



# Visual aura and Visual disturbances of Migraine

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Nothing to disclose

# Aims

1. To describe the visual disturbances associated with primary headache disorders.
2. To describe the different forms of visual aura seen in primary headache disorders.

# Introduction



- Migraine is a complex disabling headache disorder which can be preceded or accompanied by visual symptoms.
- Migraine aura (MA) is a disabling neurological condition, characterized by transient visual, and less commonly transient sensory, motor and dysphasic disturbances.
- Affects 8% of the general population.
- 15% to 1/3 rd of migraineurs experience aura.



# Definition

- According to the International Classification of Headache Disorders, Third Edition (ICHD-3) migraine aura is defined as “**recurrent attacks, lasting minutes, of unilateral fully reversible visual, sensory, or other central nervous system symptoms that usually develop gradually and are usually followed by headache and associated migraine symptoms.**”
- Visual aura symptoms are by far the most common, occurring in 90% or more of patients, followed by sensory, language, and motor symptoms.
- Typical visual aura without headache : Aura is neither accompanied nor followed by headache of any sort within 60 minutes (mis labelled as optical or ocular migraine).

# ICHD 3<sup>rd</sup> edition Migraine with aura

At least 2 attacks fulfilling criteria B and C

B. 1 or more of the following fully reversible aura:

1. visual
2. sensory
3. speech and/or language
4. motor
5. brainstem
6. retina

C. At least 3 of the following :

1. at least one aura symptom spreads gradually over  $\geq 5$  minutes
2. 2 or more aura symptoms occur in succession
3. each individual aura symptom lasts 5-60 minutes
4. at least one aura symptom is unilateral
5. at least one aura symptom is positive
6. the aura is accompanied, or followed within 60 minutes, by headache

D. Not better accounted for another diagnosis.

# Other eye symptoms

- Migraine and other primary headache disorders can have other visual symptoms like photophobia, eye pain, dry eye, and anisocoria.
- Trigeminal autonomic cephalgia TAC (paroxysmal hemicrania, short lasting unilateral neuralgiform headache attacks(SUNCT,SUNA), & hemicrania continua ) : patients will experience one or more ophthalmic complaints- conjunctival redness, tearing.
- Primary stabbing headache occur in the periorbital region producing pain.

# Introduction

- Primary headache disorders can cause multiple visual disturbances that lead patients to frequently visit ophthalmologist and neuro-ophthalmologists.
- Unfortunately, the intermittent and subjective nature of the complaints leads to frustration for patients and for providers due to the lack of objective findings on clinical examination.
- Also causes significantly reduced vision-specific quality of life.

*Hanson LL et al . Headache. 2018;58:1007–1013.*

# Clinical features

Migraine aura is gradual in onset and progression in contrast to the abrupt onset of symptoms seen in brain ischemia or hemorrhage.

Unlike ischemia, positive visual and sensory symptoms (eg, flashing lights, paresthesia) are more common than negative ones.

The clinical features of migraine aura are remarkably variable both from one individual to another as well as from one attack to the next attack.

Sensory, language, or motor aura symptoms most commonly occur in conjunction with visual symptoms, although nonvisual aura symptoms occasionally occur in isolation.

Why migraine aura tends to involve the visual cortex remains unclear.

Higher neuron-to-astrocyte ratio in the visual cortex could be involved or the distinct columnar organization of the cortex could play a role.



# Incidence and Prevalence

- In population studies, the prevalence of migraine with aura among migraineurs can range from approximately 20% to 40%.
- Relative prevalence of migraine with aura compared with migraine without aura is approximately the same in women and men.

# Visual aura

- Visual aura is the most common type of aura, happens at least in some migraine attacks.
- 30% of migraine patients experience visual aura.
- Visual disturbances may consist of positive and/or negative phenomena; may be binocular or monocular.

# Visual aura



- The typical aura is teichopsia or fortification /scintillating scotoma is a combination of scotoma” and “zigzag or jagged lines” and/or “flickering light” that starts as a small, crescent-shaped zigzag image in the paracentral field that slowly grows in size as it moves toward the periphery.
- It typically begins at the center of the visual field and expands outward, but it can also begin peripherally and propagate toward the center.
- Often has a shimmering quality, some patients may perceive colors as well.
- The visual aura may propagate throughout an entire visual field or may remain spatially limited.



