaviour problem checklist; MPQ, multidimensional personality questionnaire
Diagnostic interviews were used for the assessment of headache disorders, psychiatric disorders, and personality traits. In addition, behavioural observations of the study members by multiple observers, and hospital records were screened (for injury, perinatal complications, and neurological problems) and analysed prospectively. Importantly, the design of this study allowed us to address specificity in headache syndromes by comparing predictor variables across and within outcome groups.

Based on the injury research cited earlier, we hypothesised that head, neck, and/or back injury will be more prevalent among those diagnosed with a headache disorder than those without. However, the relation between perinatal complications (for example, preterm, antepartum haemorrhage) and childhood conditions with neurological implications (for example, seizure disorders, poisoning, meningitis, anoxia) and later occurring headache remains unknown and these analyses should therefore be considered exploratory. For psychological factors, we hypothesised that our findings will be consistent with previous reports that migraineurs are more likely to be classified as anxious (“neurotic”) and depressed people. We further expect, based on our previous finding of a significant relation between migraine and stress during midadolescence, that those with migraine and combined headache will be more likely than those with TTH to have a stress reactive personality.

**PARTICIPANTS AND METHODS**

The sample comprised 481 female and 499 male (aged 26 years (SD) 3 months) members of the Dunedin Multidisciplinary Health and Development Study. This is a longitudinal investigation of the health and behaviour of a cohort of children born in Dunedin (population about 120,000), New Zealand between 1 April 1972 and 31 March 1973 (see Silva and Stanton for details).

In brief, study members have been assessed on a wide variety of psychological and medical measures at ages 3 (n=1037), 5 (n=991), 7 (n=954), 9 (n=955), 11 (n=925), 13 (n=850), 15 (n=976), 18 (n=993), 21 (n=992), and most recently in 1998–9 at the age of 26 (n=980; 96.2% of the living sample). The health and development interviews were conducted individually and typically occurred within about 6 weeks of each study member’s birthday. Ethical approval was obtained for all aspects of the study.

**Headache classification**

**Childhood headache**

At each of the ages 7, 9, and 11 assessments, parents were asked to complete a questionnaire about their child’s behaviour that included one item about complaints of headache (Rutter child scale A’). Children who complained of headaches at least once a month in the past year at any of the ages 7, 9, or 11 assessments were defined as having a childhood history of headache (n=305; 31.1% of those assessed at the age of 26). Of the remaining study members, 59% (n=578) did not report headaches at any of these ages and were therefore classified as having a negative history and 97 were excluded because of missing data at one or more ages. In addition, about two thirds of those children identified by parental report as having a history of headache themselves responded positively to the question “do you get a lot of headaches” at the age 9 assessment.

**Primary headache at age 26**

Either a registered nurse or medical practitioner obtained a medical history at the age 26 assessment. Study members were asked if, in the previous 12 months, they had experienced headaches lasting from 30 minutes to 7 days. A positive answer to this gate question led to a series of questions concerning headache pain characteristics and symptoms abstracted from the International Headache Society classification (see Waldie for further details). In accord with the society recommendations, Study members were excluded if they had had head or neck injury in close temporal proximity to the onset of headache symptoms.

**Maternal headache**

At the age 26 assessment, study members’ biological mothers (n=915) were asked if they had frequent headaches. Historical headache information was also available for mothers who accompanied their child to the age 5, 7, and 9 assessments and completed the Rutter malaise inventory, section B. In total, 168 biological mothers (18.4%) were classified as having a history of headache based on a positive response during the age 26 assessment and on a positive response on at least one of the age 7, 9, or 11 assessment occasions.

**Physical correlates**

**Perinatal problems**

The complications experienced by the study members’ mothers during pregnancy or birth were summed (n=156 with at least one complication) and are described in detail in Stanton et al. In brief, the complications recorded at birth included: epilepsy (n=4); moderate or severe hypertension (diastolic blood pressure 100 to more than 109 mm Hg, n=35); antepartum haemorrhage (n=6); delivery other than spontaneous (forceps and rotation vertex delivery, caesarean section or breech birth, n=150); small for gestational age (10th percentile of birth weight for gestation age or less, n=94); preterm (<37 weeks gestational age, n=41); idiopathic respiratory distress syndrome (n=32); minor or major neurological signs (n=29); non-haemolytic hyperbilirubinaemia (serum bilirubin concentrations>15 mg/100 ml, n=2); and Rh incompatibility (n=2).

