

A nosographic analysis of the migraine aura in a general population

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Summary

The study presented here is the first detailed nosographic analysis of migraine aura, diagnosed using the criteria of the International Headache Society, in a sufficiently large sample for statistical analysis. Of 4000 people, 163 had migraine with aura. Sixty-two had attacks of migraine aura with headache as well as migraine aura without headache, and seven had exclusively migraine aura without headache. Visual symptoms were most frequent (99%), followed by sensory (31%), aphasic (18%) and motor (6%) symptoms. Those with several types of aura symptoms had visual aura in virtually every attack, while sensory, motor and aphasic aura were present only in a small number of their attacks. The typical visual aura starts as a flickering, uncoloured, zig-zag line in the centre of the visual field and affect the central vision. It gradually progresses towards the periphery of one hemifield and often leaves a scotoma. The typical sensory aura is unilateral, starts in the hand, progresses towards the arm and then affects the face and tongue. The

typical motor aura is half-sided and affects the hand and arm. The visual, sensory and aphasic auras rarely lasted >1 h, while the motor aura did in 67% (six out of nine). Four people had exclusively acute onset visual aura. The duration of the aura and the characteristics of the ensuing headache were typical for migraine with aura, suggesting that acute onset aura is a real phenomenon. Headache followed the aura in 93%, headache and aura occurred simultaneously in 4% and aura followed headache in 3%. The characteristic spread of each symptom and the sequence of different symptoms suggest that cortical spreading depression is the mechanism underlying the migraine aura. Our results do not suggest that alterations of the diagnostic criteria of the International Headache Society are needed. The intra-individual variation of aura symptoms shown in this study indicates that a simplification of the International Classification of Diseases, Neurological Adaptation is appropriate.

Keywords: migraine; aura; symptomatology

Introduction

The most precise descriptions of migraine aura originate from personal records made during attacks by physicians and other professionals, who had migraine with aura themselves (Airy, 1870; Jolly, 1902; Lashley, 1941; Hare, 1966; Lord, 1982), and from diary records made during attacks by a clinic population who suffered migraine with aura (Russell *et al.*, 1994). However, these records, especially those from single cases, may be criticized for lack of representativity and bias towards complicated and interesting symptomatology. Prospective records are very accurate, but there is very little published material, and that may not necessarily provide a representative description of the migraine aura. This can only be ascertained by supplementing these personal records with

the migraine history of the general population. Data from clinic populations are less appropriate, as they are biased by selection (Berkson, 1946; Rasmussen *et al.*, 1992). The diagnosis of migraine with aura is difficult. For example, photophobia can easily be mistaken for a migraine aura. For this reason only, interviews by physicians with experience in headache diagnoses can be considered valid in nosographic studies of migraine with aura (Rasmussen *et al.*, 1991; Henry *et al.*, 1992; Russell *et al.*, 1995).

This study is the first nosographic analysis of migraine aura in a representative sample of migraineurs from the general population, sufficiently large for statistical analysis. The participants were interviewed by a physician.

Material and methods

A sample of 3000 males and 1000 females, all aged 40 years, was drawn from the National Central Population Registry. The total population of the sampling area was 328 070, which is 54% of the Copenhagen County population and 6% of the total Danish population. Using data from the National Statistics, the sampling area was shown to be representative of the total Danish population regarding age, sex and marital status (Danmarks Statistik, 1993a, b). Regarding vocational categories and employment status, farming and fishing were under-represented both in the sampling area and in Copenhagen County (0.5% versus 5.4% in Denmark), and hence there were fewer self-employed individuals. Compared with the whole of Denmark, trades and services were over-represented, as were salaried employees. All people from the random sample were sent a questionnaire regarding migraine. Kappa (chance corrected agreement) was 0.87, validating self-reported migraine in the questionnaire against the diagnosis at the interview (Russell *et al.*, 1995). If the first questionnaire evoked no response, a second and subsequently a third one was issued. All people with self-reported migraine were invited to a general health examination and headache interview of 1 h duration. The study took place at the Glostrup Population Studies Section of the Department of Internal Medicine between March 1993 and June 1994. A