Courtesy Washing post

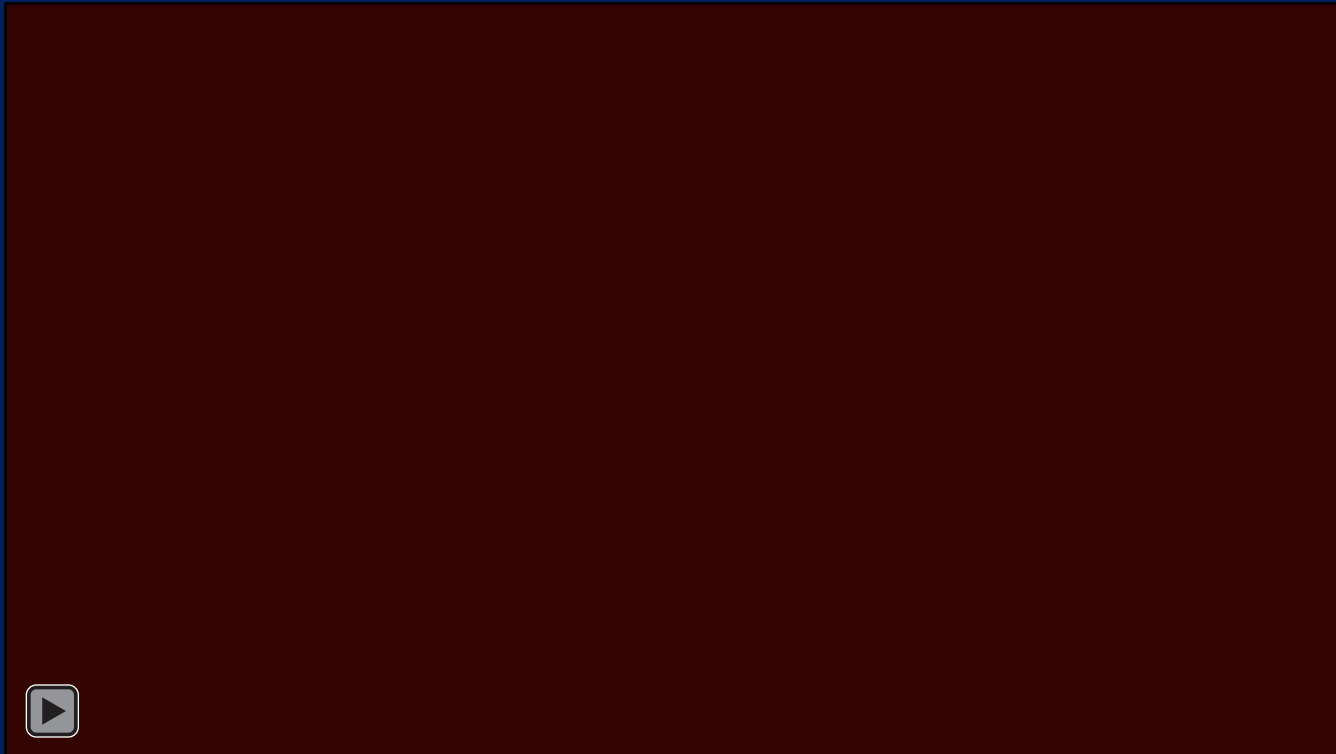
# Visual Aura

- Other common positive visual symptoms : flashes of bright light, sparkles, small bright dots/phosphenes.



# Visual Aura

- Negative visual symptoms : Foggy vision/blurred vision, scotoma, blind spots, Hemianopia, Tunnel vision.
- No consensus exists about whether blurred vision should be considered an aura.



# Perceptual Abnormalities

- Viewing through a kaleidoscope, cracked glass, or rain on a window, 'looking through heat waves or water' (Friedman).



# Perceptual abnormalities

- Polyopia and palinopsia ( trailing of images ) can also occur (Belcastro, Lee MS).



Belcastro V, et al Cephalalgia. 2011;31:999–1004.



