

The triggers or precipitants of the acute migraine attack

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The aim of this study was to evaluate and define the triggers of the acute migraine attack. Patients rated triggers on a 0–3 scale for the average headache. Demographics, prodrome, aura, headache characteristics, postdrome, medication responsiveness, acute and chronic disability, sleep characteristics and social and personal characteristics were also recorded. One thousand two hundred and seven International Classification of Headache Disorders-2 (1.1–1.2, and 1.5.1) patients were evaluated, of whom 75.9% reported triggers (40.4% infrequently, 26.7% frequently and 8.8% very frequently). The trigger frequencies were stress (79.7%), hormones in women (65.1%), not eating (57.3%), weather (53.2%), sleep disturbance (49.8%), perfume or odour (43.7%), neck pain (38.4%), light(s) (38.1%), alcohol (37.8%), smoke (35.7%), sleeping late (32.0%), heat (30.3%), food (26.9%), exercise (22.1%) and sexual activity (5.2%). Triggers were more likely to be associated with a more florid acute migraine attack. Differences were seen between women and men, aura and no aura, episodic and chronic migraine, and between migraine and probable migraine. □ *Headache, migraine, precipitants, triggers*

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Introduction

Clinical experience and a wealth of electrophysiological studies reflect the increased sensitivity of the brain of the migraineur compared with the non-migraineur. Migraineurs report excessive sensitivity to light, sound, motion, smells and other sensory stimuli in between migraine acute attacks (1). Cortical and brainstem evoked responses have reflected some of this heightened sensitivity (2). Failure of habituation of the migraine brain may underlie this altered state (3). It is therefore hardly surprising that the already sensitized brain responds readily to external and internal triggers. Many studies of these triggers have been published (4–22). Some uniformity is emerging, but differences between studies persist.

The large database used in this study, with many variables and accumulated during the normal course of patient evaluation, facilitates the study of

a large number of subjects as well as allowing the definition of frequencies and characteristics of triggers in different clinical situations.

This retrospective study was undertaken: (i) to characterize the triggers of a large group of migraineurs attending a headache clinic, (ii) to evaluate triggers in different forms of migraine (migraine with aura, migraine without aura, probable migraine, episodic and chronic migraine), (iii) to evaluate triggers in males vs. females, and (iv) to explore correlations between triggers and other characteristics of migraineurs and acute migraine attacks.

Patients and methods

Study population and study design

The study population consisted of consecutive patients treated by the author in his clinical

practice. A detailed headache evaluation was performed and all responses were recorded on a database. The evaluation included a thorough neurological history, structured headache interview and a detailed neurological examination by the author or neurologically and headache trained nurse practitioners. All patients were evaluated by the author. Data were recorded by the examiner 'face to face' in a database program designed by the author.

All patients studied met the International Classification of Headache Disorders (ICHD)-2 diagnostic criteria of 1.1, 1.2.1, 1.5.1 and 1.6 (23). Headache was present in all patients studied. Unremitting daily headache was excluded from the 1.5.1 group as it was felt that this group may not readily reflect changes induced by potential triggers.

Patients were excluded from the study if they had: (i) no headache; (ii) headaches thought to be related to trauma or injuries; (iii) complicated neurological problems, i.e. underlying brain or systemic illness related to their headaches; (iv) recent onset headaches, i.e. <1 month prior to study; (v) significant legal issues related to their headaches; (vi) been seen prior to the initiation of the database; (vii) declined to, or were cognitively not able to participate in the database interview; and (viii) language or intellectual barriers.

This was a retrospective analysis of a large clinical database. Approval was obtained from an institutional review board for the use of the patients' information. The personal identities of patients were discarded when the data were downloaded to the statistical package.

Patient symptom rating

At the initial visit the presence and characteristics of prodrome, aura and postdrome as well as duration of migraine in years and family history of migraine were recorded. Triggers were studied by two methods. Patient were asked to rate how often their migraines were precipitated by something, as well as how often individual specific triggers precipitated their migraine attacks. Triggers (as a whole; how frequently are your headaches triggered by something?, or individually including lights, weather, sleep disturbance, sleeping late, food, alcohol, not eating, neck pain, heat, hormone, stress, perfume or odour, exercise, sexual activity, and smoke) were recorded on a 0–3 scale (0, never; 1, occasional, 1–33%; 2, frequent, 34–66%; 3, very frequent, 66–100%). Headache characteristics [time to peak intensity of headache (in minutes),

