

Precortical dysfunction of spatial and temporal visual processing in migraine

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Abstract

This paper examines spatial and temporal processing in migraineurs (diagnosed according to International Headache Society criteria, 1988), using psychophysical tests that measure spatial and temporal responses. These tests are considered to specifically assess precortical mechanisms. Results suggest precortical dysfunction for processing of spatial and temporal visual stimuli in 11 migraineurs with visual aura and 13 migraineurs without aura; the two groups could not be distinguished. As precortical dysfunction seems to be common to both groups of patients, it is suggested that symptoms that are experienced by both groups, such as blurring of vision and photophobia, may have their basis at a precortical level.

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Visual symptoms are a common feature of attacks of migraine with aura, appearing to the patient as scintillations, fortification spectra, and scotomata.¹ As well as this symptomatology, it is known that visual stimuli of various kinds can act as migraine triggers.^{2,3} Patients often complain, for example, that they are unable to drive at night for fear that the glare of oncoming headlights will cause a migraine. Clinical experience suggests that this kind of photosensitivity is not confined to patients who have migraine with aura, but also occurs when ictal visual neurological signs are not present (migraine without aura).

A number of studies have looked for interictal visual abnormalities in migraine. It has generally been assumed that migraine is not associated with ocular abnormality, and attention has tended to focus on the later stages of visual processing. In particular, electrophysiological studies have compared the steady state EEGs and visual evoked responses of migraineurs with those of controls, with equivocal results. Some studies report abnormality of the resting EEG, whereas others do not; the changes reported are not specific to migraine and the situation is further complicated by shifting views of what constitutes an abnormal EEG record.⁴ There is somewhat more consensus that the visual evoked responses of migraineurs are abnormal, but little agreement as to which components of the visual evoked response waveform are necessarily affected. For example, in studies with

pattern reversal as the evoking stimulus, Kennard *et al*⁵ showed an increased latency of the P100 component, Diener *et al*⁶ found no latency differences but an increased amplitude, and Benna *et al*⁷ found no differences between migraineurs and controls in either latency or amplitude. Consequently, it has not proved possible to use visual evoked potential measures to aid the diagnosis of migraine (although the occasional claim to the contrary occurs in the literature—for example, Marsters *et al*⁸). Furthermore, as a result of the many difficulties in methodology and interpretation in EEG and visual evoked potential studies,⁴ the potential of such studies to define a pathophysiological abnormality is low.

There has been little work using psychophysical techniques to investigate visual function in migraine. Khalil⁹ found that spatial contrast sensitivity is reduced at all spatial frequencies in migraine compared with controls. He also discovered that (a) contrast sensitivity decline is correlated with the number of years a person has had migraine, (b) hemifield contrast sensitivity is reduced on the aura side in patients who have migraine with aura, and (c) in patients with consistently lateralised head pain, hemifield contrast sensitivity is asymmetric but with no systematic relation to the pain side. Khalil also found that temporal contrast sensitivity is reduced in migraine with aura (but not in migraine without aura); these reductions were greatest at 10 to 12 Hz, and again correlated with the number of years of migraine.⁹

The results of Khalil⁹ are consistent with the hypothesis that there is some form of interictal abnormality in visual processing in migraine, which is related to the laterality of the migraine aura. There are some difficulties, however, in drawing firm conclusions from his work as Khalil describes visual dysfunction in migraine but his data do not allow us to localise the dysfunction to either precortical or cortical areas. It is the aim of this paper to consider this issue by presenting data from psychophysical experiments that specifically examine precortical visual processing.

We have made use of the “background modulation method,” which was developed for the measurement of low level visual response functions involved in threshold detection of a circular target.^{10,11} For reasons explained in the methods section, the characteristics of these response functions are thought to reflect postreceptor, precortical processing in the human visual system.

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Methods

SUBJECTS

Data were collected from a total of 40 age matched subjects: 11 migraineurs with visual aura (mean age 33.4 years), 13 migraineurs without aura (mean age 39.6 years), and 16 non-headache control subjects (mean age 31.6 years) who were mainly spouses or friends of the migraineurs. There were no significant differences between the ages of the subjects in the three groups. Patients were diagnosed according to criteria set out by the International Headache Society (Headache Classification Committee of the International Headache Society)¹² by neurologists at the Princess Margaret Migraine Clinic; the same neurologists ensured that none of the control subjects had had migraine. The table gives further details of the patients.

Experiments were approved by the ethics committee of Riverside Health Authority before the investigation began, and informed consent was obtained according to the declaration of Helsinki from all those participating. Colour vision and visual acuity were assessed for each person with the Ishihara colour plates and the Snellen visual acuity chart. Although some patients with migraine responded more slowly to the Ishihara plates, all subjects gave correct responses, and all wore appropriate lenses to give visual acuity of 6/9 or better during testing to correct for refractive errors.