# Other types of visual aura

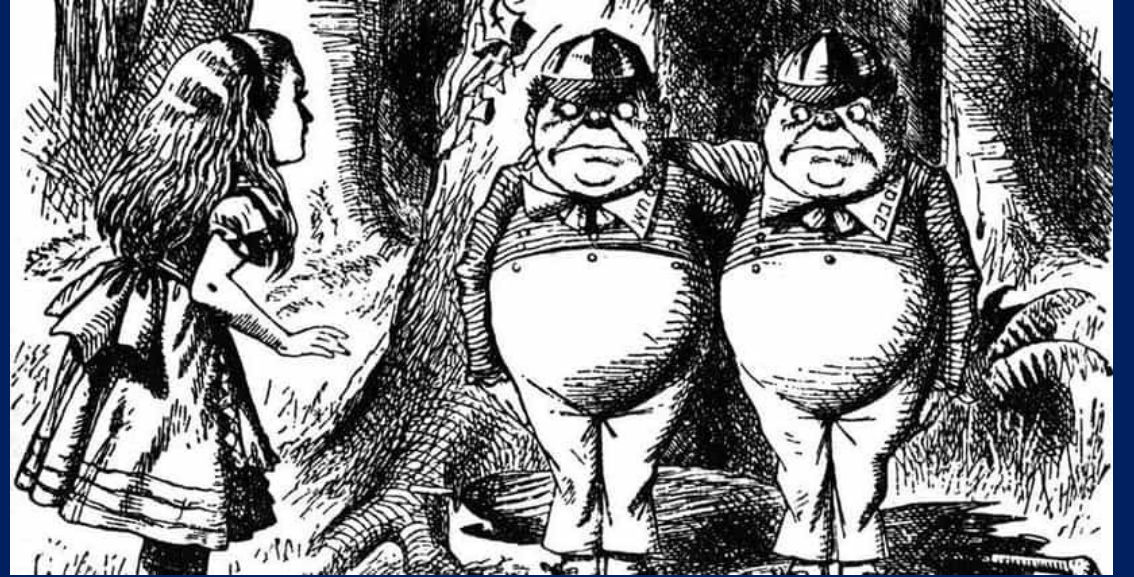
- White Spots
- 'Bean-like' forms ( crescent or C-shaped)
- Deformed images (alteration of line/ angles) / Metamorphopsia
- Curved or circular lines
- Round forms
- Oscillopsia /autokinesis (movement of stationary objects)
- Like a mosaic
- Micropsia/macropsia
- Things look closer, or look farther away than they really are
- Slanted vision

# Retinal migraine

Extremely rare cause of transient monocular visual loss, repeated attacks of scintillations, scotomata or blindness, associated with migraine headache.

- A. Attacks fulfilling criteria for Migraine with aura and criteria B.
- B. Aura characterized by both of the following:
  - 1. fully reversible, monocular, positive and/or negative visual phenomena (e.g. scintillations, scotomata or blindness) confirmed during an attack by either or both of the following:
    - a) clinical visual field examination
    - b) the patient's drawing of a monocular field defect.
  - 2. at least two of the following:
    - a) spreading gradually over  $\geq 5$  minutes
    - b) symptoms last 5-60 minutes
    - c) accompanied, or followed within 60 minutes, by headache
- C. Not better accounted for by another diagnosis, other causes of amaurosis fugax have been excluded.

# Alice in Wonderland Syndrome



- Episodic perception of distortion of one's own body or objects in the environment.
- Affects human perception to the senses of vision, hearing, touch, sensation, and phenomenon of time.
- Migraine is the most common cause, occurs in 15% patients (Blom).
- Various forms of metamorphopsia : micropsia, macropsia, teleopsia (objects appear unusually far away), pelopsia (objects appear unusually close).

# Alice in Wonderland Syndrome

- Can occur before a headache or separate from headache.
- Unclear whether this is a form of aura without headache.
- Does not meet criteria for a typical aura (Rastogi).
- Can respond to migraine preventive therapy (Beh SC, Blom ).

# Visual Snow

- A distinct entity from a migraine aura, lacks the characteristic features (Schankin CJ, White OB).
- Visual perceptual disorder closely associated with migraine, high degree of comorbidity with migraine (59%) or headache (87%).
- Patients experience a constant positive visual disturbance described as fine flickering dots similar to “television static”.
- Present throughout the entire visual field.
- Also have other visual disturbances, like palinopsia, entopic phenomena, photophobia, and nyctalopia.
- Clinical ophthalmological and neurological exam will remain normal.



*Schankin CJ, Maniyar FH, Digre KB, Goadsby PJ Brain. 2014;137:1419–1428.*

# Visual Snow - Pathophysiology



- A small functional imaging study showed hypermetabolism in the supplemental visual cortex of these patients (White SB).
- May be due to dysfunctional central sensory processing (Schankin).
- Visual snow is often refractory to treatment, but some efficacy for lamotrigine (Unal-Cevik), also used in migraine with aura, further supporting a link between visual snow and migraine.
- Migraine can aggravate this syndrome (White OB, Puleda F).