headache duration (in hours), headache intensity (0–10 scale), headache character (throbbing, aching, pressure, stabbing), headache aggravated by activity, recurrence of headache (percentage occurrence), time to recurrence (in hours), usual time of occurrence of headache (morning, afternoon, evening, night, or 'any time'), medication responsiveness, acute and chronic disability, and patient social, sleep, habits, and psychological characteristics] were graded and recorded. Patients were asked to rate their symptoms experienced during the headache for an average headache. Variables were graded on a scale of 0–3 ranging from none to most, with intensity of headache being graded from 0 to 10.

Statistical analysis

Descriptive statistics were obtained using SPSS version 11 for the Macintosh (SPSS Inc., Chicago, IL, USA). Missing data were rare but, if present, that subject was excluded from analysis for a particular category being analysed. Descriptive statistics were used. Mann–Whitney *U*-test was used to compare triggers in patients with migraine vs. probable migraine, episodic vs. chronic migraine, migraine with aura vs. migraine without aura and in female patients with migraine vs. male patients with migraine. Trigger correlations were made using Spearman ρ . In all instances, *P*-values < 0.05 were considered significant.

Results

Demographic characteristics

Of the 1750 total migraine patients seen by the author at the initial visit, 84.3% were females and 15.7% were males. The mean (\pm SD) age of patients was 37.67 ± 12.0 years, the youngest being 13.0 years and the oldest 80.5 years; 33.8% were single, 60.2% married and 6.0% divorced. Almost 50% of the patients were college graduates. Ethnicity was not studied.

Headache diagnosis

Based on headache characteristics on initial evaluation, 1750 patients were diagnosed with ICHD-2 1.1, 1.2, 1.5.1 or ICHD 1.6 (total migraine population), 1207 were diagnosed with ICHD-2 1.1, 1.2 and 1.5.1 (migraine), 716 with ICHD-2 1.1–1.2.1 (episodic migraine), 491 with ICHD-2 1.5.1 (chronic migraine) and 543 with ICHD 1.6 (probable migraine). Daily unremitting migraine was present

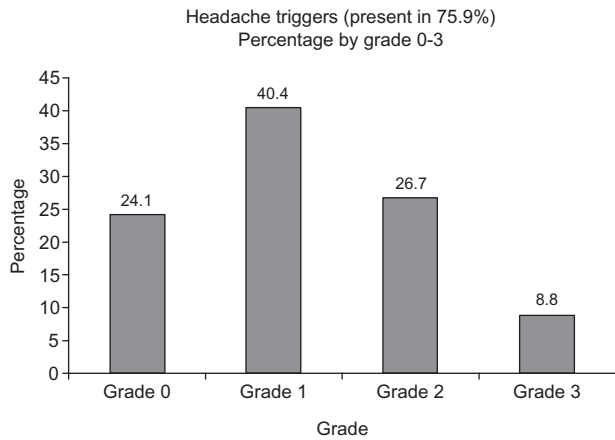


Figure 1 Percentage of migraineurs experiencing migraine triggers by asking patients to grade frequency of triggers overall (0–3). Patients were asked how frequently their migraine attacks were triggered by something (never 1–33%; 34–66%; and 67–100%).

in 133 patients, who were excluded from this study and will be the subject of a future study. These patients are different from the chronic daily headache patients who have some days without headaches. Their headache features tend to be less distinctive and their responses to triggers possibly blunted.

Characterization of triggers

Overall trigger frequency (see Fig. 1)

Migraines were triggered in 75.9% of patients, occasionally in 40.4%, frequently in 26.7% and very frequently in 8.8%. No triggers were seen in 24.1%. These frequencies were in response to querying how often migraines were triggered. Conversely, individual triggers occurred at least occasionally in 94.6% of subjects.

Individual trigger frequency (see Figs 2 and 3)

Triggers occurring at least occasionally are shown in Fig. 2. The frequency of individual triggers occurring at least occasionally varied enormously, from stress (79.7%) and hormones in women (65.1%) to, least frequently, sexual activity (5.2%). In reducing order of frequency these were: not eating (57.3%), weather (53.2%), sleep disturbance (49.8%), perfume or odour (43.7%), neck pain, specifically reported as not part of the headache but neck pain worsening and causing headache (38.4%), lights (38.1%), alcohol (37.8%), smoke (35.7%), sleeping late (32.3%), heat (30.3%), food, not specific which food (26.9%) and exercise (22.1%).