TECHNIQUES

We have examined two response functions in our patients, one of which provides a measure of spatial and the other a measure of temporal vision. These functions arise in two different spatiotemporal (ST) visual mechanisms (or filters), referred to as the ST1 and ST2 mechanisms, which are involved in threshold detection of moving targets.¹¹ Each mechanism has its characteristic spatial response, the ST1 mechanism being tuned to higher spatial frequencies than ST2, which gives it higher spatial resolution. The ST1 spatial response seems to be a more sensitive indicator of abnormal function, as it is selectively impaired in conditions such as developmental amblyopia¹³ and we chose, therefore, to measure it in our patient group. Similarly each mechanism has a characteristic temporal response,

the ST1 temporal response being low pass (sustained) and the ST2 temporal response band pass (transient).¹¹ The second seems to be derived from the first, and as it is more readily determined, we have used it to assess temporal responses in the patients.

For ease of presentation in this paper we will refer to the ST1 spatial response simply as "the spatial response" and the ST2 temporal response as "the temporal response".

The spatial response was obtained by measuring the luminance of a target at which it could just no longer be detected against a background grating. The target moved across the grating and threshold luminance was determined for a series of background gratings with different periodicities. In our experiments the target moved horizontally and the grating was orientated vertically (inset fig 1). With a Maxwellian optical view system the circular target (3.5 degrees of visual angle in diameter) moved at 15 degrees/s in a horizontal direction over the central 8 degrees of the circular background, which was 17 degrees in diameter. The direction of the target's movement was reversed on successive presentations. The alternate light and dark bars of the background grating were of equal width, giving a grating period of $(2d)^{-1}$. The grating modulation was greater than 95% and its mean luminance was 3.5 log trolands.

The temporal response was obtained by measuring the luminance of a target at which it could just no longer be detected against a uniformly illuminated flickering background. The target variables were the same as those used in measuring the spatial response, and threshold was measured as a function of the frequency f_t of the background flicker. The mean background luminance was 3.5 log trolands and it flickered sinusoidally at 100% modulation.

Threshold luminance l_t was measured as a function of $(2d)^{-1}$ to give the ST1 spatial function and of f_t to give the ST2 temporal function; l_t values were obtained by a double interleaved staircase,¹⁴ for which the target luminances were set under computer control. The observer responded to each presentation of the target by pressing one of two response buttons, denoting target "seen" or "not seen", and thresholds were set to an accuracy of 0.03 log units.

The spatial mechanism has high spatial frequency and low pass, sustained temporal frequency responses, whereas the temporal responses have low frequency spatial and band pass (transient) temporal responses. These response characteristics led Barbur and Ruddock¹⁰ and Holliday and Ruddock¹¹ to associate the spatial and temporal mechanisms with the precortical P (parvocellular) and M (magnocellular) type projection pathways respectively. Other response features are also indicative of early visual processing; both types of response are monocularly controlled, are unaffected by the preadaptation to spatial patterns, and are essentially insensitive to the target size and to the orientation of the background grating.^{10 11}

Details of the 11 migraineurs with visual aura and 13 migraineurs without aura taking part in the ST1-spatial and ST2-temporal response tests

Patient group	Number of years with migraine (mean (SD))	Medication (expressed as proportion of patients on particular regime)	Average time since last attack (months)
With visual aura:	22.8 (20.1)	A (7/11) P + A (2/11) H (1/11) N (1/11)	1.6
Without aura:	22.6 (12.7)	A (7/13) P (1/13) P + A (2/13) H + A (2/13) N (1/13)	0.9

A = acute treatment alone; P = prophylaxis (atenolol or nimodipine) alone; P + A = prophylaxis plus acute treatment; H = homoeopathy alone; H + A = homoeopathy plus acute treatment; N = no treatment.

Figure 1 ST1 spatial: mean values for 11 patients with aura, 13 patients without aura, and 16 normal control subjects. The luminance required for detection of the target is plotted against the periodicity of the background grating. Below: diagram to show stimulus presentation.

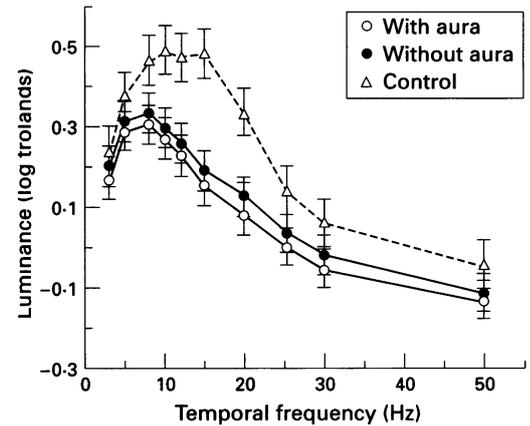
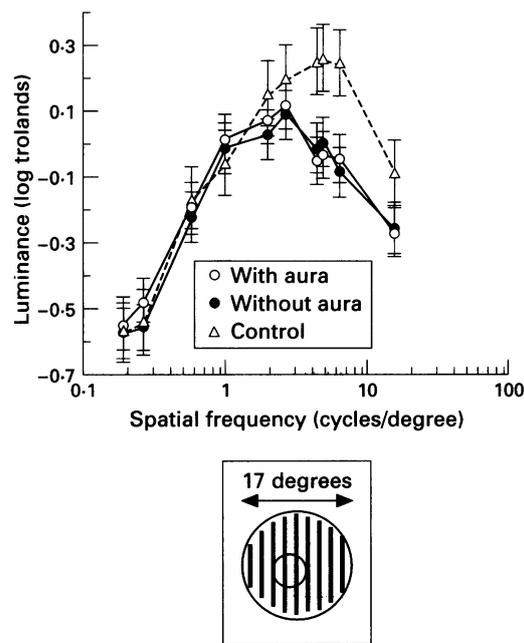


Figure 2 ST2 temporal: mean values for 11 patients with aura, 13 patients without aura, and 16 normal control subjects. The luminance required for detection of the target is plotted against the modulation frequency of the flickering background.

