

Migraine auras and the eyes of the mind

Giuseppe Nappi, MD^{a,b,d}, Cristiano Termine, MD^{c,d}

^a IRCCS “C. Mondino Institute of Neurology” Foundation, Pavia, Italy

^b Chair of Neurology, University “La Sapienza”, Rome, Italy

^c Child Neuropsychiatry Unit, Department of Clinical and Biological Sciences, University of Insubria and “Macchi Foundation Hospital”, Varese, Italy

^d University Centre for Adaptive Disorders and Headache (UCADH), Sections of Varese and Pavia, Italy

Corresponding author: Giuseppe Nappi, MD
IRCCS C. Mondino Institute of Neurology Foundation
Via Mondino 2, 27100 Pavia, Italy

What is migraine? What is migraine aura? One of the difficulties in answering these questions, which are only superficially simple and banal, lies in the great variety of ways in which these disorders can manifest themselves. Even though diagnostic practice is based on the detection of a series of symptoms and features, set out in the ICHD-II (1), clinical observations show that migraine is highly heterogeneous. It can evolve in very different ways in different individuals and, over time, even in the same individual (2). The frequency and intensity of the attacks, the accompanying neurovegetative symptoms, the response to symptomatic drugs, and the impact on the patient's life can all vary considerably. In short, we are faced with a complex disease: a range of possibilities that may be manifested in a myriad of neurological symptoms named aura. The most frequent aura type is visual (3), while a minority of patients may experience sensory (4), motor (5) or language disturbances (6), prosopagnosia, dyschromatopsia, ideational apraxia, alien hand syndrome, proper name anomia, or aphasia (7), indicating that other areas of the cortex distinct from the occipital lobes must be affected.

Visual migraine auras are windows onto the visual brain. Because they occur in awake, aware individuals whose self-reports are not subject to the uncertainties of other conditions that would qualify as hallucinations (i.e. visions without a stimulus), such as dreaming, psychoses or drug-induced states (8), they provide a valuable route for studying the neural mechanisms of visual awareness. The range of visual aura symptoms is wide (9) even though the majority of patients present, as a cardinal feature of the phenomenon, simple positive and/or negative (scotoma) components. The most common reports are of visual phosphenes and simple geometric patterns. The positive components are always described as very bright, usually white or silver but coloured in some instances, and as scintillating, flashing, or flickering. A second striking property of many, but not all, visual auras is that they spread in a stereotyped pattern across the visual field.

The most familiar descriptions of visual auras refer to the form known as fortification spectra. One historical example of such descriptions is that of Sir JFW Herschel, which dates back to 1866 and reads: “I was startled by a singular shadowy appearance at the outside corner of the field of vision of the left eye. It gradually advanced into the field of view and then appeared to be a pattern in straight-lined angular forms, very much in general aspects like the drawing of a fortification, with salient and re-entering angles, bastions, and ravellings with some suspicion of faint lines of colour between the dark lines” (10).

Lashley's 1941 self-report (11) clearly illustrates why visual aura can be used as a window onto the visual brain. Lashley described the progression of fortification spectra across his visual field during his own migraine aura and mapped these onto his visual cortex, concluding that the aura moved across his visual cortex at a rate of approximately 3 mm/min. A few years after this, Leão found that noxious stimulation of the exposed cortex of a rabbit produced a spreading decrease in electrical activity (cortical spreading depression, CSD) that moved at a rate of 2-3 mm/min (12). Some time later, Milner made the connection between Leão's CSD and Lashley's fortification spectra, proposing that CSD is the mechanism of aura (13). Whether or not Leão's CSD is the mechanism underlying migraine aura, it is nevertheless now widely accepted that a “spreading depression-like” process underlies the visual aura in migraine (14). Several recent studies using magnetoencephalography and high-field strength, high-resolution magnetic resonance imaging have established a link between migraine aura and CSD (15,16). For example, the propagation of CSD within the human primary visual cortex during migraine visual aura has been found to be congruent with the retinotopic progression of the visual percept that is generated by the phenomenon (16). The wavefront of neural excitation operating on intrinsic cortical networks is presumed to underlie the positive hallucinations and the subsequent neuronal depression, the scotoma (8). Auras generally precede headache onset and

experimental data, showing that CSD activates the trigeminovascular system (17,18), suggest that it is this activation that provokes the headache (19). The question that remains unanswered is how CSD is triggered in the human cortex during migraine aura. It has been suggested that genetic and environmental factors may modulate individual susceptibility by lowering the CSD threshold, and that cortical excitation may raise extracellular K^+ and glutamate levels sufficiently to initiate CSD (20).