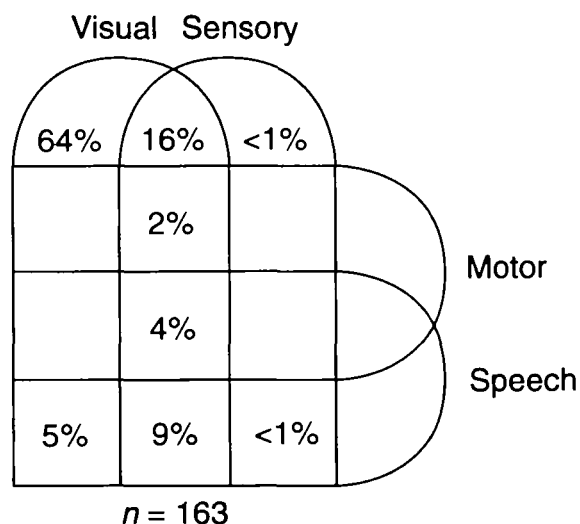


Fig. 1 Venn diagram illustrating the distribution of the various aura symptoms.

semi-structured headache interview was used. The examination included a physical and a neurological examination in order to exclude other medical or neurological disorders. The subjects not responding to the invitation were interviewed by telephone. The operational diagnostic criteria of the International Headache Society were used (Headache Classification Committee of the International Headache Society, 1988). One neurological research fellow (M.B.R.), experienced in headache research, took care of all the clinical examinations and interviews. A detailed description of the study design, representativeness of the population, and characteristics of the non-participants has been published elsewhere (Russell *et al.*, 1995). The project was approved by the Danish ethical committees.

Statistical analysis

All data were processed using SSPS Data Entry II and SPSS Base System for Windows 6.1.

Results

Of the 163 people (95 male and 68 female) who suffer migraine with aura, 62 people (36 male and 26 female) had attacks of both migraine aura with headache and migraine aura without headache and seven people (three male and four female) had exclusively attacks of migraine aura without headache.

General characteristics of aura symptoms

Visual aura was the most frequent symptom (99%), followed by sensory (31%), aphasic (18%) and motor (6%) aura. The various combinations of aura symptoms are illustrated in Fig. 1. Only visual aura frequently occurred in isolation, whereas sensory, motor and aphasic aura were nearly always experienced in association with visual aura. Table 1 shows the percentage of attacks with occurrence of the specific aura symptoms. Only visual auras were experienced in almost every attack (99%), whereas sensory, motor and aphasic aura were only present in a small percentage of an individual's total number of attacks. Migraine aura without headache was experienced by 42% of those with migraine with aura, but

Table 1 The percentage of attacks with occurrence of specific aura symptoms

| Percent of attacks | Visual aura ($n = 161$) | | Sensory aura ($n = 51$) | | Motor aura ($n = 9$) | | Aphasic aura ($n = 29$) | | Aura without headache ($n = 69$) | |
|--------------------|------------------------------|-----|------------------------------|-----|---------------------------|-----|------------------------------|-----|---------------------------------------|-----|
| | % | n | % | n | % | n | % | n | % | n |
| 1-24 | <1 | 1 | 35 | 18 | 44 | 4 | 31 | 9 | 36 | 25 |
| 25-49 | — | — | 16 | 8 | 22 | 2 | 14 | 4 | 13 | 9 |
| 50-74 | <1 | 1 | 14 | 7 | 11 | 1 | 10 | 3 | 29 | 20 |
| 75-99 | — | — | 2 | 1 | — | — | 7 | 2 | 12 | 8 |
| 100 | 99 | 159 | 33 | 17 | 22 | 2 | 38 | 11 | 10 | 7 |

only 10% of them had migraine aura without headache in every attack.