**Neurological problems**

Neurological problems that were experienced by study members (birth to age 13) were noted by a neurologist or paediatrician during the early assessments and/or were obtained from hospital, neurological, and neuropsychological testing records (n=117 with at least one neurological complication). Recorded problems included possible (1) CNS insult (n=1: anoxia n=5, multiple injuries with questions of abuse n=2, fainting episodes with mirror movements n=1, possible brain damage, n=10); (2) seizure disorders noted in hospital records (n=11; fits and blackouts, convulsions, petit and grand mal), febrile seizures associated with measles, mumps, or gastroenteritis with severe dehydration documented at age 3 (n=19); (3) poisoning with CNS active toxins resulting in hospital admission (n=14; for example, kerosene, heart medication, antidepressant drugs, tranquillisers); (4) meningitis (n=7); (5) congenital syndromes with neurological implications (n=9; for example, cerebral palsy, Down’s syndrome, hemiplegia, hypothyroidism); and (6) suspected neurological abnormality (n=39 from hospital, paediatrician and neuropsychological testing records, see McGee, et al for further details).

**Injuries**

Injury information was gathered from the age 3 through to the age 26 assessments (for a review of these injuries, see Gaford et al). At each assessment until the age of 13, the study member’s caregiver was asked to provide details about any injuries received since the last assessment that resulted in their child receiving medical attention (taken to a general practitioner, hospital, or the accident and emergency service after the injury). From age 15–21 years, study members themselves were asked to provide injury information in the years since the last assessment. Injury information was confirmed (date, nature, severity, and circumstances of the injury) from
the accident and emergency department of the Dunedin Hospital where possible. At the age 26 assessment, Study members were asked “From age 21, have you had a serious injury that has limited your activities for more than 6 months? If yes, please describe the injury.”

For mild traumatic head injury, study members were required to have evidence of an injury to the head resulting in a concussion that required admission to hospital for less than 24 hours between the ages of 3 and 21 (n=124). Study members with a record of severe head injury (loss of consciousness and admission to hospital >24 hours, n=11) were excluded from this study according to International Headache Society recommendations. For neck or back injury, Study members were required to have evidence that an injury of the bone, muscle, or nerve (for example, dislocation, fracture, crush, nerve damage, strain/sprain) occurred in the region of the neck or the back (n=82 from ages 3 to 21).

### Psychological correlates

#### Childhood behavioural problems

Parents were asked to complete the Rutter child behaviour scales (form A) at each of the age 5, 7, and 9 assessments. The questionnaire includes various behavioural and emotional problems (previous 12 months), rated on a three point Likert scale (“does not apply” to “certainly applies”). The following subscales were used in the present study and averaged across the three assessment periods: (1) worry/fearful (for example, “worried about many things”, “often appears miserable, unhappy, tearful, or distressed”); (2) antisocial (for example, “frequently fights with other children”, “often tells lies”); and (3) hyperactive (for example, “squirming, fidgety child”).

At the age 13 and 15 assessments parents completed the 64 item revised behaviour problem checklist (RBPC). The RBPC consists of six subscales: conduct disorder, aggression, inattention, hyperactivity, anxiety, and psychotic symptoms (see Feehan et al. for details).

### Multidimensional personality questionnaire (MPQ)

At the age 18 assessment, 937 study members completed a modified version of the multidimensional personality questionnaire (MPQ) (form NZ approved by Tellegen for use in New Zealand). The MPQ is a self report personality instrument designed to assess a broad range of individual differences in affective and behavioural style and has well established psychometric properties. The 177 question questionnaire consists of 10 different subscales measuring the following traits: wellbeing (11 items), social potency (18 items), achievement (17 items), social closeness (19 items), stress reaction (14 items), alienation (17 items), aggression (18 items), control (20 items), harm avoidance (22 items), and traditionalism (22 items). These subscales can be combined into four higher order superfactors (constraint, negative emotionality, communion, agency). This study focused on the 10 subscales, however, because of their specificity and relative independence from each other. A brief description of each subscale and internal consistency coefficients are presented in Table 1.

### Mental health

At age 18 (n=930) and age 21 (n=961), study members were administered a modified version of the diagnostic interview schedule (DIS version III-R comorbid disorders). Modifications consisted of: (1) including only those questions pertaining to the assessment of DSM-III-R criteria; (2) assessing only the symptoms that occurred within the past 12 months (rather than lifetime prevalence); and (3) assessing only the more commonly occurring diagnoses for this age group.