# Persistent aura without infarction

- Defined as an aura that is prolonged or remains continuous for a minimum of 1 week, with cases lasting as long as 28 years (Thissen).
- Such cases however merit evaluation for cerebral ischemia.

# Photophobia

- Means increased light sensitivity, exacerbation of the headache by light, or ocular discomfort due to bright lights.
- Believed to be mediated by the trigeminal autonomic system (Evans).
- Migraine is the most common reason for photophobia, can occur in the premonitory phase, also persist between migraine attacks because of baseline CNS hypersensitivity in the interictal period.
- Photophobia also reported in TAC and tension type headache.





# Photophobia

- One of the most common causes of eye pain in both ophthalmology and neurology clinics (Bowen).
- Fluorescent (FL)-41 filters may provide symptomatic relief in migraine and other disorders of photophobia (Katz BJ).



# Diplopia

- Migraineurs may have diplopia, monocular or binocular.
- Monocular diplopia could suggest symptomatic dry eye.
- Binocular diplopia is exceedingly rare in primary headache disorders and should merit evaluation for secondary etiologies like Idiopathic intracranial hypertension ( sixth nerve palsy).

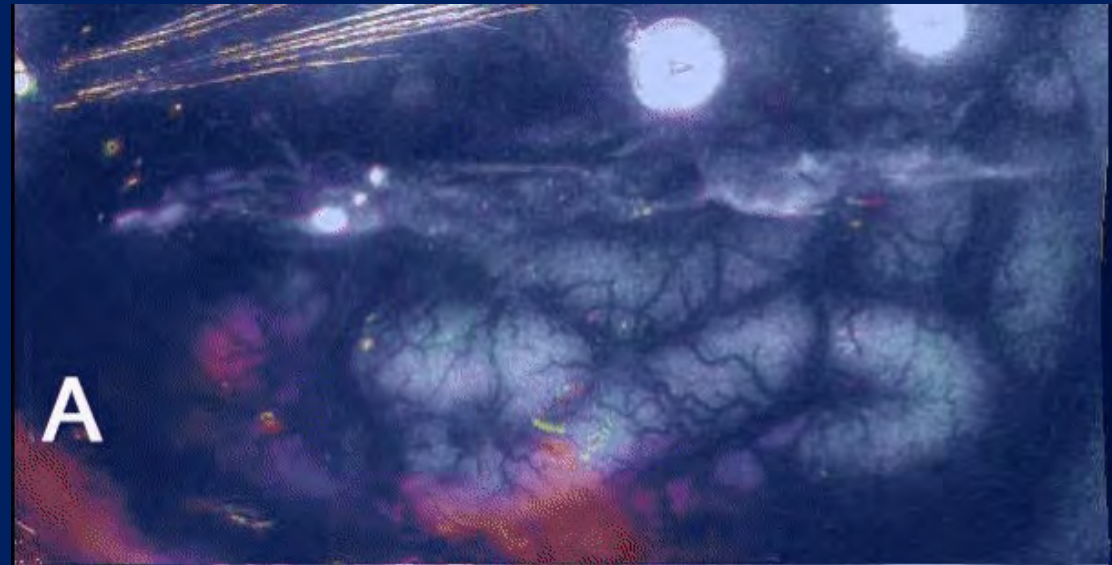


# Ophthalmoplegic migraine

- “Ophthalmoplegic migraine” is now understood to be a form of inflammatory cranial neuropathy; also termed “recurrent painful ophthalmoplegic neuropathy.”
- Need at least 2 attacks of unilateral headache associated with ipsilateral paresis of one or more ocular motor nerves.
- MRI head may show abnormal enhancement of the oculomotor nerve during the attack, usually at the nerve root exit zone in the interpeduncular cistern (Gelfand AA).

# Pathophysiology of migraine aura

- The positive and negative aura correspond with cortical spreading depression.
- CSD is an intense but self-limited neuronal and glial depolarization wave that slowly propagates (2-3 millimeters/minute) in the gray matter by way of chemical contiguity, a wave of excitation followed by inhibition and oligemia that spreads through the cortex.
- Slowly propagated waves of reduced blood flow over broad areas of the cortex have been reported in both migraine with and without aura.



# Pathophysiology of migraine aura

- A binocular phenomenon, but many patients perceive it as monocular.
- Both photoreceptor cells (rods and cones) and intrinsically photosensitive cells (melanopsin-producing cells) transmit signals to the trigeminovascular system that plays a key role in photophobia and pathophysiology of migraine and TAC.
- Marked efflux of cellular potassium and glutamate contributes to the cortical spreading depression that forms the electrophysiological basis of migraine aura phenomena.

