Palinopsia, Perservation, Sparkle and Scintillations

Making Sense of Visual Hallucinations
Visual disturbance

- Altered visual perception is a frequent presenting complaint in the clinical setting.
- Often the examination is not always helpful and reliance on the history becomes critical in assessing the underlying source of the complaint.
- There is utility in characterizing the specifics of the hallucination.
- The most value in determining etiology comes from a knowledge of co-existent medical history.
Visual Hallucinations

• Used in a general sense, a sensory perception in the absence of an external stimulus

• Illusions are a misperception or distortion of true external stimulus

• Similar to evaluating any other subjective complaint, history, context, co-morbidity and time course are key in establishing likely underlying etiologies.
Key historical features

- Monocular versus binocular (helps to localize where in visual pathway) Also if binocular is the image identical in each eye.
- Formed versus unformed
- **Time of onset, duration and evolution**
- Provoking factors
- Other medical history, medications
- Other associated symptoms
Temporal course

- Tempo of onset
  - Evolution or expansion
  - Maximal at onset

- Duration of symptoms
  - Seconds (retinal detachment and/or vitreous traction, outer retinal pathology, seizure)
  - Minutes (TIA, migrainous aura)
  - Hours (infarction or prolonged aura, other degenerative or structural brain lesions)
Monocular versus Binocular

- Many patients have not thought to check
- I always make sure that they are actually covering each eye separately
- If they are sure they are bilateral it is useful to assess if they are seeing the same exact disturbance in both eyes, retrochiasmal pathology is usual the same with either eye viewing but there can be ocular pathology that is bilateral as well
Formed versus unformed

- Unformed also sometimes called simple are lines, circles, dots, trails, streaks, sparks, occasional other shapes but are not complex structural images.
- Formed or complex include people, animals, insects, objects, scenes.
Provoking factors

- Do certain backgrounds or lighting trigger it?
- Positionally dependent?
- Present only at night or in the dark.
- Began after a change in medication or medical therapy?
Ocular pathology

- Retinal pathology
  - Usually simple, brief with intact insight
  - Can be binocular but should at least be different with each eye
  - Often include light and sometimes motion
  - Photopsias can be associated with some of the outer retinal pathologies or cancer associated retinopathy as well as some of the retinal dystrophies
  - Should be promptly evaluated to r/o retinal detachment, hole or tears.
Ocular pathology

- Corneal edema related to elevated of IOP
  - Acute angle closure
  - Pigment dispersion syndrome, a disorder where pigment is lost from the posterior surface of the iris and can clog the trabecular meshwork leading to IOP elevation

- Some clues can be symptoms that occur following exercise or are related to positioning.

- Usual bilateral but may be different in each eye. Generally cause halos sometimes colored/rainbow like.
Migraine Aura

- By far one of the commonest cause of visual hallucination, often is diagnosed by excluding other potential etiologies.
  - Drug prescription and illicit toxicity or withdrawal
  - Metabolic derangement
  - Psychiatric
  - Neurodegenerative
  - Focal CNS pathology (stoke, tumor, AVM)
  - Release hallucinations
  - Seizures
Alcohol and drug use and withdrawal

- Toxicity

- In a general sense any drug that effects the central nervous system has the potential to induce an altered mental status to include visual hallucinations and make occur in the absence of any other symptoms of confusion or delerium. Can be a toxic effect or withdrawal

- Often are complex and vivid, full field and binocular
Withdrawal hallucinations

• Often accompanied by other tactile hallucination, formed, persistent and full field.

• With alcohol usually occurs 24 hours after last ingestion, (also seen with other sedative withdrawal)

• Accompanied by agitation, tremulousness, and other excessive adrenergic symptoms.

• Less likely to see hallucinations with opioid or cocaine withdrawal.
Drug toxicity

- Can be seen with prescription as well as illicit drugs.
- Hallucinations are bincoular sometimes stimulus dependent and long lasting.
- Can be formed or simple or causing a color cast to the vision.
- Pathology can localize to the retina or CNS
Drug toxicity

- Digoxin can cause Xanthopsia which is a predominance of yellow tones in one’s vision, seen in up to 15% of patients with digoxin toxicity (Br J Ophthalmol. 2002 Nov; 86 (11): 1259-1261).
- Sildenafil can cause cyanopsia, a term for seeing everything with a bluish tint.
- In both of these toxicity states the pathology is at the retinal level and has been demonstrated with electrophysiologic testing of the retina.
- Anticholinergic and dopaminergic medications can be associated with more vivid formed hallucinations and possibly associated with confusion.
Xanthopsia, “yellow vision”
Cyanopsia
Drug effects

