Review

Migraine: association with personality characteristics and psychopathology

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The relationship between migraine and psychopathology has been discussed far more often than it has been systematically studied. Twentieth-century investigators have frequently described the obsessional, rigid, angry personality postulated to characterize migraine sufferers. More recent population-based studies have demonstrated associations between migraine and depression and migraine and panic disorder. This article discusses the relationship of migraine and personality and migraine and psycho-pathology. • *Cormorbidity, depression, dysthymia, mania, migraine, panic disorder, personality, psychopathology*

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The relationship between migraine and psycho-pathology has been discussed far more often than it has been systematically studied. One ancient view suggests that migraine was caused by evil spirits. More recently, Andrew Pope, in *The Rape of the Lock,* suggested a relationship between depression (spleen) and migraine.

When screen'd in shades from day's detested glare, Spleen sighs forever on her pensive bed, Pain at her side, and megrim at her head (1).

Twentieth-century investigators have frequently described the obsessional, rigid, angry personality postulated as characterizing migraine sufferers (2). More recent population-based studies have demonstrated associations between migraine and depression and migraine and panic disorder.

In this article, we discuss the relationship of migraine and personality and migraine and psychopathology. After addressing the methodologic issues important to these studies, we review both clinic-based and population-based data. We close with a summary of alternative explanations for the association between migraine and psychopathology and speculate on the mechanism of the association.

Methodologic issues

Selection bias

Many early studies of migraine and psychopathology were conducted in subspecialty centers. As most migraine sufferers do not receive a medical diagnosis and only 2% consult headache specialists, observations from subspeciality clinics are subject to referral bias (3, 4). Factors that lead to consulting headache specialists may be mistaken for attributes of the disease (5- 7). If patients with obsessional personality traits are more likely to seek out specialists, obsessional personalities may be over-represented among migraine sufferers who attend a headache-clinic (8). Even if migraine and obsessional personality are not associated, they might appear to be associated in a clinic-based sample. Thus, findings from clinic-based samples must be confirmed in samples of the general population before they are accepted as valid. Henryk-Gutt and Rees found that migraineurs selected from headache clinics had more psychopathology than migraineurs identified by screening civil servants in London (9).

Diagnosis and measurement

Case-definitions of migraine have varied substantially across studies. While some studies have relied on a clinician's implicit diagnosis without specifying diagnostic criteria, others have used the imprecise ad hoc criteria developed by Friedman et al. (10). A few recent studies have used the explicit diagnostic criteria proposed by the International Headache Society (IHS) (11), but even these criteria have important limitations (12, 13).

Studies have also varied in their approaches to assessing personality or psychopathology. Personality (patterns of perceiving, relating to, and thinking about the environment and oneself that are exhibited in a wide range of social and personal contents) refers to relatively stable individual characteristics that vary along a continuum without any direct

implication about abnormal function (14). Psychopathology refers to marked deviations from normal function (15). Personality characteristics and psychopathology can both be assessed using dimensional or categoric systems of measurement. Diagnostic systems for headache (IHS) and for psychopathology (DMS-IV) use categoric systems to identify individuals with specific disorders, such as migraine, major depression, or panic disorder (16). A contrasting approach, which grew out of the psychometric research, measures personality characteristics or psychopathology using dimensional scales (16). In general, it is easier to detect statistically significant group differences (between migraine and non-migraine groups) using dimensional rather than categoric variables.

Migraine and personality

Introduction

Over the years, many studies have focused on particular personality traits of migraineurs. Basic assumptions are that: (i) migraineurs share common personality traits, (ii) these traits are enduring and measurable, and (iii) these traits differentiate migraineurs from controls (17). The notion of a migraine personality first arose from clinical observations of the highly selected patients seen in sub-specialty clinics.

In 1934, Touraine and Draper (18) reported that migraineurs were deliberate, hesitant, insecure, detailed, perfectionistic, sensitive to criticism, and deeply frustrated emotionally. They were said to lack warmth and to have difficulty making social contacts. Wolff found his migraineurs to be rigid, compulsive, perfectionistic, ambitious, competitive, chronically resentful, and unable to delegate responsibility (2). They had troubled relationships with their parents, protected themselves from intimacy, and attempted to dominate their environment. Friedman reported that some, but not all, of his migraineurs were orderly, overly conscientious, and meticulous in appearance. He observed that patients with migraine showed hostility, irritability, withdrawn social behaviour, and transitory and prolonged depressions (19).

While these descriptions are based on uncontrolled observation of highly biased patient samples, they have passed into the general culture. For example, in *The White Album,* Joan Didion's physician focuses on aspects of the migraine personality: "You don't look like a migraine personality ... Your hair's messy. But I suppose you're a compulsive housekeeper" (20). Her response reflects a higher level of scientific rigor than her physician's question: "Actually my house is kept even more negligently than my hair." But the doctor was right nonetheless; perfectionism can also take the form of spending most of a week writing and rewriting a paragraph. But not all perfectionists have migraine, and not all migrainous people have migraine personalities (20).