Visual aura

The characteristics of the visual aura are shown in Table 2. Seven people had exclusively visual aura without headache. Five people had acute onset visual aura, of these three had exclusively visual aura and headache and one had exclusively visual aura without headache. A fifth person had gradually progressing sensory and motor auras after the sudden onset of visual aura. The acute onset visual aura had a sudden onset in four people and developed during 1 min in the fifth person. It was flickering in three of the five people, and was unilateral in one person and bilateral in four people. Of the 49 people with bilateral visual aura, 21 had unilateral headache and 28 had bilateral headache. The typical visual aura starts as a flickering, uncoloured, unilateral zig-zag line in the centre of the visual field, it gradually progresses towards the periphery, often leaving a scotoma. The gradual progression lasted <30 min and the total duration of visual auras was ≤ 60 min. Only few had prolonged visual aura. Those who had visual aura exclusively tended to have shorter mean gradual progression and duration of their aura than those with visual aura in association with sensory, motor or aphasic aura (gradual progression \pm SD: 25 ± 19 min, versus 33 ± 42 min, $P < 0.20$; duration \pm SD: 33 ± 50 min versus 44 ± 63 min, $P < 0.30$).

Table 2 Visual aura symptoms

| Symptoms | Visual aura (<i>n</i> = 161) | |
|---|----------------------------------|----------|
| | % | <i>n</i> |
| Acute onset visual aura | 3 | 5 |
| Gradually developing visual aura | | |
| 5–30 min | 82 | 132 |
| 31–60 min | 11 | 17 |
| >60 min | 4 | 7 |
| Duration | | |
| 5–30 min | 69 | 111 |
| 31–60 min | 20 | 32 |
| >60 min | 8 | 13 |
| Location | | |
| Unilateral | 69 | 108 |
| Bilateral | 31 | 49 |
| Starting in the centre of the visual field | 62 | 94 |
| Starting in the periphery of the visual field | 28 | 42 |
| Scotoma | 50 | 79 |
| Preserved central vision | 22 | 36 |
| Zig-zag lines (fortification) | 81 | 128 |
| Flickering light | 87 | 138 |
| Colour | | |
| White | 47 | 74 |
| Yellow | 3 | 5 |
| Black | 3 | 5 |
| Rainbow colours | 12 | 18 |
| Other colours | 21 | 33 |
| No particular colour | 14 | 21 |

Sensory aura

The characteristics of the sensory aura are shown in Table 3. The sensory aura frequently affected the hand and face, whereas the body and the legs were rarely involved. Cheiro-oral symptoms were experienced by 97% (33 out of 34) of those with sensory aura in the face. The typical sensory aura is unilateral, starts in the hand and progresses up in the arm, then affects the face and tongue. The gradual progression lasted <30 min and the duration was ≤ 60 min. About one-fifth had prolonged sensory aura. Those with sensory aura not associated with motor aura tended to have shorter mean gradual progression and had significantly shorter duration of their sensory aura than those who had sensory aura in association with motor aura (gradual progression \pm SD: 32 ± 52 min versus 49 ± 50 min, $P < 0.05$; duration \pm SD: 74 ± 221 min versus 245 ± 460 min $P < 0.05$).

Motor aura

The characteristics of the motor aura are shown in Table 4. The nine people with motor aura had this in association with both visual and sensory aura (Fig. 1). No part of the body was affected by motor aura which was not also affected by sensory aura. However, four people experienced sensory aura and no motor aura in their face, while both sensory and motor aura were present in the hand. The motor aura was unilateral and affected the hand and arm. The duration was

Table 3 Sensory aura symptoms

| Symptoms | Sensory aura (<i>n</i> = 51) | |
|-----------------------------------|----------------------------------|----------|
| | % | <i>n</i> |
| Acute onset sensory aura | 2 | 1 |
| Gradually developing sensory aura | | |
| 5–30 min | 82 | 42* |
| 31–60 min | 2 | 1 |
| >60 min | 14 | 7 |
| Duration | | |
| < 5 min | 2 | 1* |
| 5–30 min | 67 | 34 |
| 31–60 min | 12 | 6 |
| >60 min | 20 | 10 |
| Location | | |
| Unilateral | 84 | 42 |
| Bilateral | 16 | 8 |
| Sensation of sensory aura | | |
| Face | 67 | 34 |
| Tongue | 62 | 31 |
| Hand | 96 | 49 |
| Arm | 78 | 40 |
| Foot | 24 | 12 |
| Leg | 24 | 12 |
| Body | 18 | 9 |

*One person experienced a gradually developing sensory aura of 3 min duration. The sensory aura affected the hand. It was preceded by a typical visual aura of 25 min duration and followed by headache.