• Hallucinogenic persisting perception disorder (HPPD)
  • After taking hallucinogenic drugs up to 25-50% experience flashbacks (a feeling of being under the influence of the drug)
    • most commonly associated with lysergic acid diethylamide but can be seen with psychodelic mushrooms, MDMA or ecstasy and cannabis.
    • Light streaking, trailing, palinopsia, visual snow, photopsias.
    • Can be provoked by entering into dark room or motion.
    • Medications that can provoke it can be phenothiazines, amphetamines, anti-parkinsonian drugs, SSRIs
Drug effects, Palinopsia

- Palinopsia or after imagery, is a particular type of visual hallucination, where there is the persistence of visual imagery after the stimulus is removed.

Palinopsia

- Hallucinatory
  - Not affected by environment
  - Long lasting, high resolution and complex
  - Lesion of posterior visual pathway lesions, seizures.
  - Cortical deafferentation leads to unregulated or uncontrolled neuronal discharges that are unaffected by environmental stimuli.
  - Etiologies include stroke, neoplasm, infection and arteriovenous malformation.
Illusory Palinopsia

- Illusory
  - Unformed, indistinct and are affected by light and motion.
  - Prescription drugs, illicit drugs, migraine, head trauma.
  - Postulated to be secondary to alterations in cortical excitability.
  - Depend heavily on background contrast, stimulus intensity, motion, flickering.
### Medications associated with Palinopsia

- Topiramate
- Clomiphene
- Trazodone
- Nefazodone
- Risperidone
- Mirtazapine
Metabolic encephalopathy

- Visual hallucinations can occur as part of a more generalized delerium
  - Confusion, agitation and other tactile hallucinations and delusions may be present.

- Differential diagnosis in addition to drug toxicity or withdrawal include
  - Infection, ischemia, hepatic or renal disease, other metabolic or endocrinologic derangement.
### Psychiatric Hallucinations

- Auditory hallucinations are twice as common
- Carefully consider drug/alcohol toxicity or withdrawal.
- Careful medication history
- Consider other etiologies that may be evaluated or treated differently.
Neurodegenerative Disease

- Often seen as a common clinical feature in the parkinsonian syndrome of dementia with Lewy bodies (DLB) often accompanied by delusions and other neuro-psychiatric manifestations.
  - Is second to Alzheimer's as the most common form of dementia
  - May be one of the early disease manifestations
  - May manifest prior to other Parkinsonian features being recognized.
  - Hallucinations are often complex and formed and may be accompanied by hallucinations of other senses such as touch or hearing.
  - Insight is invariably preserved depending on other cognitive deficiencies.
  - They often have fluctuations of cognition being intact and alert at times alternating with confused periods.
  - If suspect inquire about falls, cognition, confusion
Neurodegenerative disease

- Visual hallucinations can also be seen with Parkinson’s disease
  - More common later in the disease
  - Often dopaminergic medications contribute substantially to visual hallucinations
  - Other contributing factors include advanced age, impaired vision, sleep disturbance, impaired cognition
Neurodegenerative Disease

- Hallucinations relatively uncommon with Alzheimer’s dementia and when present concern should arise to acute superimposed delirium, medication toxicity or withdrawal or impaired vision.
Neurodegenerative Disease

- Creutzfeld-Jakob disease
  - Heidenhain variant termed to represent cases with early prominent visual complaints
  - Cooper, SA et al in Br J Ophthalmol. 2005 Oct; 89 (10): 1341-1342 reviewed 594 cases of pathologically confirmed CJD.
    - 22 had isolated visual symptoms at
    - Visual distortion and palinopsia were some of the symptoms identified
    - Most were followed by a rapid cognitive decline and myoclonus after a few weeks.
Seizures

- Like most seizures epileptic hallucinations are brief, (seconds) and stereotypical.

- Depending on localization of epileptic focus can be simple or complex with more simple localizing more occipitally and complex ones more temporally.

- Often do no occur in isolation, and often at some point may have other seizure manifestations.