Didion's comment gets to the essence of the matter. Do migraineurs have enduring personality profiles different from those of the general population? The migraine personality has rarely been investigated in population-based samples of patients. This review focuses on studies of population or general practice samples to avoid the problems of selection bias that limit findings from clinic-based studies. Studies using the Minnesota Multiphasic Personality Inventory (MMPI) are addressed in a separate section.

Population-based studies (Table 1)

Most investigations have used psychometric instruments such as the MMPI or the Eysenck Personality Questionnaire (EPQ). The EPQ is a well-standardized measure which includes four scales: psychoticism (P), extroversion (E), neuroticism (N), and lie (L).

Brandt et al. (21) used the Washington County Migraine Prevalence study to conduct the first population-based case-control study of personality in migraine (Table 1). Over 10 000 12- to 29-year-olds selected using random-digit dialing received a diagnostic telephone interview. A sample of subjects who met the criteria for migraine with or without aura (n = 162) were compared to subjects without migraine. Each subject received the EPQ, the 28-item version of the General Health Questionnaire (GHQ), and a question about headache laterality.

Subjects with migraine scored significantly higher than controls on the EPQ N scale, indicating that they were more tense, anxious, and depressed than the control group. In addition, women with migraine scored significantly higher on the P scale than controls, indicating that they were more hostile, less interpersonally sensitive, and out of step with their peers. Both men and women with migraine had significantly lower mean L scores than controls, suggesting that they were less defensive than the control group. Migraine sufferers of both sexes scored significantly higher than controls on the GHQ, with higher levels of anxiety, insomnia and depression, and more somatic complaints and social dysfunction.

Rasmussen (22) screened a population-based sample to identify migraine and tension-type headache (TTH) sufferers, with classification based on clinical assessment using the IHS criteria. They found no association between these disorders and cohabitation, employment status, marital status, educational level, or occupational category. TTH occurring alone was associated with high N scores on the EPQ. Persons with pure migraine (that is, without TTH) did not score above the norms on the N scale, although persons with migraine, with and without

Table 1. **Migraine and personality: epidemiologic studies (community).**

	Sample Subjects N DX	Age	Source	Controls	instrument	Findings
Brandt et al., 1990 (21)	162 Mig RR = 94.2%	12-29	Community telephone survey of 10, 169	162 matched for sex and age-no headache	EPQ	EPQ-N: Both F & M Mig higher than controls. EPQ-P: F Mig higher than controls.
Rasmussen 1992 (22)	77 Mig 167 TTH RR = 76%	25-64	Random sample of 1000 selected from the National Central Person Registry	496 non-headache	EPQ	EPQ-N: (1) Higher for TTH and Mig vs rest. (2) No difference b/t "pure" mig vs rest.
Merikangas et al., 1993 (23)	11 Cls 91 Corn 63 TTH 50 Sxs Only	28-29	Community survey in Zurich-longitudinal	158 non-headache	Freiburg Personality Inventory	Cls sign. higher than other groups on nervousness, depressiveness, inhibition, decreased levels of resilience.

Abbreviations: Com = common migraine; Cls = classic migraine; Combo = combination; EPQ = Eysenck Personality Questionnaire; EPQ-E = EPQ: Extraversion; EPQ-N = EPQ: Neuroticism; EPQ-P = EPQ: Psychoticism; EPQ-L = EPQ: Lie; HA = headache; MC = muscle contraction; Mig = migraine; Mixed = mixed headache type; PT = post trauma; RR = response rate; SMCH = scalp muscle contraction; TTH = tension type headache.

TTH, showed a tendency to score above the norms on the N scale. None of the headache groups showed any association with the L scale. Clearly, the inclusive migraine group is more representative of migraine sufferers than the pure migraine group, as most migraineurs in that study also reported TTH. For this group, findings paralleled those of Brandt et al. on the N scale.

Merikangas et al. (23) investigated the cross-sectional association between personality, symptoms, and headache subtypes as part of a prospective longitudinal study of 19- and 20-year-olds in Zurich, Switzerland, when the subjects were 29 to 30 years old. Personality was assessed by the Freiburg Personality Inventory (FPI). The symptoms checklist 90 (SCL-90) was used to examine somatic and psychologic symptoms. Migraineurs scored higher on indicators of neuroticism than did non-migraine subjects. This difference reached statistical significance only in subjects with migraine with aura (n = 11). Somatization was the only subscale on the SCL-90 which discriminated between subjects with migraine and those without migraine. TTH subjects did not differ from controls on any of the personality or symptom scales.

