SYLLABUS

TC26: Neuro-ophthalmology

Tuesday, November 15, 2011 09:00 - 12:30 Hall L

Marrakesh, Morocco, November 12-17, 2011

XXth WORLD CONGRESS OF NEUROLOGY

XXth WCN 2011 MARRAKESH World Congress of Neurology

WFN

SMN SOCIETE MAROCAINE DE NEUROLOGIE

WCN Education Program

Tuesday, 15 November, 2011

09:00-12:30

NEURO-OPHTHALMOLOGY

Chairperson: **Christopher Kennard**, *UK*

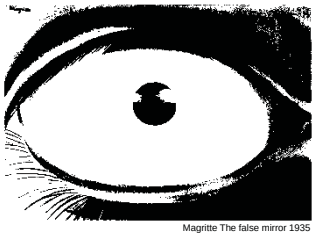
UNDERSTANDING THE VISUAL BRAIN AND DIAGNOSING CENTRAL DISORDERS OF VISION
Christopher Kennard, *UK*

WHAT THE EYES SAY ABOUT THE BRAIN: DIAGNOSING CENTRAL DISORDERS OF EYE MOVEMENT
Tim Anderson, *New Zealand*

WHEN THE EYES DON'T MOVE TOGETHER: DIAGNOSING PERIPHERAL AND CENTRAL CAUSES OF DIPLOPIA
John Leigh, *USA*

10:30-11:00 *Coffee Break*

Understanding the visual brain and diagnosing central disorders of vision



Magritte The false mirror 1935

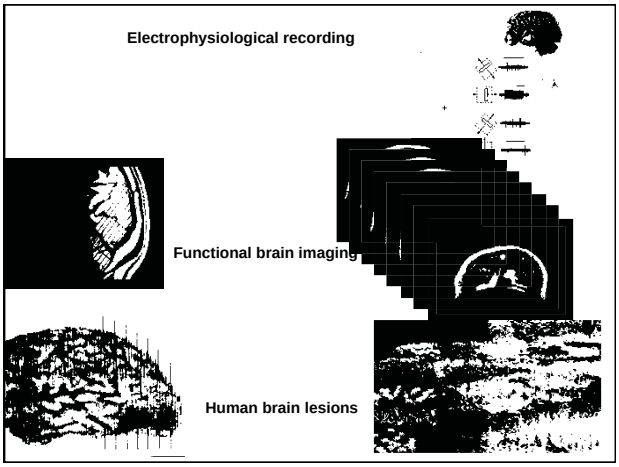
Christopher Kennard
Nuffield Department of Clinical Neurosciences
University of Oxford

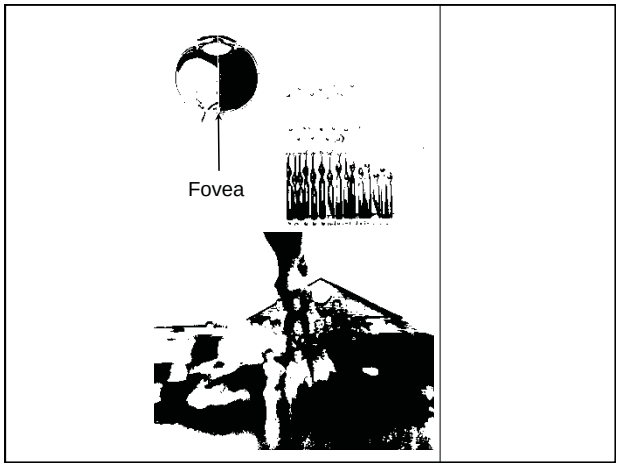
WCN 2011, Marrakech
15th November 2011

Topics and Questions to be discussed in this lecture

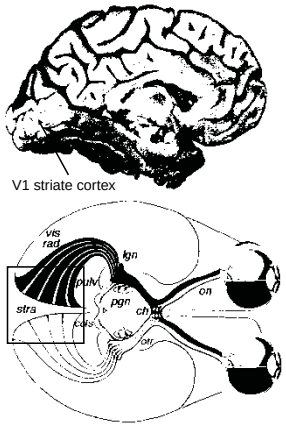
- how does the brain process the image of the visual world?
- does the visual brain provide a perfect representation of the outside visual world ie is it a passive process like a camera, or is the reality of what we see created by our mind
- what are the disturbances of vision which occur when different parts of the visual system are damaged?
- visual illusions and hallucinations
- Visuo-spatial neglect