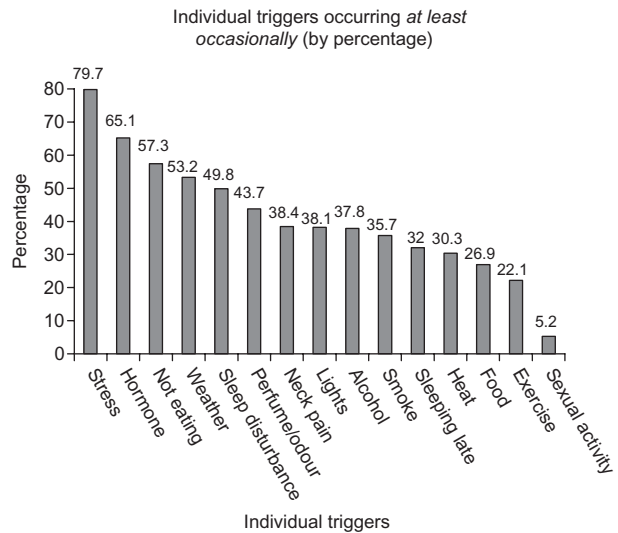


Figure 2 Percentage frequency of individual migraine triggers occurring at least occasionally (>33% of headaches). Hormone trigger refers only to women.

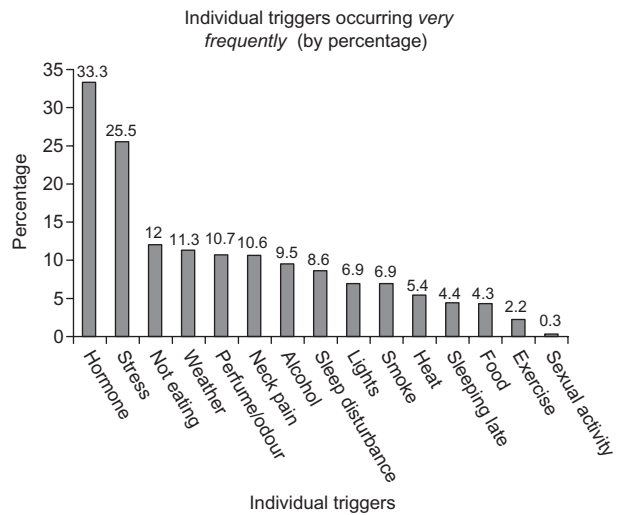


Figure 3 Percentage frequency of individual migraine triggers occurring very frequently (>66% of headaches). Hormone trigger refers only to women.

Triggers occurring very frequently are shown in Fig. 3. The commonest was hormones in women (33.3%) and stress (25.5%). The rest were much less common, as seen in Fig. 3.

Number of triggers per subject (see Fig. 4)

The mean number of triggers was 6.7 (SD 3.88), median 7.7; 23.2% patients had one to three triggers, 61% had between four and nine triggers and only 0.4% had all 15 triggers.

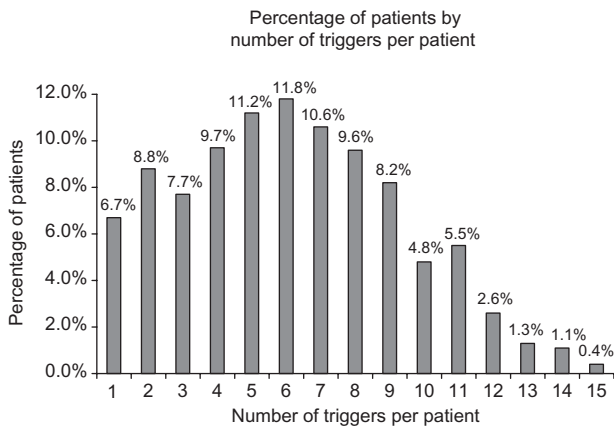


Figure 4 The distribution of the number of triggers per patient.

Comparison of triggers in different forms of migraine

Comparison of triggers in patients with migraine (ICHD-2, 1.1 and 1.2.1) and patients with probable migraine (ICHD-2, 1.6, see Table 1)

Patients with migraine had more hormone, light, alcohol, food and fewer sexual triggers than patients with probable migraine.