Samples of convenience (Tables 2 and 3)

Passchier et al. (25) recruited adult headache patients and healthy control subjects through advertisements in a local newspaper (Table 2). Subjects with headache disorders were offered behavioral therapy, while control subjects were paid. Migraine and TTH subjects both showed elevated achievement motivation, while rigidity was present mainly in the TTH group. Neither migraineurs nor TTH subjects showed elevations on the neuroticism or obsessive-compulsive scales. These findings are limited because the recruitment and incentive procedures may have introduced selection bias. Headache sufferers who desire behavioral therapy may have different psychologic profiles than do headache sufferers in general.

Passchier et al. (24, 25) studied a stratified sample of schoolchildren in Holland. About 57 000 children were chosen, and headache was measured using Waters' headache questionnaire. Compared to children without headache, children with migraine and TTH were characterized by a high motivation to achieve and by a fear of failure (24).

Schmidt et al. (17) recruited subjects from a large metropolitan city in western Canada using a press release. From the initial screening, 125 subjects with migraine (103F, 22M) between the ages of 20 and 55 years were selected; all received the Jackson Personality Inventory. No differences were found between migraine sufferers and historical norms for anxiety, tension, or orderliness. Lower scores were found on complexity, risk-taking, and social participation scales and higher scores on responsibility and value orthodoxy scales. A potential response bias may have affected the results, as subjects who respond to a press release may differ from other migraine sufferers. Response bias might be especially likely because the study did not use a control group of persons who responded to a press release.

Table 2. **Migraine and personality: convenience samples (recruited by press release).**

	Subjects N	DX	Age	Source	Controls	Instrument	Findings
Passchier et al., 1984 (25)	56 32	Mig TTH	16-55	Subjects recruited by ads in local paper- offered therapy for HA	26 matched for sex, age non-medical treatment, and education	(1) Inadequacy and rigidity subscales from the Dutch Personality Q. (2) Achievement motivation test (3) Inventory of daily beh. (4) Impulsiveness scale (IMP) Defense Mechanism I.	(1) Mig and TTH patients more achievement oriented than controls. (2) TTH more rigid than controls. (3) Combined groups more rigidity, achievement motivation, debilitating anxiety and less impulsiveness than controls.
Schmidt et al., 1986	125	Mig	18-55	Recruited by press release announcing study of Mig HA		Jackson Personality Inventory (16 scales)	Complexity, responsibility, risk taking, social participation, and value orthodoxy lower for Mig group than test norms.

Abbreviations: Com = common migraine; Cls = classic migraine; Combo- combination; EPQ = Eysenck Personality Questionnaire; EPQ-E = EPQ: Extraversion; EPQ-N = EPQ: Neuroticism; EPQ-P = EPQ: Psychoticism; EPQ-L = EPQ: Lie; HA = headache; MC = muscle contraction; Mig = migraine; Mixed = mixed headache type; PT = post trauma; RR = response rate; SMCH = scalp muscle contraction; TTH = tension type headache.

Henryk-Gutt and Rees (9) interviewed a random sample of civil servants with migraine with aura, migraine without aura, non-migrainous headache, and non-headache to obtain information on personal, medical, and family histories (Table 3). Groups were matched for age, sex, marital status, and civil service grade. Migraineurs, compared to non-migraine headache patients and non-headache controls, had significantly increased N scores on the EPQ, increased anxiety and somatization scores on the MMPI (women only), and increased hostility scores on the Buss Scale. Women migraine clinic patients had even higher N scores, anxiety, and hostility scores (9), a finding that might reflect high rates of comorbid diseases among the clinic patients.

Phillips (26) studied patients with migraine and "muscular tension" headache. Questionnaires were mailed to a sample of approximately 1500 patients selected from a general practice register. A sample of 68 headache cases (the basis of selection is uncertain) completed the EPQ. The group consisted of 39 migraineurs, 24 muscular tension-headache patients, and 5 individuals with both conditions. (Migraine was defined by the presence of two or more of the following symptoms: unilateral headache, nausea and/or vomiting, and sensory prodromata. Muscular tension headache was defined as headache with no more than one of the above symptoms (with the exception of vomiting).) The groups did not differ from each other on N, E, P, or L scales of the EPQ. A different sample of tension-headache patients, selected on the basis of their desire for treatment and their headache severity, had significant elevation of N scores. Perhaps this was a sample of patients with transformed migraine (27), since the higher N score was associated with higher medication use. This study did not have non-headache controls and used historical norms.

Crisp et al. (28) surveyed every fifth adult from a group practice in a small English town (5000 adults). Patients were interviewed and given the Middlesex Hospital questionnaire. Women with migraine were significantly more anxious and depressed than were non-migraine subjects, many of whom had other headache types. (Diagnostic criteria for common migraine were a throbbing headache (unilateral or bilateral) associated with nausea and/or vomiting and/or severe photophobia. Classic migraine required a preceding "warning".) There was no control group.