Joseph Mallord William Turner 1844
Rain, steam and speed - the Great Western Railway

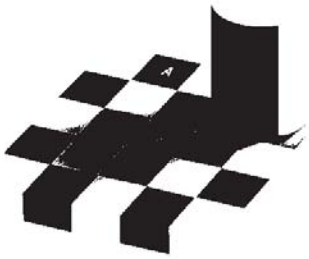


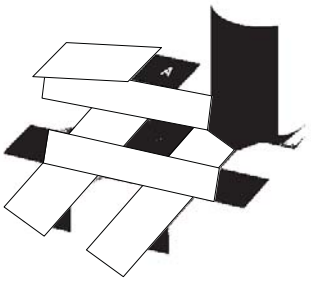


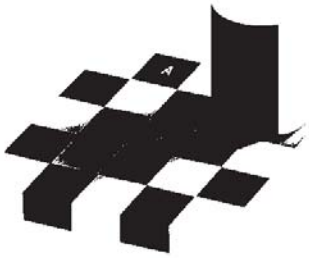
An example of global perceptual effects ie individual neurons can integrate information over large areas of the visual cortex



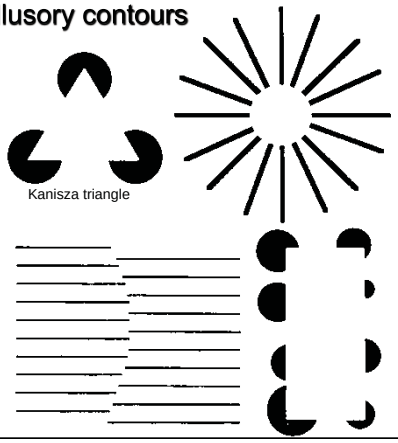
Does vision reconstruct reality?







Illusory contours

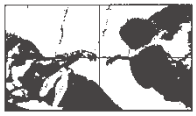


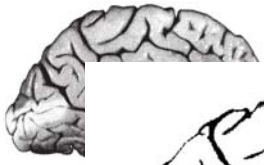
selves through the usual round of work and play, a degree
ness and a desire for rest are characteristic of
migraine. A vascular h
head m
only, or even the chief, mechanism at work. M
during an attack and exhibit diminished tone of skeleta
drowsy.
The relation of sle
one, and we will ha
contexts: the i
migraine (migr
migraines o
relation to t
attention to th
of intense dro
the occasional alle
and the typical protracted
natural termination.
Nowhere in the literature can we find more vivid and
descriptions of migrainous stupor than in Liveing's monogr

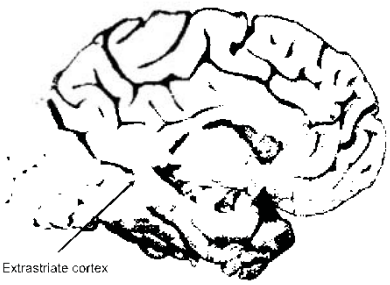
Medieval Naarden, Holland

The visual aura of migraine with scintillating fortification spectra (a wave of excitation followed by inhibition across orientation columns)

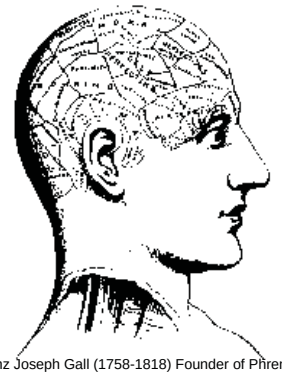
Homonymous hemianopia





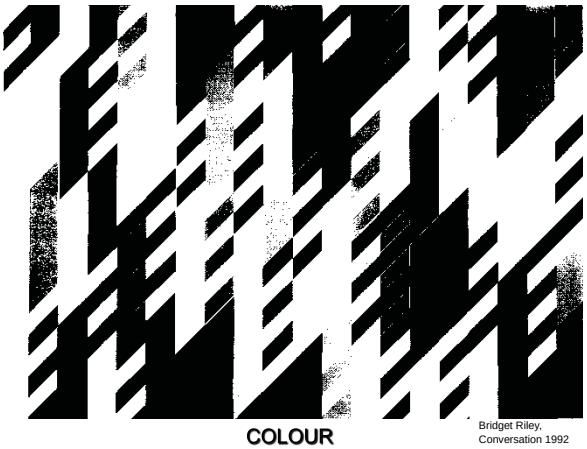


Extrastriate cortex



Functional specialisation?