- Typically binocular, homonymous but can be misinterpreted
Release hallucinations

- Associated with visual loss or field loss regardless of underlying cause.
- Can be simple or complex
- Can be monocular or binocular or restricted to the involved field of visual loss.
- Simple or complex
Migrainous Aura

- Probably one of the most common sources of positive visual phenomenon and one of the most fascinating.
  - Can be worrisome to be patients and their physicians (concern for stroke or other more worrisome condition)
  - Can be associated independantly with disabilty to include inability to drive or work.
  - Sufficient to ground aviators.
Migraine
Aura (without headache) IHS classification ICHD-II

- Visual and/sensory symptoms with or without speech symptoms.
- Gradual development
- Duration of no longer than 1 hour
- Mix of positive and negative features
- Complete reversibility of symptoms
- Persistent Aura without infarction, aura symptoms present greater than 1 week
Visual Aura

- By far the most common type of aura
- Something unique about the occipital cortex (more on this to follow)
- 20% of patients will have migraine with aura
- 90+% will have a visual aura (of these most 70-80% will have homonymous phenomenon)
IHS classification

- Retinal migraine
  - Repeated attacks of monocular visual disturbance, including scintillations, scotomata or blindness associated with migraine headache.
  - Diagnostic criteria
    - A. At least 2 attacks fulfilling criteria B and C
    - B Fully reversible monocular positive and/or negative visual phenomena (scintillations, scotomata or blindness confirmed by examination during an attack or by the patient’s drawing of a monocular field defect during an attack
    - C Headache fulfilling criteria B-D for Migraine with aura begins during the visual symptoms or follows them within 60 minutes
    - D Normal ophthalmological examination between attacks
    - E Not attributable to another disorder
  - Appropriate investigations to exclude other causes of transient monocular blindness.
“Late Life Migrainous Accompaniments”

- C.M. Fisher emphasized the benign nature of aura and published collection of cases first in 1980.
  - 93 patients with positive phenomenon
    - 75% with “brightness”
    - 50% with flickering
    - 50% with color
    - 75% with “buildup” spreading or expansion
“Late Life Migrainous Accompaniments”

CM Fisher’s criteria

- Scintillations or other visual display in the spell (paresthesias, aphasia, dysarthria and paralysis)
- Buildup of scintillations (over minutes)
- “March” of paresthesias (over minutes)
- Progression of one accompaniment to another
- The occurrence of two or more similar spells
- Headache in the spell
- Episodes of 15-25 minutes
- Mid-life flurry (around age 50)
- Benign course and exclusionary workup
Consider Further Evaluation:

- Unusual, prolonged or persistent aura
- Increasing frequency, severity or change in clinical features
- First, worst or neurologically cursed!
- History of malignancy
- Post-traumatic
Aura Pathophysiology

- Current understanding of migraine mandates that migraine attacks originate in the brain and can be triggered by various conditions.
  - This argues in favor of a threshold that governs the incidence of attacks (similar to epilepsy)
  - This would imply that there are areas of the brain with transient or persistently exaggerated hyperexcitability of neurons.
Aura Pathophysiology

- 1938 Graham and Wolf, demonstrated that the amplitude of arterial pulsations could be decreased with use of IV ergotamine with reduction of headache pain.

- 1941 Lashley observed the progression of his own aura and deduced that the phenomenon must be moving across his occipital cortex at a rate of 3mm/min.

- 1944 Leao reported on the phenomenon of cortical spreading depression in rabbits.
Migraine as a state of abnormal brain hyperexcitability.

- For decades the dogma that migraine aura was due to vasoconstriction and that headache that was due to vasodilatation had been firmly entrenched
- **Migraine is an abnormal state of the brain**
- Vascular changes occur but they are not primary
- Primary event is neuronal
Migraine as episodic state of altered brain function

- Can be viewed as an interaction of environmental factors in a susceptible host.
- Evidence suggests that individuals with migraine have hyperexcitable brains and do not habituate to normal stimuli.
- Vascular changes are an epiphenomenon.
- Primary phenomenon is cortical hyperexcitability.
Occipital Cortical Hyperexcitability

- The threshold for transcranial magnetic stimulation of the occipital cortex required to produce phosphenes is significantly lower in patients with migraine who experienced aura between their headaches than it was in normal controls.

- Valproic acid was able to reduce this hyperexcitability in one study.

- Migraineurs are often more sensitive to sensory input (smells, sound, touch, visual input)
Enhanced Neuronal excitation

Enhanced Neuronal excitation coupled with firing in a localized area of cortex is known to result in the local build up of potassium which depolarizes adjacent neurons and causes the phenomenon to spread.