Table 4 Motor aura symptoms

| Symptoms | Motor aura (n = 9) | |
|-----------------------------------|-----------------------|---|
| | % | n |
| Acute onset motor aura | 11 | 1 |
| Gradually developing sensory aura | | |
| 5–30 min | 56 | 5 |
| 31–60 min | 11 | 1 |
| >60 min | 22 | 2 |
| Duration | | |
| 5–30 min | 33 | 3 |
| 31–60 min | — | 0 |
| >60 min | 67 | 6 |
| Location | | |
| Unilateral | 100 | 9 |
| Bilateral | — | 0 |
| Sensation of motor aura | | |
| Face | 44 | 4 |
| Tongue | 44 | 4 |
| Hand | 89 | 8 |
| Arm | 89 | 8 |
| Foot | 56 | 5 |
| Leg | 56 | 5 |
| Body | 33 | 3 |

Table 5 Aphasic aura symptoms

| Symptoms | Aphasic aura (n = 29) | |
|---|--------------------------|----|
| | % | n |
| Duration | | |
| 5–30 min | 59 | 17 |
| 31–60 min | 24 | 7 |
| >60 min | 17 | 5 |
| Paraphasia | 76 | 22 |
| Impaired production of language (not due to paraphasia) | 72 | 21 |
| Impaired comprehension of language (not due to headache) | 38 | 11 |

prolonged in two out of three of those with motor aura. The mean gradual progression \pm SD and duration \pm SD of motor aura were 46 \pm 54 min and 13 \pm 18 h, respectively.

Aphasic aura

The characteristics of the aphasic aura are shown in Table 5. Only those with paraphasia, otherwise impaired production of language or impaired comprehension of language (not due to headache) were included as having an aphasic aura. Of the 29 people with aphasic aura, 15 also experienced dysarthria. Two people had exclusively dysarthria (not included as aphasic aura). Few had prolonged aphasic aura. The mean duration of the aphasic aura \pm SD was 43 \pm 43 min.

Succession of aura and headache

The headache followed the aura in 92.6% (137 out of 148), they occurred simultaneously in 4.7% (seven out of 148),

and aura followed headache in 2.7% (four out of 148). Information was missing in eight people. The specific succession of aura and headache was as follows.

Visual aura and headache. Headache followed the visual aura in 92% (86 out of 94), occurred simultaneously in 7% (seven out of 94) and visual aura followed headache in 1% (one out of 94).

Visual and sensory aura and headache. Visual aura was followed by sensory aura and then headache in 72% (18 out of 25), visual aura was followed by headache and sensory aura in 16% (four out of 25), headache was followed by visual and then sensory aura in 8% (two out of 25), and sensory aura followed by visual aura and then headache in 4% (one out of 25).

Visual, sensory and motor aura and headache. Visual aura was followed by sensory aura, motor aura and then headache in 50% (four out of eight), and sensory/motor or motor/sensory aura was followed by visual aura and then headache in 50% (four out of eight). Six of the nine people had co-occurrence of aphasic aura, but specific information was missing in four of them. One person had motor and sensory aura followed by aphasic aura, visual aura and then headache and the other person had visual aura followed by sensory and motor aura, aphasic aura and then headache.

Visual, sensory and aphasic aura and headache. Visual aura was followed by aphasic aura, sensory aura and then headache in 46% (six out of 13), visual aura was followed by sensory aura, aphasic aura and then headache in 31% (four out of 13), visual aura was followed by headache and then sensory and aphasic aura in 8% (one out of 13) and sensory aura was followed by aphasic aura and then visual aura and headache in 15% (two out of 13).