# Migraine aura and vascular changes

- Risk of ischemic stroke is significantly increased in migraine with aura.
- Combined hormonal contraception (with estrogens) significantly increases the risk of stroke in women with migraine with aura (Tietjen et al).
- Although multiple organizations including WHO and the American College of Obstetricians and Gynecologists recommend against the use of estrogen-containing oral contraceptives in women with migraine with aura because of increased risk of stroke, the evidence supporting this recommendation is mixed and has many confounding factors.

# Migraine aura and vascular changes

- While substantial evidence clearly exists for the association between migraine with aura and stroke, the mechanism(s) for this association remains unclear.
- During migraine aura, brain hypoperfusion may occur as indicated by positron emission tomography (PET), MRI perfusion, and arterial spin labeling studies.
- Hypoperfusion may also extend to regions of the brain beyond those related to aura or occur in patients without clinical symptoms of aura.

# Migraine aura and vascular changes

- Hyperperfusion has also been reported in some cases during aura and in other cases following aura symptoms.
- Neither the hypoperfusion nor the hyperperfusion are strictly correlated temporally or spatially with either aura or headache, indicating that the blood flow changes are not primarily responsible for aura symptoms.
- It is extremely rare for the hypoperfusion associated with migraine aura to reach the threshold for ischemia, **migrainous infarction is rare.**
- While migraine aura itself does not result in stroke, migraine aura mechanisms may worsen stroke when it occurs because of causes other than migraine .



# Red flag symptoms

- Fever, weight loss
- Persistent visual symptoms
- Pulsatile tinnitus
- Neurological symptoms- focal weakness, gait instability, change in speech
- Comorbid conditions – malignancy, immunosuppression, pregnancy
- Precipitated by Valsalva like activity
- Headache worsened with postural changes
- Acute change in headache
- Age above 50 years
- Abrupt onset of symptoms

Think : infection, mass lesion, venous sinus thrombosis, optic nerve ischemia, stroke, intracranial hypertension, intracranial hypotension.

# Migraine aura needing evaluation

- Homonymous hemianopia reported in migraine, can be permanent(Wakakura) and seen on automated perimetry during acute migraine (Luu).
- r/o acute ischemic stroke, headache can occur in posterior circulation strokes in a minority (Pollak).
- Ascertain that the visual disturbance especially when occurring first time is consistent with migraine and not a vascular disorder.
- Migraine aura is difficult to distinguish TIA and stroke.
- Migraine is 3<sup>rd</sup> most common stroke mimic, accounts for 18% of all improper thrombolytic treatment( Terrin A).
- When TIA cannot be completely ruled out, aspirin therapy can be used for migraine prevention and vascular prophylaxis (Baena).

# Differential diagnosis

- Cerebrovascular disorders
- Giant cell arteritis
- Retinal detachments
- Increased intracranial pressure
- Epilepsy
- Occipital lobe epilepsy can also cause visual aura but , this has abrupt onset, duration is < 5 minutes, image remains lateralized in a single hemifield and fixed, but migraine aura can alternate sides and/or cross the vertical midline with slow spread( Hartl E).

# Treatment

- Most currently available acute therapies for migraine primarily target the headache phase with limited effectiveness in managing aura.
- Preventive treatments are often considered, especially if the headache and aura are intrusive and frequent.
- No treatments are specifically indicated for the prevention of migraine with aura.

# Treatment

- Migraine with aura may be less responsive to triptans than those without aura.
- Some neurologists hesitate to use triptans in patients with aura due to concerns regarding possible vasoconstrictive effects.
- However magnetic resonance angiography (MRA) studies indicate that triptans do not, in fact, constrict intracranial blood vessels and no evidence supports a contraindication to triptans as acute therapies in attacks of migraine with aura.
- Two randomized controlled trials concluded that triptans had reduced effect when administered during the aura
- An open label study found that oral sumatriptan given during the aura had a higher success rate for reducing headaches than it did when given 4 hours after the onset of pain (89 vs. 21% of patients).

# Treatment

- Studies have provided evidence that ketamine may be helpful for migraine with prolonged aura, but this approach has not been widely adopted.
- Animal studies have shown that ketamine, an antagonist of the NMDA glutamate receptor, blocks CSD propagation.
- Intranasal ketamine has been shown to reduce the severity but not the duration of visual aura in a group of 18 patients with migraine and prolonged aura.