Comparison of triggers in patients with episodic migraine (ICHD-2, 1.1, 1.2.1) with patients with chronic migraine (ICHD-2, 1.5.1, see Table 1)

Patients with episodic migraine had less stress, not eating, perfume/odour, neck pain, smoke, sleeping late and exercise triggers than patients with chronic migraine.

Comparison of triggers in patients with migraine with aura (ICHD-2, 1.2.1) and patients with migraine without aura (ICHD-2, 1.1, see Table 1)

Patients with migraine with aura had more stress, not eating, weather, sleep disturbance, sleeping late, perfume/odour, lights, alcohol, heat, food and exercise triggers than patients with migraine without aura.

Comparison of triggers in females and males

Comparison of triggers in female patients with migraine and male patients with migraine (all ICHD-2, 1.1, 1.2.1 and 1.6, see Table 1)

Female patients with migraine had more weather, perfume/odour and heat triggers than male patients with migraine.

Table 1 Mann-Whitney U, comparing triggers in patients with migraine vs. probable migraine, episodic vs. chronic migraine, no aura vs. aura, and female vs. male patients

	Migraine vs. probable			Episodic vs. chronic			No aura vs. aura			Female vs. male			
	N	N	Z	N	N	Z	N	N	Z	N	N	Z	P
Headache triggers	1014	447	-3.170	808	343	-2.630	987	552	-2.732	877	145	-1.903	0.057
Stress trigger	1204	542	-0.040	674	276	-1.448	784	454	-0.703	878	144	-0.717	0.473
Hormone trigger	986	434	-3.448	808	343	-2.592	987	552	-3.159	878	144	-4.315	0.000
Not eating trigger	1205	543	-0.876	808	343	-0.058	987	552	-2.212	877	144	-1.921	0.055
Weather trigger	1205	542	-1.097	807	343	-1.841	985	551	-4.108	877	144	-4.315	0.000
Sleep disturbance trigger	1204	541	-0.173	807	343	-1.591	987	551	-3.099	877	144	-4.315	0.000
Perfume/odour trigger	1204	543	-1.172	808	342	-2.266	986	552	-1.165	878	143	-0.121	0.903
Neck pain trigger	1202	543	-0.302	808	343	-0.118	986	551	-5.577	878	144	-0.294	0.769
Lights trigger	1205	541	-2.278	773	324	-1.152	919	522	-2.213	846	128	-0.561	0.574
Alcohol trigger	1147	499	-2.566	618	270	-2.131	854	419	-1.306	687	110	-1.193	0.233
Smoke trigger	953	420	-1.368	628	282	-2.349	873	427	-4.108	703	115	-0.233	0.816
Sleeping late trigger	975	426	-0.053	773	332	-0.876	978	523	-2.552	845	139	-2.249	0.025
Heat trigger	1165	523	-0.297	809	343	-0.482	987	553	-3.487	878	145	-0.648	0.517
Food trigger	1206	543	-2.396	771	331	-2.243	975	522	-2.586	843	138	-1.539	0.124
Exercise trigger	1160	523	-0.957	728	312	-1.803	899	492	-0.242	808	122	-1.594	0.111
Sexual activity trigger	1100	470	-2.213	808	343	-2.630	987	552	-2.732	877	145	-1.903	0.057

Numbers in each group, Z scores and P-values are given in each category. Significant variables with $P \leq 0.05$ are in bold.

Table 2 Significant Spearman correlations of triggers as a whole

	No	Spearman's ρ	P-value
Family number of headaches	851	0.135	0.000
Headache duration in years	864	0.102	0.003
Prodrome premonitory symptoms	860	0.145	0.000
Postdrome syndrome	844	0.089	0.010
Throbbing quality	864	0.115	0.001
Pressure quality	864	0.075	0.028
Stabbing quality	864	0.128	0.000
Nausea	864	0.068	0.045
Photophobia	864	0.068	0.045
Running of nose/tearing of eyes	859	0.073	0.033
Osmophobia	818	0.139	0.000
Taste abnormality	675	0.099	0.010
Headache wakes from sleep	860	0.091	0.008
Choose to sleep/rest with headache	812	0.089	0.012
Headache response to acute medication	858	0.156	0.000
Percentage headache recurrence	666	0.107	0.009
Abnormal sleep rating	861	0.078	0.021
Trouble staying asleep	662	0.085	0.028
Anxiety	864	0.134	0.000
Depression	862	0.084	0.013
Mood swings	864	0.082	0.016
Aches and pains in general	863	0.070	0.039

Patients were asked how frequently their migraine attacks were triggered by something (never 1–33%; 34–66%; and 67–100%) compared with other variables. Migraineurs ICHD-2, 1.1, 1.2.1. Number of patients with data available, Spearman's ρ and P-values ≤ 0.05 are shown.