Hundleby and Loucks compared 91 young adult migraineurs with 126 non-migraine controls recruited from students who completed a headache questionnaire. Measurements included the Personal Data Form, the 16P-F, the Jackson Personality Research Form (Form E), the Depression Adjective Checklist (Form A), stimulation-seeking scales, and other selected objective tests of personality. Anxiety and cortertia (a measure of alertness and arousal) scores were significantly higher in the migraineurs

Table 3. **Migraine and personality: convenience samples (practice enrollees, civil servants and students).**

	Sample Subjects N	DX	Age	Source	Controls	Instrument	Findings
Henryk-Gutt & Rees, 1973 (9)	50 50 50 RR = 54%	Cls Com Ha	17-64	1859 Questionnaire distributed to civil servants in London	50 HA free 18 Mig clinic patients 19 men w/asthma	EPQ	*EPQ3/4N:* (1) Cls + Com higher than HA + no HA (both M & F). (2) Cls + Com lower than clinic patients (both M & F). (3) Cls vs. Com-no difference HA v. No HA no3/4 difference. *EPQ3/4E:* Male Mig sign. lower than rest of males.
Phillips, 1976 (20)	39 TTH Mixed	Mig 24 5		1500 Questionnaire sent to patients in general practice		EPQ	No difference b/t Mig and TTH so combined. *EPQ3/4*N: No group differences. *EPQ3/4L:* Higher scores for female HA than controls.
Crisp et al., 1977 (28)	41 reported 60 other HA RR = 72%	Self-Mig	Adult	1000 Questionnaire sent to adults from one group practice		Middlesex Hospital Q (self-rating scales)	(1) Female Mig vs. no Mig higher on anxiety, somatic dep, and hysteria scales. (Males higher but not significant). (2) Mig vs. No Mig-no excessive obsessional trait.
Hundleby & Locks, 1985 (29)	91	Mig	Early 20s	2131 Students completed a questionnaire. All mig and random sample of non-mig selected for study	126 non-mig	Personality Research Form, Depression Adjective Checklist, Stimulation seeking scales)	(1) Anxiety and cortertia sign. different b/t Mig and Non-Mig. (2) No relationship w/stimulation seeking behaviour.
Kohler & Kosanic, 1992 (30)	69	Mig	Mean= 40.9	Patients of neurologic and psychiatric practice	69 sex and age matched	3 scales: ambition orderliness rigidity	No sign. differences b/t mig and controls on the 3 scales (*t*-tests).

(29). The authors concluded that the differences, while detectable, were meager at best.

Köhler and Kosanic (30) found no difference between 69 migraineurs and age- and sex-matched controls in ambition, orderliness, and rigidity. Controls were patients from a neurologic and psychiatric practice; the patients had phobias, insomnia, or marital problems and agreed to fill out the personality questionnaire in the waiting room. This is clearly not a healthy control group.

In summary, studies that used the EPQ or similar personality measures and compared persons with migraine to non-migraine controls have reported an association between migraine and neuroticism (22, 24-26). (Results from one study (22) were consistent with this conclusion although not statistically significant.)

MMPI studies (Table 4)

Most investigators (31-34) have found that MMPI scores in migraineurs fall within the normal ranges, in contrast to the abnormalities found in patients with chronic TTH or mixed headache disorders (Table 4) (35). However, the original MMPI-I was developed on the basis of item responses from psychiatric patients (36) and has a distinct psycho-pathologic bias. It may not be sensitive to the personality traits found in non-psychiatric populations in general and in migraineurs specifically.

Kudrow and Sutkus (33) found that patients with migraine and cluster headache scored lowest, those with TTH and "combination headache" in the intermediate range, and those with post-traumatic headache scored highest on the neuroticism scales of