The experiments were performed monocularly (right eye), with the contralateral eye covered by a patch. Subjects were dark adapted for about 15 minutes before the start of testing. Testing took about two hours in total so that subjects could take frequent breaks to maximise their compliance. Patients in particular were encouraged to inform the investigator if they wished to stop testing at any time, but all were happy to complete the tests.

Results

Figure 1 presents the spatial responses. The log threshold luminance of the target required for its detection is plotted against the periodicity of the background grating (in cycles/degree). Figure 2 presents the temporal data, with log threshold luminance plotted as a function of the background flicker frequency (in Hz). Data are given in the form of mean (SEM) values.

Results for the spatial responses (fig 1) indicate that the control subjects generally required a higher luminance for detection of the target than both migraine groups, particularly against background gratings of higher spatial frequencies. This suggests that the spatial filter mechanisms responding to the background field were strongest in the non-migraineur group. An average peak response was obtained for the control subjects at a background frequency of 4.81 cycles/degree, similar to that reported by Barbur and Ruddock,¹⁰ whereas for both the migraineurs with aura and the migraineurs without aura, peak responses were obtained at 2.52 cycles/degree. It is also of interest to note that the two patient groups, diagnosed as distinct on the basis of International Headache Society criteria, could not be distinguished in our results.

The results for the temporal responses (fig 2) showed that a higher luminance level for target detection was again required by the control subjects, compared with both groups of patients who could not be distinguished. This reached significance ($p = 0.05$) for each of the frequencies between 10–20 Hz. The average peak response for the control group was obtained at 10 to 15 Hz, similar to that found by Holliday and Ruddock,¹¹ whereas for both patient groups peak responses occurred at 5 to 8 Hz.

Discussion

Both migraineurs with aura and migraineurs without aura showed a loss of sensitivity in response to those spatial structures to which normal subjects exhibit maximum sensitivity—that is, to spatial frequencies around 4 to 5 cycles/degree. Although the differences between the values recorded by either patient group and the normal subjects were not statistically different at the 0.05 level (t test) at any single frequency there was a consistent reduction in the values recorded for the patients at frequencies greater than 1 cycle/degree. At frequencies below this value all subject groups gave similar responses. The abnormal response pattern recorded with the patients differs from that found in other abnormal conditions, such as amblyopia for which the frequency response is displaced laterally, to one side of the normal function.¹⁴ With the computational methods described by Barbur and Ruddock,¹⁰ it can be shown that the spatial frequency response data for the migraineurs (fig 1) imply that the spatial resolution of the spatial mechanism is reduced, and that the centre-surround antagonistic organisation of its receptive field is abnormal.

Temporal responses also seem to be affected, as migraineurs showed a loss of sensitivity to temporal frequencies in the range 10 to 20 Hz, and as for the spatial responses patients with and without aura gave similar temporal responses. The values recorded for

either patient group differed significantly for each of the frequencies between 10 Hz and 20 Hz, and they were consistently lower than the normal values for all frequencies above 5 Hz. These results imply that the time constant for the temporal mechanism is abnormally long, and that its temporal resolution is impaired.

As discussed in the methods section the response mechanisms studied in these experiments seem to reflect precortical activity. The results indicate abnormalities in the responses associated with both mechanisms, which implies that both parvocellular and magnocellular projection pathways are disturbed. For both patient groups the measurements were made between attacks, and thus the changes in visual function could not have resulted from cortical visual disturbances or any other factor such as headache associated with an acute attack. This suggests that the disturbances of visual processing may represent intrinsic abnormalities in the connectivity of the magnocellular and parvocellular precortical visual pathways.

Alternatively, they may be a consequence of repeated migraine attacks with associated ischaemia, or of persisting interictal abnormalities of cerebral blood flow in the occipital lobe.^{15 16} Although Khalil⁹ found a correlation between the degree of abnormality in contrast sensitivity and the number of years of migraine attacks such a disturbance could arise at any level in the visual pathways, whereas our findings specifically relate to the precortical visual pathways. These pathways may be involved in ocular migraine,¹⁷ but this is an unusual form of migraine which was not present in any of our patients, and we know of no evidence for ischaemia in precortical visual pathways during attacks of uncomplicated migraine with or without aura. There is, however, a rich back projection from the striate cortex to the lateral geniculate nucleus that involves considerably greater fibre numbers

than the ascending geniculostriate pathway. It is conceivable therefore, that repeated dysfunction at a cortical level may give rise to retrograde geniculate disturbances, so altering the precortical visual responses.

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