The majority of positive migraine auras fall into the elementary hallucination category. Ictal blindness (scotoma) may accompany the positive features or may present alone in a variety of forms including complete hemianopia and tunnel vision. Much less frequent are auras classifiable as illusions or distortions. These include objects or persons appearing to be split, along fracture lines of varying form and orientation, into two or more parts that may be displaced and separated from each other ("illusory splitting") (21); the visual illusion of an extra edge around an object ("corona phenomenon") (22); the breaking up of the visual image into crystal-like facets ("mosaic vision") (23); the loss of smooth movements of observed scenes ("cinematic vision") (23); altered perception of shape (metamorphopsia) and size (micropsia and macropsia) (24), and impaired sense of the passing of time ("Alice in Wonderland syndrome") (24); out-of-body experiences, like the visual sensation of perceiving the environment from a location in space outside one's physical body ("autoscopy"), or the somaesthetic sensation of a duplicate of the body ("parasomatic body") (25). In addition, a patient may see little people, brightly coloured and clearly defined, tiny animals or fantastic creatures. In these latter cases, reality judgement may be well preserved, with the accompanying affective state characterised by feelings of delight and joy and only rarely by fear or terror ("Lilliputian hallucinations") (26).

But how does migraine aura impact on the lives of patients? Some people manage to live with their migraine and its aura manifestations quite well, leading a practically normal life, while others are heavily penalised on a personal, family, social and professional level. Furthermore, if, moving on from the observation of migraine aura's multiple clinical manifestations, we also consider the psychological aspects of this disease and the adaptive strategies patients employ, we find that the level of heterogeneity increases still further.

Aura is a visual disturbance, an "experience" that does not impair cognitive abilities. From a clinical point of view, this characteristic is so important that it is one of the criteria for the differential diagnosis of migraine aura. Indeed, during aura, a patient, in a state of perfectly lucid consciousness, can observe, describe and draw the phenomena that he or she experiences and consider them rationally and this is a fundamental factor differentiating the aura experience from dreaming and from psychosensorial phenomena (epileptic or induced by hallucinogenic drugs). These peculiarities are at the root of the emergence and development of "migraine art" (27), a phenomenon that arose in Britain in the 1980s out of the decision of the British Migraine Association (since re-named the Migraine Action Association) and Boehringer Ingelheim UK Limited jointly to sponsor an art competition open only to migraine sufferers. A good 900 paintings were submitted, but since some of the artists wanted their work back, only 562 are today included in the resulting collection of migraine art, an archive of extraordinary importance from a research perspective. For the patient, "migraine art" is a way of illustrating his pain, of expressing how he feels and what he sees during a migraine attack; it is also a way of highlighting the social consequences of migraine. In this field, the different pictorial techniques available can provide efficient and sometimes even the best possible means of expressing and conveying the patient's experiences, both the symptoms themselves and the migraine patient's reactions to his disturbances (e.g. 21,22,25,26). The word "art" is here used in its widest sense, without reference to specific aesthetic values.

The pattern of migraine aura manifestations is highly personal, whereas the far more frequent visual phenomena are, in most cases, surprisingly similar, being characterised by constant, recurring shapes. However, some "creative migraineurs" such as Giorgio de Chirico, Friedrich Nietzsche, Gerolamo Cardano, Lewis Carroll, and Hildegard of Bingen can be credited with turning what for some is merely disability into an opportunity for the spreading of knowledge and awareness. For individuals such as these, migraine provides the initial stimulus for a complex elaboration (technical, stylistic, cultural or philosophical), this process of elaboration being the element that distinguishes art from everything that is not art (28). Hence, de Chirico's statues suspended in emptiness, his disconnected atmospheres, his forms which evolve into seemingly impossible constructions, and the strong sense of suspended time exuded by his paintings are all brilliant and highly personal variants of a language whose vocabulary manages to overcome the purely subjective dimension (29) (Fig. 1).