Table 4. **Migraine and personality: MMPI (neurotic triad*) studies.**

	Subjects		Sample			
	N	DX	Age	Source	Controls	Findings
Kudrow & Sutkus, 1979 (33)	49 49 41 52 30 34	Mig SMCH Cluster Combo PT Conv	18-70	Patients in a speciality HA clinic	30 non-HA subjects	Patients with migraine and cluster scored lowest. Patients with SMCH or combination headache scored next lowest. Patients with post-traumatic or conversion headache scored highest. Significant conversion V patterns found in women with SMCH, post-traumatic, and conversion headache, and men with combination headache.
Sternbach et al. 1980 (32)	83 41 58	Vascular MC Mixed	20-70	Patients seen for HA at pain treatment center	Data on MMPI from 50 000 patients, compared on age and sex	Vascular less depressed and less neurotic than MC and Mixed. All groups combined vs. controls sign. higher on scales Hs, D, Hy. Males with MC higher on paranoid than females. Females in all HA groups higher on Hy, Hs than males.
Andrasik et al., 1982 (37)	29 39 12 22	Mig MC Cluster Mig + MC	18-68	Physician-referral or self-referral	30 friend or relative of patient matched on age, sex, ses, marital status	Control subjects no meaningful elevations on any scale. None of HA types showed sign. scale elevations. Sign. c^2 tests for *t*-score elevations ³ 70 vs < 70 by the 5 HA groups for scales Hs, Hy.
Weeks et al., 1983 (34)	50 50	Mig Combo	Not speci-fled	Outpatients evaluated for treatment at HA center		Combination headache sign. Higher than mig on Hy, D, Hs.
Levor et al., 1986 (38)	20 9 5	Com Cls Mixed	23-63	Patients recruited from physicians specializing in treatment of HA	Data from days prior to a migraine day were matched with the same person's data prior to headache-free days	Mild, subclinical elevations on Hs, D, Hs for all HA groups vs. norms.
Ellertsen & Klíve, 1987 (39)	12 33	TTH Mig	16-70	Neurology patients	34 HA-free, muscle pain in neck/ shoulder patients recruited by ads	Muscle pain group: males scored higher on Hs than females. TTH: Males and females had elevated scores on Hs and D (m vs. f not sign. diff). Female Mig and TTH groups had similar profiles.
Rappaport et al., 1987 (41)	48 47 28	Mig MC Mixed	18-66	Recruited by newspaper and radio advertise-ments		MMPI profiles do not distinguish different diagnostic categories. May be related to headache frequency or underlying personality.
Dieter & Swerdlow, 1988 (42)	82 48 58 61 53	Mig SMCH PT Mixed Cluster	Not speci-fled	Random selection from general practice population	68 HA free people solicited from the staff of the hospital	SMCH, Mig/Cluster, Mixed/PT each sign. different from control group on scales Hs, D, Hy. Clinically elevated scores from Mixed and PT on Hs (both males and females). Clinically elevated scores for Mixed and PT on D (males only). Clinically elevated scores for Mixed and PT on Hy (both males and females).
Invernizzi et al., 1989 (31)87	148 183 Mixed	Mig TTH	16-70	to HA center	Patients referred Hs, D and Hy.	Mixed vs. Mig and Mixed vs. TTH sign. diff. for

Continued overleaf

Table 4. **(Continued)**

	Sample					
	Subjects					
	N	DX	Age	Source	Controls	Findings
Pfaffenrath et al., 1991 (43)	160 95 30 149	Mig TTH Cluster Mixed	14-70	Patients in a speciality headache center		Slight increase in T mean values to over 60 but still within 25 D of population normals. No statistically significant differences between groups or between patients with or without analgesic abuse.
Robinson et al., 1991 (44)	88 46 130 130 91	Mig TTH Mixed PT Cluster		Outpatient headache clinic		MMPI profiles do not discriminate between different diagnostic categories.
Inan et al., 1994 (45)	44 36	Mig TTH	Not speci-fled	Patients referred to clinical psychologist	36 healthy controls	Female TTH higher on Hs, D, Hy than controls. Female Mig higher scores on Hy than female controls. Differences between TTH and Mig not sign. different.

*MMPI Neurotic Triad includes: D = depression, Hs = hypochondriasis, Hy = hysteria.

Abbreviations: Com = common migraine; Cls = classic migraine; Combo = combination; Conv = conversion; EPQ = Eysenck Personality Questionnaire; EPQ-E = EPQ: Extraversion; EPQ-N = EPQ: Neuroticism; EPQ-P = EPQ: Psychoticism; EPQ-L = EPQ: Lie; HA = headache; MC = muscle contraction; Mig = migraine; Mixed = mixed headache type; PT = post trauma; RR = response rate; SMCH = scalp muscle contraction; TTH = tension-type headache.

the MMPI. This is similar to the pattern found in chronic pain patients, who show characteristic "neurotic" MMPI profiles, with elevation of the first three clinical scales: Hypochondriasis (Hy), Depression (D), and Hysteria (Hs).

Sternbach et al. (32) studied 182 patients with vascular headache (migraine), muscle contraction headache, and mixed headache, and controls, and noted statistically significant differences on the MMPI in the Depression and Psychasthenia (anxiety) scales. While vascular headache patients tended to be less depressed and anxious than the muscle contraction and mixed headache group, the statistically significant differences were not considered clinically significant.

Andrasik et al. (37) compared 99 headache sufferers (participants in a research project) (migraine, muscle contraction, mixed, and cluster) to 30 matched non-headache controls using the Ad Hoc criteria. None of the headache types had significant scale elevations, although all possessed moderate elevations that increased in frequency, beginning with cluster and continuing through migraine, mixed, and muscle contraction headache.