If cellular homeostasis cannot contain the glutamate release and restore ionic concentrations then a wave of spreading depression is generated.

This is known as cortical spreading depression.
Cortical Spreading Depression

- A slowly moving wave of suppressed electrical activity that moves across the cortex at a rate of 2-5 mm/min.
- Glial cells maintain K+ homeostasis
- In humans the lowest glial to neuron ratio is found in the human occipital cortex.
- Increasing evidence that cortical spreading depression is causally related to migraine aura
Migraine pain is generated by the activation of the trigeminal vascular system.

As depolarization moves across the cortex, nitrous oxide, arachidonic acid, H+ and K+ ions are released.

TNC is activated and neuronal output to the vasculature occurs.

Trigeminal neurons release calcitonin gene-related peptide, Substance P and neurokinin A.

The vessels dilate and become inflamed.
CSD and Migraine Aura

- Functional imaging studies (fMRI-BOLD) demonstrated clinical features of CSD in patients with spontaneous migraine with aura
  - Eight characteristics of CSD were observed and were time locked to the perception of the visual aura
  - Initial hyperemia (increased blood flow implying increased neuronal activity)
  - Characteristic duration and velocity
  - Followed by hypoperfusion

\(\text{(Hadjikhani et al 2001, Cao et al. 1999)}\)
Sustained visual cortex hyperexcitability

Chen et al in Brain 2011, 134;2387-2395

- Magnetoencephalography, a technique for brain mapping by measuring magnetic fields produced by electrical currents.

- Looked at persistent aura, episodic migraine (some during and some in between headache, chronic migraine patients and healthy controls).

- Only the patients with persistent visual aura had potentiation of the responses suggesting persistent hyperexcitability and thought to be due to reverberating CSD circuits.
Visual Snow
Persistent Positive Visual Phenomenon

- Liu et al 1995 in Neurology 10 cases - full field persistent positive visual phenomena
  - 3 patients had no previous migraine or aura
  - Small particles like TV static, snow, lines of ants, dots or rain
  - Bothersome but not visually disabling
  - Medical trials (TCAs, Ca channel blockers, beta blockers and analgesics were unhelpful).
Persistent positive phenomenon

- International Headache Society’s defines:
- Persistent aura without infarction
  - Patients with previous migraine aura have a similar aura that persists for longer than a week
- Migraine aura status
  - At least 2 aura episodes per day for at least 3 days
Visual Snow

- Resemblance to TV static or snow as described by patients. Also terms pixelated vision.
- Both eyes, entire visual field, often with flickering of the background.
- Long duration, has high impact on quality of life and has proven difficult to treat.
Visual Snow


- Appears to be distinct than typical migraine aura, proposed diagnostic criteria.
  - A. Dynamic, continuous, tiny dots in the entire visual field lasting longer than 3 months.
  - B. Presence of at least 2 of 4
    - Palinopsia
    - Enhanced entoptic phenomenon (excessive floaters in both eyes, excessive blue field phenomenon, self-light of the eye or spontaneous photopsia)
    - Photophobia
    - Nyctalopia
  - Symptoms not c/w typical migraine aura
  - Not explained by another disorder (especially normal eye exam)
Visual Snow

- PET scans have demonstrated hypermetabolism in the right lingual gyrus (region of secondary visual cortex thought to modulate visual processing) and left anterior lobe of the cerebellum.

- Appears to be distinct from migraine and migraine with aura though there is likely a close relationship with common issues of cortical hyperexcitability playing a role.

- Related to screen time? Phones, computer use?
An approach

- If hallucinations are simple or illusory palinopsia
  - Try to establish if possible monocular/binocular
  - Rule out ocular pathology, include field assessment.
  - Drug/medication toxicity withdrawal
  - Migraine history
    - Evolution of symptoms
    - Binocular
    - Positive phenomenon
    - Time of duration and tempo of evolution
  - Other associated Neurologic signs or symptoms
  - History of head trauma
An approach

- Try to get patient to characterize symptoms better.
- If has well formed complex hallucinations
  - Get good medication/drugs of abuse history
  - Assess for any areas of visual loss (release hallucinations)
  - See if any risk factors/signs of accompanying neurologic disease (cognitive decline, parkinsonian features)
  - Consider metabolic abnormalities
  - Psychiatric disease