Correlations of triggers in migraineurs

Correlations of patients with migraine (ICHD-2, 1.1 and 1.2.1, see Table 2)

Migraine patients with triggers as a whole (rather than individual triggers) were more likely to have a higher number of family members with migraine, have longer duration of headache in years, more premonitory symptoms, postdrome, throbbing, pressure, stabbing, nausea, photophobia, running of nose/tearing of eyes, osmophobia, taste abnormality, headache waking from sleep, were more likely to choose to sleep or rest with headache, greater response to acute medication, have a higher percentage of headache recurrence, more trouble staying asleep, more anxiety, depression, mood swings, have more aches and pains in general. Migraineurs with triggers were less likely to rate their sleep as normal. Individual trigger correlations were not addressed in this study.

Discussion

Migraine management appears to have reached a plateau. Acute treatment paradigms have modified,

by not radically improved, responses to triptans in the past decade. Advances in preventive medication have widened the choice of treatment, provided a different range of side-effects and often, by so doing, allowed comorbid treatment. However, the success rate is still limited in a large number of migraineurs. The genetic underpinning of migraine cannot be modified. Therefore it seems appropriate to study the triggers of migraine in an attempt to reduce the frequency of the acute attack. Triggers may also be helpful in the diagnosis of migraine (4) as well as in understanding its pathophysiology.

Trigger evaluation and comparison with other studies

There are no comprehensive studies evaluating how many migraine attacks in an individual are actually recognized as being 'triggered' by a defined precipitant (although presumably all headaches are 'triggered' by something). Trigger evaluation is fraught with difficulties (5), not least of which may be the large number of 60 suggested potential triggers (6). At times it may be difficult to recognize the trigger, as sometimes the 'trigger'

such as light may also be part of the migraine attack, as in photophobia, or the trigger may be inconsistent. Furthermore, triggers may sometimes be difficult to distinguish from the premonitory symptoms. Sometimes there may be multiple triggers occurring at the same time, such as stress, not sleeping and weather changes, which may summate to trigger the headache. The trigger may be dose dependent, or the response time to the trigger delayed, making the association between the 'trigger' and the acute headache difficult to determine. Furthermore, triggers may change over time in the life of the migraineur or be modified by preventive medication.

The current study shows that trigger frequency is reported in 75.9% of patients when asked whether they have triggers for the migraine attack in general, and this figure rises to 94.6% when subjects are responding to a specific list of triggers. This compares with 85% (8), 79.3% without aura and 64.9% with aura (9), and 96.1% (8) in other studies.

The mean number of triggers per patient (Fig. 4) was 6.7, with almost two-thirds of patients having four to nine triggers. A median of three triggers per individual has been reported (7). Not documented in this study were rarer triggers such as crying (9, 10), laughing (10), reflux (13), medication triggers and the occurrence of triggers in combination.

The commonest individual triggers (Fig. 2) were stress (79.7%), hormones in women (65.1%), not eating (57.3%), weather (53.2%), sleep disturbance (49.8%) and perfume or odour (43.7%). Individual trigger frequencies were different when frequently occurring triggers were reported (see Fig. 3). In this instance, stress (33.3%) and hormones in women (25.5%) dominated the triggers. Thus, on a frequency basis, most individual triggers are identified by only a minority of patients, supporting other findings (8). Some of the trigger frequencies reported in other studies are summarized in Table 3 (4, 7, 8, 24, 13–20) and also thoroughly reviewed elsewhere (21).

Triggers in different forms of migraine and trigger gender differences

In the current study differences in individual triggers are seen between migraine and probable migraine, episodic and chronic migraine, migraine with aura and migraine without aura and females and males. Aura vs. no aura had more differences than the comparisons in the other groups, although a previous study showed only light to be a more frequent trigger in patients with aura, and

menstruation in patients without aura (24). There is no consistent pattern to these differences and more research in this area is appropriate. In another study, differences were found between females and males with regard to missing a meal, sexual activity, weather changes, perfume and smoke (18). The current study found females with migraine had more weather, perfume/odour and heat triggers than males with migraine.