Weeks et al. (34) compared, using standard norms and the Ad Hoc criteria, 50 migraineurs to 50 combination headache patients in a tertiary care center. Patients with combination headaches had higher scores than migraineurs on the Hs, D, and Hy scales. None of the T scores showed significant elevations above > 70.

Levor et al. (38) studied 33 patients who had migraine, either with or without aura (common or classic, Ad Hoc criteria) recruited from physicians specializing in headache treatment. Twenty-four migraine patients also had muscle contraction headaches. These subjects had mild subclinical elevations of the Hs, D, and Hy scales.

Ellersten and Klíve (39) compared MMPI profiles in men and women with chronic muscle pain to the profiles of chronic tension-type headache patients and women migraineurs. Elevation of the Hs, D, and Hy subscales was found in all groups. A "conversion V" profile was found in women migraineurs but not in women with chronic tension-type headache.

Ellersten (40) prospectively studied a group of female migraineurs, comparing MMPI profiles before and after biofeedback and autogenic training. There were no differences on the MMPI between the most improved and the least improved patients before the start of treatment, suggesting that the MMPI has no value in predicting outcome. At 2 years, however, there were significant differences between these sub-groups. The most improved patients had significant improvement on five MMPI scales, suggesting that the headache disorder and the MMPI profile improve in parallel. The authors suggest that the psychologic problems reflected in the MMPI improve when the pain problems decrease, although other interpretations are possible. These findings suggest that the MMPI profile does not invariably reflect enduring personality characteristics; it may reflect "state" characteristics associated with having severe headache. The least improved group showed a slightly more elevated V configuration, but profiles were essentially unchanged. The resistant patients

may continue to have the "state" characteristics associated with headache; alternatively they may have a comorbid psychiatric illness that is associated with abnormal MMPI profiles.

Rappaport et al. (41) compared MMPI profiles in headache sufferers who had IHS criteria migraine, muscle contraction, or mixed headaches. Within this headache population, four MMPI cluster profiles were found that did not correlate with their headache diagnosis.

Dieter and Swerdlow (42) found the MMPI profiles of 505 individuals with various headache diagnoses, including migraine, to be less pathologic than those reported in prior studies (Table 4). Clinically significant elevations of the Hy, D, and Hs scales occurred only in the post-traumatic and mixed headache groups. All five headache diagnoses had a significantly greater proportion of "conversion V" (muscle contraction headache (12.5%), migraine (18.3%), cluster headache (20.7%), mixed headache (24.6%), and post-traumatic headache (31%)), than headache-free controls (0%). There were no significant differences among the headache conditions in "conversion V" frequency. (This is one of the few convenience-based samples with a control group.) When the items in the MMPI that address headache or their associated symptoms were deleted and the scores recalculated, there was a decrease in both the Hy and Hs scales to below the 70t clinical threshold. These data suggest that MMPI abnormalities result in part from accurate reporting of pain and its associated symptoms, and that there is a large intra-group variance in MMPI scores.

Invernizzi et al. (31) studied 418 patients with migraine, tension, and mixed headache, not using the IHS criteria. Patients with mixed headaches showed significantly elevated scores (Hs, D, Hy, and PT) on the MMPI compared to norms. Migraine and tension headache patients did not have elevated scores. No correlation was found between the MMPI scores and duration of illness.

Pfaffenrath et al. (43) studied 434 patients who had IHS classified cluster, migraine, or tension-type headache, or migraine and tension-type headache. The patients all had slightly elevated Hs, D, and Hy scales compared to test norms. No significant differences were found between patients who abused analgesics and those who did not.

Robinson et al. (44) attempted to see if there was any relationship between MMPI cluster profiles and the Ad Hoc criteria diagnostic categories. Cluster group analysis did not discriminate between different diagnostic categories. Differences may reflect patients' global response to pain rather than a headache-related personality.

Inan et al. (45) compared the MMPI profiles of Turkish women migraineurs with TTH patients and controls using the IHS criteria. Migraine sufferers had significantly higher scores on the hysteria sub-test, while TTH patients had higher scores on the neurotic subtests (Hy, D, and Hs).

Most MMPI studies have been clinic-based, limiting their generalizability and creating opportunities for selection bias. Some have not used control groups, relying instead on historical norms. Many have not used explicit diagnostic criteria for migraine. Despite these limitations, most studies show elevation of the neurotic triad, although this is not statistically significant.