The following DSM-III-R diagnoses were obtained for study members meeting criteria at both ages 18 and 21: any anxiety disorder (panic disorder, generalised anxiety disorder, social phobia, simple phobia, agoraphobia, obsessive-compulsive disorder, n=75), any depressive disorder (major depressive episode, dysthymia, n=63), and any substance dependence (alcohol or cannabis, n=75). Feehan et al. and Newman et al. give details of diagnostic procedures, reliability, and validity of DSM-III-R diagnoses in this sample.

### Statistical analysis

Physical and psychological correlates were analysed with χ² and binary logistic regression. Logistic regression is analogous to multiple regression and the odds ratio (OR) with 95% confidence intervals (95% CIs) is typically used in retrospective analyses to approximate relative risk. Univariate unadjusted ORs were used to identify unique risk factors and ORs adjusted for other terms in the model were used to determine the effects of shared risk factors (physical and psychological) for the outcome groups.

### RESULTS

Of the 979 members of the cohort who completed the medical interview at age 26, 24.5% reported frequent headache in the past year (n=240, 66.7% women). Of these, over 7% fulfilled International Headache Society criteria for migraine (n=72, 79.2% women), 11.1% for TTH (n=109, 62.4% women), and 4.3% (n=42, 64.3% women) were diagnosed with both migraine and TTH. The sex ratio (women:men) was 2.4:1 for combined headache. Of the 979 members of the cohort who completed the medical interview at age 26, 24.5% reported frequent headache in the past year (n=240, 66.7% women). Of these, over 7% fulfilled International Headache Society criteria for migraine (n=72, 79.2% women), 11.1% for TTH (n=109, 62.4% women), and 4.3% (n=42, 64.3% women) were diagnosed with both migraine and TTH. The sex ratio (women:men) was 2.4:1 for combined headache.

### Childhood and maternal headache history

Women were no more likely than men (n=165, 54.1%) to have a childhood history of headache. The likelihood of childhood

### Table 1. Multidimensional personality questionnaire (MPQ) subscale descriptions and internal consistency coefficients

<table>
<thead>
<tr>
<th>MPQ Scale</th>
<th>α</th>
<th>Description of a high scorer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Traditionalism</td>
<td>0.63</td>
<td>Desires a conservative social environment; endorses high moral standards</td>
</tr>
<tr>
<td>Harm avoidance</td>
<td>0.71</td>
<td>Avoids excitement and danger, prefers safe activities even if they are tedious</td>
</tr>
<tr>
<td>Control</td>
<td>0.79</td>
<td>Is reflective, cautious, careful, rational, patient</td>
</tr>
<tr>
<td>Aggression</td>
<td>0.78</td>
<td>Hurts others for own advantage; will frighten and cause discomfort for others</td>
</tr>
<tr>
<td>Alienation</td>
<td>0.76</td>
<td>Feels mistreated, victimised, betrayed, and the target of false rumours</td>
</tr>
<tr>
<td>Stress reaction</td>
<td>0.80</td>
<td>Is nervous, vulnerable, sensitive, prone to worry</td>
</tr>
<tr>
<td>Achievement</td>
<td>0.69</td>
<td>Works hard, enjoys demanding projects and working long hours</td>
</tr>
<tr>
<td>Social potency</td>
<td>0.76</td>
<td>Is forceful and decisive; fond of influencing others, fond of leadership roles</td>
</tr>
<tr>
<td>Wellbeing</td>
<td>0.67</td>
<td>Has a happy, cheerful disposition; feels good about self and sees a bright future</td>
</tr>
<tr>
<td>Social closeness</td>
<td>0.75</td>
<td>Is sociable, likes people and turns to others for comfort</td>
</tr>
</tbody>
</table>
headache was raised among those with migraine (52.4%) compared with those with TTH (28.4%; OR 2.8, 95% CI 1.4 to 5.3) and controls (32.6%; OR 2.3, 95% CI 1.4 to 3.8). Positive history of headache was also significantly more frequent among study members with combined headache (46.2%) compared with TTH (OR 2.2, 95% CI 1.0 to 4.6). A positive maternal history of headache doubled the likelihood of being diagnosed with migraine (OR 2.1, 95% CI 1.1 to 4.6) or combined headache (OR 2.2, 95% CI 1.2 to 3.8) but was not associated with TTH (OR 0.83, 95% CI 0.51 to 1.3).