# Treatment

- Currently, the only treatment specifically indicated for the acute treatment of migraine with aura is single-pulse transcranial magnetic stimulation (approved for use by the US (FDA)).
- When applied to the cerebral cortex, currents are induced that may influence cortical excitability and block waves of cortical spreading depression.
- Another noninvasive treatment is vagus nerve stimulation applied within 20minutes from headache onset, which was shown to abort migraine in 21% of patients compared with 10% of controls.

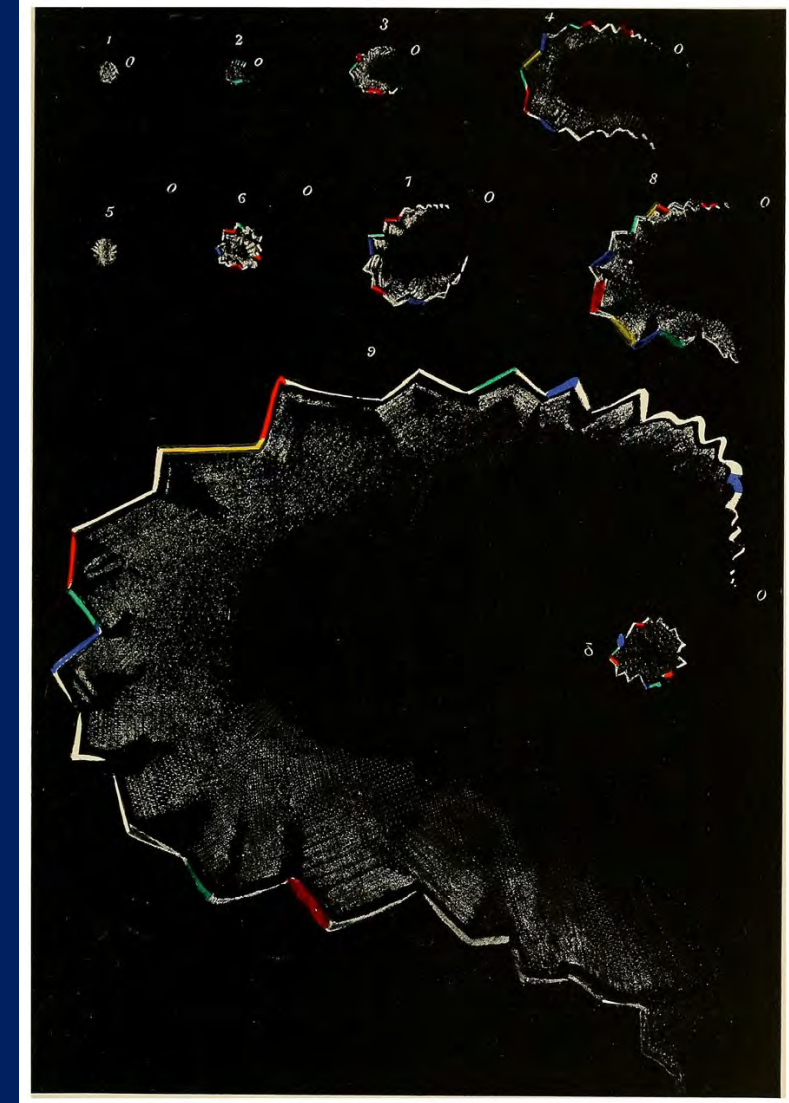
# Psychiatric comorbidities

- Migraine with aura has been reported to be associated with a number of psychiatric comorbidities including depression, bipolar disorder, panic disorder, and suicidality.
- Interestingly, however, patients with migraine aura without headache were reported to have reduced affective disorder and suicidality compared to those with headache.
- The mechanisms underlying these associations remain unclear but could include shared pathophysiology regarding neurochemical function or cortical excitability.



# Conclusions

- Migraine and other primary headache disorders cause a variety of neuro-ophthalmic complaints that may be distressing for the patient.
- Usually, examination is normal during the episodes or in between.
- Physicians should become familiar with headache disorders and associated visual symptoms.
- Should also recognize when a patient's symptoms are atypical and consider further investigation for secondary causes.



# Conclusions

- The migraine aura is a dramatic neurologic event with complex neural and vascular mechanisms.
- Refined understanding of its clinical features, comorbidities, patterns of propagation in the human brain, and specific responses to therapy can add important new insight into the pathophysiology of migraine and its optimal therapy.

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