Studies on migraine and personality have generally not controlled for drug use, headache frequency, or headache-related disability. One group found a slight non-significant increase in some T values of the MMPI in patients with drug abuse (44). Furthermore, they have not controlled for major psychiatric disorders (such as major depression or panic disorder), which occur more commonly in migraineurs (see next section). Comorbidity of migraine and major psychiatric disorders might confound the assessment of the relationship between migraine and personality traits. Neuroticism, in particular, is associated with depression and anxiety, which occur with increased prevalence in migraineurs (see next section). Differences in neuroticism across studies might reflect variations in the role of comorbid psychiatric disease. The available data suggest that migraineurs may be more neurotic than non-migraineurs. The stereotypical rigid, obsessional migraine personality might reflect the selection bias of a distinct subtype of migraine that is more likely to be seen in the clinic. Because of inconsistencies across studies, further research is needed before a definitive generalization can be made.

Migraine and psychopathology and psychiatric disorders

In contrast to the numerous studies on the relationship of migraine to personality traits or psychologic distress, there are only a few studies on the relationship of migraine to specific psychiatric disorders (46-53). Several clinic-based studies have reported an increased prevalence of migraine in patients with major depression and an increased prevalence of major depression in patients with migraine (41, 42). Three population-based studies have examined a wide range of psychiatric disorders in addition to major depression (43-47).

Merikangas et al. (43) reported on the association of migraine with specific psychiatric disorders in a random sample of 457 adults aged 27 to 28 years in Zurich, Switzerland. Persons with migraine (n = 61) were found to have increased 1-year rates of affective and anxiety disorders. Specifically, the odds ratio for major depression (OR (2.2, 95% CI 1.1-

4.8)), bipolar spectrum disorders (OR (2.9, 95% CI 1.1-8.6)), generalized anxiety disorder (OR (2.7, 95% CI 1.5-5.1)), panic disorder (OR (3.3, 95% CI 0.8-13.8)), simple phobia (OR (2.4, 95% CI 1.1-5.1)), and social phobia (OR (3.4, 95% CI 1.1-10.9)) were significantly higher in persons with migraine compared to persons with no migraine. The odds ratio is used in retrospective case-controlled studies to approximate the relative risk. Because subjects in case-controlled studies are selected by the presence or absence of *disease* rather than by exposure status, the odds ratio is defined in terms of probabilities of exposure instead of probabilities of disease. The interpretation of the odds ratio is straightforward. The odds ratio for migraine and major depression implies that the odds of migraine are 2.2 times greater in persons with depression than in those without depression. Because the 95% confidence interval does not include 1.0, this difference is statistically significant at the $p = 0.05$ level.

Migraine with major depression was frequently complicated by an anxiety disorder. In persons with all three disorders, Merikangas et al. suggest that the onset of anxiety generally precedes the onset of migraine, whereas the onset of major depression follows the onset of migraine. Merikangas believes that migraine associated with psychiatric morbidity may be a distinct syndrome, with different manifestations at different times in the life cycle. Anxiety may appear in early childhood, followed by migraine and then depression. Disease duration may be more important than attack frequency in determining the presence of associated psychologic conditions. If there is a subtype of migraine associated with anxiety and depression, it may require, or respond differently to, different treatment (44).

Stewart et al. (45) reported on the relationship of migraine to panic disorder and panic attacks in a population-based telephone interview survey of 10 000 Washington County, Maryland residents aged 12 to 29 years. The highest rates of migraine headaches occurring in the last week were reported by men and women with a history of panic disorder. The proportion of migraine headaches reported by those with a history of panic attacks (who did not meet the criteria for panic disorder) was intermediate, whereas the proportion of migraine headaches in persons with no history of panic attacks was lowest. The relative risk of migraine headache during the previous week associated with a history of panic disorder was 6.96 in males and 3.70 in females. The associations of panic disorder and panic attacks with other types of headaches (i.e., muscle contraction symptoms, forehead pain only, and other) were considerably weaker (45).

Stewart et al. (46), in a follow-up study of the same population, found that 14.2% of women and 5.8% of men with a headache in the previous 12 months consulted a physician for the problem. An unexpectedly high proportion of those who consulted a physician for headache had a history of panic disorder. Of those who recently saw a physician, 15% of women and 12.8% of men between the ages of 24 and 29 years had a panic disorder. In contrast, only 5% of women and 3.1% of men in the same age group who had never seen a physician for headache had a history of panic disorder. This suggests that comorbid psychiatric disease is associated with seeking care for headache disorders and that the association between migraine and panic disorder would be overestimated in a clinic-based study (Berkson bias) (54).

Women with panic disorder who had recently seen a physician for headache had more severe, complex, frequent, and debilitating headaches, and often had extended disability. Migraine headache was very common (36%) among those with panic disorder who sought care for headache. This epidemiologic study clearly demonstrates that a comorbid condition may be more highly ,represented in a clinic-based population.