### Physical correlates

The proportion of study members in each outcome group at age 26 with a positive history of perinatal complications, neurological concerns between the ages of 3 to 13, mild traumatic head injury from the ages of 3 to 21, or neck/back injury from the ages of 3 to 26 is presented in table 2.

As shown in table 2, the likelihood of TTH at the age of 26 was reduced if perinatal problems were experienced (OR 0.44, 95% CI 0.21 to 0.89) but there was no significant relation between neurological complications and any headache diagnosis. There were no significant differences between headache diagnoses in the number of injuries that occurred from the age 3 to 26 assessments. However, study members diagnosed with TTH at the age of 26 were significantly more likely than controls to have had a neck or back injury before the age 13 assessment (OR 2.4, 95% CI 1.1 to 5.1). These neck/back injuries were also more likely to occur in those who had headaches as children (63.6% vs 36.4% without childhood headaches; $\chi^2(1)=7.6, p<0.01$).

### Psychological correlates

To determine if behaviour and/or personality styles differed as a function of headache diagnosis, we analyzed data (Z-scored) from (1) the behaviour subscales of the Rutter behaviour questionnaire at ages 5, 7, and 9; (2) behaviour subscales of the RBPC at ages 13 and 15; and (3) personality subscales of the MPQ at age 18 (see fig 1). The percentage of study members in each outcome group at age 26 who received a psychiatric diagnosis at age 18 and at age 21 is presented in table 3.

**Migraine**

After adjusting for sex, childhood, and maternal history of headache, the likelihood of having migraine at age 26 was significantly increased among those with high ratings on the worry/fearful subscale averaged across ages 5 to 9 (OR 1.3, 95% CI 1.03 to 1.67); high scores on the RBPL anxiety scale at age 13 and age 15 (OR 1.4, 95% CI 1.06 to 1.80); high scores on the stress reaction subscale at age 18 (OR 1.4, 95% CI 1.06 to 1.76); and for those diagnosed with an anxiety disorder at the age 18 and 21 assessments (OR 1.9, 95% CI 1.11 to 3.29).

**TTH**

After adjusting for sex and early neck/back injury (the only previously observed correlate of TTH), the relation between TTH and low antisocial scores in childhood (OR 0.85, 95% CI 0.68 to 1.01) and low aggression in adolescence (OR 0.83, 95% CI 0.69 to 1.07) approached significance. The likelihood of TTH was increased among those diagnosed with anxiety disorder at ages 18 and 21 but not significantly so (OR 2.0, 95% CI 0.96 to 3.8).

**Combined headache**

The likelihood of combined headache was almost threefold for female study members with both a childhood history of headache and anxiety disorder at ages 18 and 21 (OR 2.8, 95% CI 1.0 to 7.8). No other behaviour problem or psychiatric disorder was associated with combined headache or significantly interacted with a childhood history of headache.

### DISCUSSION

There is controversy over whether migraine and TTH are separate clinical entities or whether they are part of a continuum of disorder varying in severity. Convincing evidence from Rasnussen et al. regarding pain features and characteristics...
suggests that migraine and TTH should be considered separate entities. Their data also suggest that patients with combined headache have two distinct forms of headache, rather than the TTH being simply a milder form of migraine.

Findings from the present study, which prospectively examined some developmental correlates of headache in a birth cohort, generally support the view that headache disorders are separate entities. Several differences in the physical and psychological profiles between headache groups were found, with comparatively few similarities among headache subtypes. The findings also suggest that those with combined headache share certain characteristics that differentiate them from those with both pure headache disorders. These shared characteristics, discussed below, may predispose these patients to both types of recurring headache.

**Correlation between maternal and childhood headache**
A positive history of headache among biological mothers significantly increased the risk of their offspring having frequent headaches in childhood, as well as migraine and combined headache at the age of 26. That there was a strong relation between migraine and maternal headache is consistent with previous reports and may reflect a combination of learned behaviour and genetic predisposition. Interestingly, a childhood history of headache also significantly increased the risk of migraine or combined headache at the age of 26, independent of their mothers’ headache status. Among those with childhood headache, over one quarter were diagnosed with a headache disorder at the age of 26 and a further 29% continued to have frequent headaches at age 26 but did not meet International Headache Society operational criteria for a headache diagnosis. It was notable that a maternal or childhood history of headache was unrelated to TTH at the age of 26.