Visual and aphasic aura and headache. Visual aura was followed by aphasic aura and then headache in 100% (seven out of seven).

Sensory aura and headache. Information was missing.

Sensory and aphasic aura and headache. One person had headache followed by sensory aura and then aphasic aura.

Migraine aura without headache

Of the 62 people with attacks of both migraine aura with headache and migraine aura without headache, 52 had exclusively visual aura in all attacks of migraine aura without headache. Five people had visual and sensory aura without headache (one of them had aphasic aura as well), three people had visual, sensory and motor aura without headache (one of them had aphasic aura as well), one person had

visual and aphasic aura without headache, and one person had purely sensory aura without headache. Among those with attacks of both migraine aura with headache and migraine aura without headache, the mean duration of the visual aura tended to be longer in attacks accompanied by headache than in attacks without headache (38 ± 52 min and 26 ± 21 min, respectively, $P < 0.10$). Among the seven people with exclusively migraine aura without headache, the mean duration of the visual aura was 25 ± 13 min.

Discussion

Methodological considerations

The present study is the first nosographic analysis of the migraine aura in a group of thoroughly characterized people from the general population, which is sufficiently large to secure representative results. The skewed sample was chosen on the basis of our previous survey data in order to obtain approximately equal numbers of affected males and females with the different subtypes of migraine. The age of 40 years was chosen since onset of migraine most often occurs in the first four decades of life (Selby and Lance, 1960; Rasmussen and Olesen, 1992). The data are not presented separately for males and females, since we found no differences by gender. The sensitivity of self-reported migraine is 79% (Rasmussen *et al.*, 1992). This means that 21% of the migraineurs from the general population were not included in our material. However, it is most likely of only minor importance, since the four people without self-reported migraine and a clinical diagnosis of migraine with aura had very similar symptomatology to the 159 people with self-reported migraine and a clinical diagnosis of migraine with aura (Russell *et al.*, 1995). Thus, the results of the present study are considered valid and representative for the general population. In order to maximize descriptive accuracy, all interviews were performed by one neurological research fellow (M.B.R.) experienced in headache research. One interviewer is desirable, since the involvement of more interviewers invariably increases diagnostic variability (Leone *et al.*, 1994). Collection of exact information about migraine with aura is complicated by different types of bias. Both recordings during attacks as well as the migraine history may be biased by the individual's difficulties in describing important characteristics, especially if the person is confused during the attack. The episodic nature and the intra-individual variability (Russell *et al.*, 1992, 1994) may cause bias towards the more severe, recent or interesting attacks. The present data are collected using a high diagnostic standard, but are limited by the memory of the participants. The data represent characteristics of the 'typical' attack. In order to ascertain information about intra-individual variability, each participant was asked how often the specific aura symptoms occurred, and whether the aura always was associated with headache.

A more detailed discussion of the methodology has been published elsewhere (Russell *et al.*, 1995).