Figure 1 - Giorgio de Chirico: "Return to the Castle" (Ritorno al castello), 1970.

Hildegard of Bingen (1098-1179), a German abbess and mystic with extraordinary intellectual insight and literary prowess, experienced throughout her life (starting in early childhood) “visions” of which she left remarkable accounts in two illuminated books: *Liber Scivias* and *Liber divinorum operum simplicis hominis*. Close examination of these accounts and illustrations suggest that her visions were of migrainous origin. Hildegard wrote: “The visions I have come to me not in sleep, in dreaming, or in folly. I perceive them not with my carnal eyes or ears, or in hidden places; fully alert, I perceive them in wakefulness, with the eyes of my soul and with my inner ears; I see them clearly through the eyes and according to the will of God.” Hildegard’s visions, charged with this feeling of ecstasy and full of profound religious and philosophical significance, contributed to her choice to live a deeply devout life. They provide a rare example of how a physiological event, which most people would dismiss without second thought as a nuisance or simply as a source of discomfort and distress, can become, in a heightened consciousness, the substrate of supreme ecstatic inspiration (23) (Fig. 2).

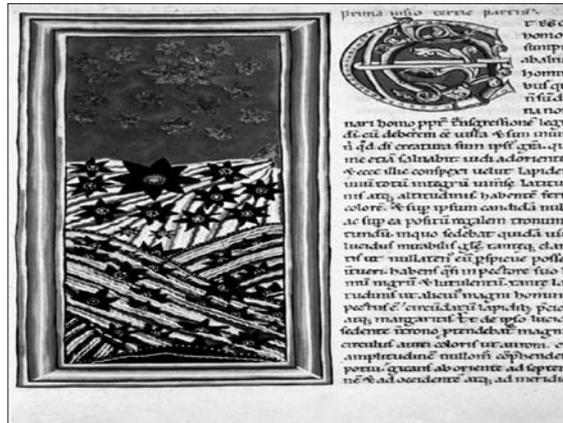


Figure 2 - Hildegard of Bingen: “The Fall of the Angels” (from *Liber Scivias*), 1141.

How is it that some people can transform migraine aura and migraine into a “short route to consciousness”, a source of creative inspiration? Perhaps more in-depth investigation (particularly using the new functional neuroimaging techniques) of the neurophysiological bases underlying these phenomena will enable us to tackle, with greater knowledge of the facts, questions that have, until now, been confined to the “grey area” between science and philosophy. Is there a physiological basis for those recurrent visual patterns that in the past have been called archetypes, paradigms, and even Platonic ideas, mental pictures and letters from the language of the Gods? Is the brain truly capable of “visual thought” (along the lines of Giordano Bruno’s hermetic diagrams), as well as propositional and symbolic thought? Is there a physiological basis for what is known, in philosophical tradition as the “mind’s eye”? The fact is that today we are able to approach migraine aura as a “window” onto the mind and on to its modular functioning, and we have Giorgio de Chirico, Hildegard of Bingen and other “creative” migraineurs to thank for helping us to open it.