Trigger correlations with migraine and other patient characteristics

The study shows a marked number of correlations of patients with triggers (studied as a whole rather than individual triggers). These migraineurs with triggers had more family members with migraine, longer lifelong duration of migraine, a more florid migraine profile as well as more comorbidity and sleep difficulties than migraineurs without triggers. Similarly, a correlation between the frequency and duration of attacks was found (7).

Management of triggers

Patients are generally advised to avoid triggers. Keeping a detailed calendar can help to define some triggers. Triggers such as lights, smoke, certain foods, alcohol, sleep disturbance, sleeping late, not eating, heat, neck pain, perfume or odour, sexual activity and exercise can be modified or avoided to some degree. Weather change trigger is not easy to anticipate or avoid. Hormonal triggers can be manipulated to some degree and this is an area with great potential for improvement. Stress management may offer a range of possibilities. The timing of the stress may be important. In one small study of 13 patients for 6 months stress was more likely to be found on the day before and the first day of the acute migraine attack, but not 2 or 3 days before the headache (22). In another study stress was more likely to occur in the 4 days preceding headache days than the 4 days before headache-free days (25). Stress in the current study occurred very frequently in 33.3% and in another study as the usual trigger in 32.9% (8). However, the timing of the stress was not defined in the current study. The effort to avoid triggers may itself act as a source of stress (8). Biofeedback, cognitive therapy (26, 27) and appropriate medication regimes clearly need consideration in up to one-third of patients with very frequent stress as a trigger.

Elimination diets and some trigger avoidance strategies can impose severe lifestyle restrictions

Table 3 Summary of other studies listing references, population studied, number of subjects, triggers as a whole and individual triggers

	Current study*	7†	24‡	8*	13‡	14*	15‡	16†	17*	18*	19*	20*	4*
No. of subjects	1207	217	484	289‡	500	69	132	385		494	77	429	38
Triggers	75.9	85.0	79.3/64.9§	96.1									
Stress	79.7	48.8	37.8/40.0§		79.0	72.4	51.1	42.0	76.0	62.0			84
Hormone	65.1	48.0	64.0		64.0		53.6	32.0	39.0	50			57
Not eating	57.3				44.0		58.9/35.3¶		48	40			82
Weather	53.2						54.4/37.5¶				50.6/62.3**		71
Sleep disturbance	49.8						37.2/56.3¶††		49	31			74
Perfume/odour	43.7						44.0/35.3			29			61
Neck pain	38.4												
Light	38.1				33.8					38			50
Alcohol	37.8	51.6	12.2/34.2§						28			30.2	42
Smoke	35.7		5.4/0.9§							26			61
Sleeping late	32.0						37.2/56.3¶††		27	24			
Heat	30.3												
Food	26.9	44.7			30.0				46	30		16.5	58
Exercise	22.1		6.8/14.5§						20	15			42
Sexual activity	5.2						10.9/11.8¶		3	5			

*Headache Clinic population.

†General population.

‡Chronic headache.

§No aura/aura.

¶Female/male.

**Documented/perceived by individual.

††Not specified whether sleep disturbance or sleeping late.

and more stress. Furthermore, it is hypothesized that avoiding triggers may not allow desensitization and, ultimately, relative immunity from the trigger to develop (28).

Potential shortcomings of the study

This study suffers from some limitations. It was centred on a single headache clinic and was not a population cross-sectional study. No diary documentation was available on the initial assessment, although some patients had documented headache profiles from prior provider evaluations. The large number of correlations performed in this study almost guaranteed that some would be statistically significant by chance. Also lacking is the study of the consistency of the triggers in individuals from headache to headache and over the lifespan of the individual. Furthermore, some patients (21% on the first office visit) were on preventive medication(s), which could have influenced some of the data being analysed.

Conclusion

Three-quarters of migraineurs have triggers at least occasionally for the acute attack, with stress, hormones in women, not eating, weather and sleep disturbance being the commonest. Triggers are more likely to be associated with a more florid acute migraine attack. Differences are seen between women and men, aura and no aura, episodic and chronic, and between migraine and probable migraine. Management of triggers may be an important aspect of migraine management.

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