**Physical correlates**
In this study, perinatal problems or the presence of a neurological problem did not significantly increase the risk of
adult diagnosed migraine (with or without coexisting TTH) or “pure” TTH. For those who had a mild traumatic head injury before the age of 13 the likelihood of experiencing childhood headache doubled, consistent with findings showing that headache is the most common complaint 1 year after mild head injury. By contrast, there was no relation between mild traumatic head injury at any age and primary headache in adulthood.

Earlier studies have found that headache is a common sequelae of neck or back injury. For example, about one third of those with minor back injuries report chronic headache 1–2 years after the accident and early onset of pain is predictive of chronicity. About 3% of school children have been found to have both back pain and headache and in the present study 4.8% of study members had experienced a neck or back injury in addition to experiencing frequent headaches by the age of 13. By the age of 26, study members diagnosed with TTH were significantly more likely to have had childhood neck or back injuries (17.4%) than headache free controls (10.8%). Most of these study members also had childhood headaches (63.6% vs. 36.4% who did not). This is consistent with the finding that headaches after neck or back injuries typically occur in those with a history of recurrent headache.

Taken together, these results suggest that perinatal and neurological problems and mild traumatic head injury early in life have little relation to primary headache in young adulthood. However, it seems that childhood neck or back injury may increase the risk of TTH in adulthood. Others have similarly found that headaches can be triggered months or years after an injury. For example, a neck or back injury may lead to an increased vulnerability in the skeletal and peripheral muscles. The time between the injury and the diagnosis in the present study suggests that other intervening factors may contribute to headache onset.

**Psychological correlates**

In accord with other population based headache studies, migraine was strongly and consistently related to anxiety (childhood through to young adulthood) and stress reactive personality (nervousness, sensitivity, and proneness to worry) independent of sex, headache history, or maternal headache status. "Neurotic" characteristics have been similarly found to predict incident migraine in prospective analyses. The early identification and counselling of children with persistent anxiety, possibly in conjunction with use of antidepressive agents, may help reduce the risk of developing migraine.

Our findings are also consistent with the idea that those with migraine inherit a nervous system that is more sensitive to and more easily aroused by its surroundings. For example, sensation seeking behaviour is lower in migraineurs than controls and electrophysiological studies have shown a relatively higher level of cortical arousal (with lack of habituation) in migraineurs between attacks.

By contrast with the above findings, we found that only the female study members with combined headache had a significantly higher risk of developing comorbid anxiety disorder. Maternal headache also increased the risk of combined headache, particularly in association with childhood headache. Patients with combined headache have been acknowledged by general practitioners as being particularly difficult to treat. This study suggests that those with a strong familial and personal history of headache may benefit from early prophylactic therapy along with techniques such as relaxation or biofeedback training.

Previous studies have found that those with TTH have higher levels of indirect hostility than migraineurs or controls and are more likely to be anxious due to repressed anger and resentment. In this study, however, we found that TTH was slightly (but not significantly) associated with lower antisocial subscale scores during childhood and lower scores on the personality trait of aggression during adolescence.

**Summary**

Study members diagnosed with migraine at the age of 26 were largely defined by a history of headache, “neurotic” behaviour, and personality traits, and anxiety disorder. By contrast, those with coexisting migraine and TTH were not distinguishable from controls on behavioural measures during childhood and up to midadolescence. However, a history of childhood headache seemed to confer a particular risk for anxiety disorder at ages 18 and 21 as well as combined headache in adulthood. This group was also more likely to have a maternal history of headache than the group with pure headache disorders. There was a slight tendency for those with TTH to have been non-aggressive, non-antisocial youngsters, with a higher incidence of childhood neck or back injury.

Although anxiety was associated with severe headache in general, the relation differed between groups, supporting the view that primary headache disorders may be distinct entities. For example, high levels of anxiety were evident in migraineurs from an early age and the association with anxiety seems unlikely to solely reflect the adverse psychological effects of migraine attacks. Nevertheless, it remains unclear if high levels of anxiety are a precipitant of headaches or an early correlate with shared pathophysiology. It is possible that anxiety and migraine are characterised by disturbed serotonergic systems in platelets and in the brain. Further work should explore this possibility and attempt to replicate the present findings.

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