Breslau et al. (47) reported on the association of migraine (using the IHS criteria) with specific psychiatric disorders in a sample of 1007 young adults aged 21 to 30 years in southeast Michigan. Persons with a history of migraine ($n = 128$) had significantly higher lifetime prevalences of affective disorder, anxiety disorder, illicit drug-use disorder, and nicotine dependence. Sex-adjusted odds ratios were 4.5 for major depression (95% CI 3.0-6.9), 6.0 for manic episode (95% CI 2.0-18.0), 3.2 for any anxiety disorder (95% CI 2.2-4.6), and 6.6 for panic disorder (95% CI 3.2-13.9) (55). The psychiatric comorbidity odds associated with migraine with aura were generally higher than the comorbidity odds associated with migraine without aura (47). Migraine with aura was found to be associated with increased lifetime prevalence of suicidal ideation and attempts, controlling for sex, major depression, and other co-occurring psychiatric disorders (56).

Using follow-up data gathered 3.5 years after baseline, Breslau et al. (57) reported on the prospective relationship between migraine and major depression in their cohort of young adults. The relative risk for the first incidence of major depression during the follow-up period associated with prior migraine was 4.1 (95% CI 2.2-7.4). The relative risk for first migraine during the follow-up period associated with prior major depression was 3.3 (95% CI 1.6-6.6). Although the onset of migraine was reported to have preceded the onset of major depression in more than one-half of the comorbid cases, partially confirming the report by Merikangas et al. (42-44), the relative risk for the first onset of migraine in persons with prior major depression was nearly as high as the relative risk for the first onset of major depression in persons with prior migraine.

In summary, recent epidemiologic studies support the association between migraine and major depression previously reported in clinic-based studies. Analysis of prospective data indicates that the observed cross-sectional or lifetime association between migraine and major depression could result from a bidirectional influence, from migraine to subsequent onset of major depression and from major depression to first migraine attack. Furthermore, these epidemiologic studies indicate that persons with migraine have increased prevalence of bipolar disorder, panic disorder, and one or more anxiety disorders. An association with illicit drug use disorder was reported by Breslau et al. (47), but this was not detected in the Zurich cohort surveyed by Merikangas et al. (43). An association with nicotine dependence reported by Breslau et al. (47) replicated previous reports of an increased prevalence of smoking in women with migraine (58, 59).

Alternative explanations and suspected mechanism

Associations between migraine and psychiatric disorders might be accounted for by two alternative explanations: (i) migraine is the cause of psycho-pathology or, conversely, is caused by it; and (ii) migraine and the psychiatric disorders associated with it have shared genetic or environmental risk factors.

Research to date has focused primarily on the migraine-major depression comorbidity. It has been proposed that major depression in persons with migraine might represent a psychologic reaction to repeated, disabling migraine attacks. Such an interpretation is consistent with the observation that, on the average, migraine has a younger age of onset than major depression and persons with comorbidity generally report an earlier age of onset of migraine than of major depression. Nonetheless, several lines of evidence suggest that, despite the typical chronologic pattern, major depression in comorbid cases cannot be adequately explained as a psychologic response to migraine attacks.

One line of evidence comes from a study of a biologic marker of depression in patients with migraine. Jarman et al. (60) administered the tyramine test to 40 migraine patients, 16 of whom had a lifetime history of major depression. Low tyramine conjugation, a trait marker for endogenous depression, was strongly associated with a lifetime history of major depression in subjects with comorbid disease, regardless of their current psychiatric status. The authors argue that the association of the trait marker with major depression in patients with migraine rules out the possibility that the depression is a psychologic reaction to migraine attacks.

A second line of evidence comes from the findings of Breslau et al. (51) demonstrating a bidirectional relationship between migraine and depression. In particular, the increased risk for the first onset of major depression in subjects with migraine weakens the hypothesis that major depression in persons with migraine is a psychologic response to disabling headache. The psychologic explanation for major depression associated with migraine would have predicted that the influence is only in one direction, that is, from migraine to subsequent major depression. Furthermore, Breslau and Davis (61) reported that the risk for new episodes of major depression (and/ or panic disorder) did not vary by the proximity of migraine attacks. Specifically, the incidence of major depression in persons whose last migraine attack had occurred more than 1 year before baseline was 15.4%, compared to 13.1% in persons with migraine attacks during the preceding year. A higher incidence of new psychiatric disorders in persons with active compared to past migraine would have supported the secondary (reactive) depression hypothesis.

Despite several parallels between migraine and major depression in neurotransmitter abnormalities and pharmacologic treatment, there is little direct evidence of shared mechanisms (62, 63). Based on two family studies of the co-segregation of migraine with major depression, Merikangas et al. (44) reported that there was no evidence that the association between the two disorders was transmissible within families by genetic or environmental mechanisms. It is possible that both disorders are accounted for by a common underlying condition. One possibility is that dysregulation in a neurochemical system within the brain, for example the serotonergic system, gives rise to both disorders. It is also possible that each condition somehow increases the risk for the other (56, 57, 64). The data regarding these choices are not clear at this time.

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