References

1. Headache Classification Subcommittee of the International Headache Society. The International Classification of Headache Disorders – 2nd Edition. *Cephalalgia* 2004;24 (Suppl 1):9-160
2. Nappi G, Costa A, Tassorelli C, Santorelli FM. Migraine as a complex disease: heterogeneity, comorbidity and genotype-phenotype interactions. *Funct Neurol* 2000;15:87-93
3. Cologno D, Torelli P, Manzoni GC. Migraine with aura: a review of 81 patients at 10-20 years’ follow-up. *Cephalalgia* 1998;18:690-696
4. Jensen K, Tfelt-Hansen P, Lauritzen M, Olesen J. Classic migraine. A prospective recording of symptoms. *Acta Neurol Scand* 1986;73:359-362
5. Thomsen LL, Olesen J. Sporadic hemiplegic migraine. *Cephalalgia* 2004;24:1016-1023
6. Almeida DB, Arruda WO, Ramina R, Pedrozo AA, Raskin S. Migraine with aphasia. Report of a family [Article in Portuguese]. *Arq Neuropsiquiatr* 1999;57:111-113
7. Vincent MB, Hadjikhani N. Migraine aura and related phenomena: beyond scotomata and scintillations. *Cephalalgia* 2007;27:1368-1377
8. Wilkinson F. Auras and other hallucinations: windows on the visual brain. *Prog Brain Res* 2004;144:305-320
9. Queiroz LP, Rapoport AM, Weeks RE, Sheftell FD, Siegel SE, Baskin SM. Characteristics of migraine visual aura. *Headache* 1997;37:137-141
10. Herschel JFW. Familiar lectures on scientific aspects. London; Alexander Straham 1866:406
11. Lashley KS. Patterns of cerebral integration indicated by scotomas of migraine. *Arch Neurol Psychiatr* 1941;46:331
12. Leão AAP. Spreading depression of activity in cerebral cortex. *J Neurophysiol* 1944;7:359-390
13. Milner P. Note on a possible correspondence between the scotomas of migraine and spreading depression of Leao. *Electroencephalogr Clin Neurophysiol* 1958;10:705
14. Sanchez Del Rio M, Reuter U. Migraine aura: new information on underlying mechanisms. *Curr Opin Neurol* 2004; 17:289-293
15. Cao Y, Welch KM, Aurora S, Vikingstad EM. Functional MRI-BOLD of visually triggered headache in patients with migraine. *Arch Neurol* 1999;56:548-554
16. Hadjikhani N, Sanchez Del Rio M, Wu O et al. Mechanisms of migraine aura revealed by functional MRI in human visual cortex. *Proc Natl Acad Sci USA* 2001;98:4687-4692
17. Moskowitz MA, Nozaki K, Kraig RP. Neocortical spreading depression provokes the expression of c-fos protein-like immunoreactivity within trigeminal nucleus caudalis via trigeminovascular mechanisms. *J Neurosci* 1993;13:1167-1177
18. Bolay H, Reuter U, Dunn AK, Huang Z, Boas DA, Moskowitz MA. Intrinsic brain activity triggers trigeminal meningeal afferents in a migraine model. *Nat Med* 2002;8: 136-142

19. Moskowitz MA. The neurobiology of vascular head pain. *Ann Neurol* 1984;16:157-168
20. Ayata C, Jin H, Kudo C, Dalkara T, Moskowitz MA. Suppression of cortical spreading depression in migraine prophylaxis. *Ann Neurol* 2006;59:652-661
21. Podoll K, Robinson D. Illusory splitting as visual aura symptom in migraine. *Cephalalgia* 2000;20:228-232
22. Podoll K, Robinson D. Corona phenomenon as visual aura symptom in migraine. *Cephalalgia* 2001;21:712-717
23. Sacks O. *Migraine*. London; Faber and Faber 1991
24. Todd J. The syndrome of Alice in Wonderland. *Can Med Assoc J* 1955;73:701-4
25. Podoll K, Robinson D. Out-of-body experiences and related phenomena in migraine art. *Cephalalgia* 1999;19:886-896
26. Podoll K, Robinson D. Recurrent Lilliputian hallucinations as visual aura symptom in migraine. *Cephalalgia* 2001;21: 990-992
27. Wilkinson M, Robinson D. Migraine art. *Cephalalgia* 1985; 5:151-157
28. Nicola U, Podoll K. *L'aura di Giorgio de Chirico*. Milan; Ed. Mimesis 2003
29. Nappi G, Nisticò P, Nicola U, Podoll K. *Artemicrania? Opere e parole tra mal di testa e metafisica*. Rome; Il Cigno Galileo Galilei 2003