Characterization of the migraine aura

The migraine aura is most frequently visual followed by sensory, aphasic and motor aura. Visual and sensory auras were slightly more and motor aura slightly less frequent than in a previous less extensive population based survey made in the same area (Rasmussen *et al.*, 1992). The frequencies of sensory, motor and aphasic aura are higher in clinic populations (Jensen *et al.*, 1986; Peatfield, 1986), which can be explained by selection bias (Berkson, 1946; Rasmussen *et al.*, 1992). Attacks with sensory, motor and aphasic aura are really rare, since only a minority of those with migraine with aura ever have these types of aura and only in a minority of their attacks. The fact that only two people never experienced a visual aura, and that visual aura accompanied nearly all attacks in the other 161 people, suggests that sensory, motor and aphasic aura which are not associated with visual aura should be suspected of having another aetiology. A large family with familial hemiplegic migraine associated with cerebellar ataxia did not experience visual aura (Bisgård *et al.*, 1993), but our participants without visual aura did not have ataxia. The existence of acute onset aura has previously been doubted, but both the present and previous studies confirm its existence (Fisher 1980, 1986; Russell *et al.*, 1994). The duration and other characteristics of the acute onset auras were typical of migraine with aura which supports that the episodes were migrainous. However, data by history are subject to recall bias and some of the acute onset auras may in fact have been gradually progressing auras. Therefore, acute onset aura may be even rarer than what we find and it should be documented by prospective recordings using an aura diary (Russell *et al.*, 1994). The majority of people had aura prior to the headache, and only few had headache prior to the aura. Even this small number may be due to reporting bias. Information obtained during attacks indicates that aura symptoms always precede the migraine headache (Olesen *et al.*, 1990; Russell *et al.*, 1994). If the headache occurs prior to the aura it is usually a tension-type headache (Russell *et al.*, 1994). Thus, these rare attacks may be explained by an attack of tension-type headache followed by an attack of migraine with aura rather than biological variation of the attacks. Unilateral migraine, according to most previous studies, is equally often ipsilateral and contralateral to aura symptoms (Selby and Lance, 1960; Bradshaw and Parsons, 1965; Peatfield *et al.*, 1981; Manzoni *et al.*, 1985; Bana and Graham, 1986). However, information obtained during attacks indicates that only a minority of attacks have ipsilateral symptoms (Olesen *et al.*, 1990; Russell *et al.*, 1994). Due to this reporting bias we have refrained from recording headache and aura laterality. A surprisingly high number of people had attacks of both migraine aura with headache and migraine aura without headache, but only a minority of attacks in the individual participant were migraine aura without headache (Table 1). It is a general experience that attacks of migraine aura without headache become increasingly frequent with age.

Significance of results

The aura symptoms in the present study developed in a way which indicates a gradual spread in the great majority of people. Except for five people who only had acute onset aura, the other 158 people had gradually developed aura compatible with a contiguous spread of symptoms. This was also the case if more than one aura symptom occurred. We conclude from our nosographic analysis that cortical spreading depression remains the most likely explanation for the migraine aura (Leão, 1944). Although spreading depression most likely triggers the migraine aura, it is not always a sufficient trigger for the headache, since nearly half of the migraineurs also experienced migraine aura without headache. The severity of the migraine aura is variable, and sometimes it may be too weak to precipitate a headache. This is indirectly supported by the observation that migraine aura tended to be of longer duration if it was followed by headache. The hypothesis that migraine aura is triggered by spreading depression gets some support from a recent PET study during a spontaneous migraine attack (Woods *et al.*, 1994). The study clearly showed oligemia, but according to the description it was not a typical attack of migraine with aura, whether this is due to reporting bias (the attack occurred during the PET scan) is not clear. The criteria of the International Headache Society were easy to apply to people from the general population. The criterion of gradual development of aura symptoms over >4 min is essential, and caution is necessary in diagnosing migraine with acute onset aura. The gradual development of visual and sensory auras usually lasted <30 min, while the development of motor aura often lasted >1 h. The latter may be caused by memory bias, because of the long duration of motor symptoms. We could not set suitable rules for defining gradual development of aphasic aura and therefore only recorded the duration of this symptom. The duration of visual, sensory and aphasic aura were usually <60 min, confirming the validity of this criterion of the International Headache Society. However, motor aura can last for several hours. The classification of the International Headache Society, according to the present study, functions well in the general population and our results do not suggest alterations of the diagnostic criteria of the International Headache Society. The International Classification of Diseases, Neurological Adaptation subdivides migraine with aura in order to identify specific types of neurological symptoms (World Health Organization, 1993). Distinction is made between hemianoptic and other visual migraine, hemisensory migraine, migraine with aphasia, multiple types of aura, and other specified migraine with aura. Our results indicate that this subdivision is not useful, since attacks differ in each individual, and virtually no person had attacks with exclusively sensory, motor or aphasic aura. Hence most people would be coded hemianoptic and other visual migraine (G43.1) or multiple types of aura (G43.7). We suggest that future editions of the International Classification of Diseases,

Neurological Adaptation limits the subdivision of migraine with aura to comprise visual migraine, multiple types of aura, migraine aura without headache, basilar migraine and familial hemiplegic migraine.

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