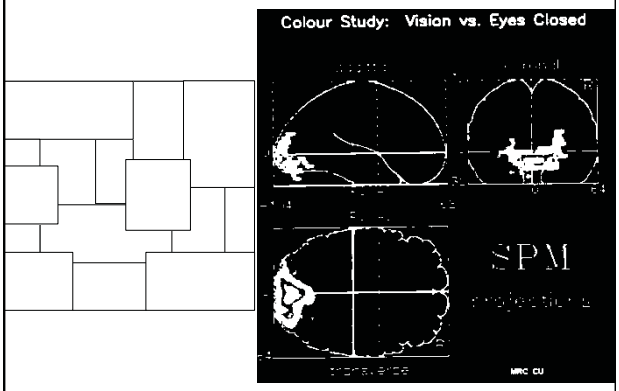
Franz Joseph Gall (1758-1818) Founder of Phrenology



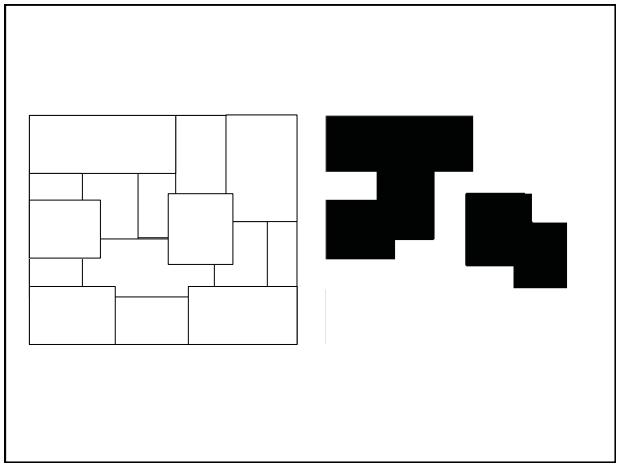
Bridget Riley, Conversation 1992

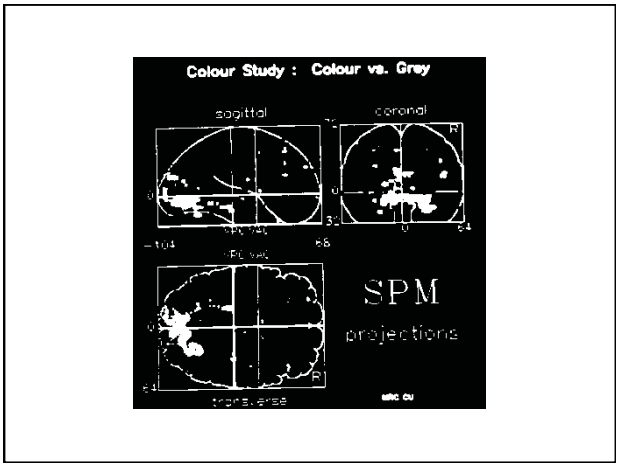
Henri Rousseau Le repas du lion 1907

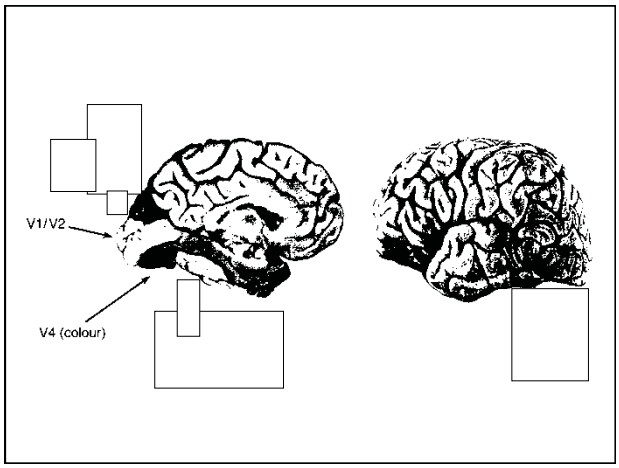
Henri Rousseau Exotic landscape 1908



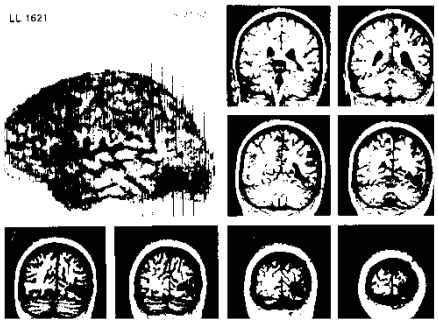
Lueck et al 1989



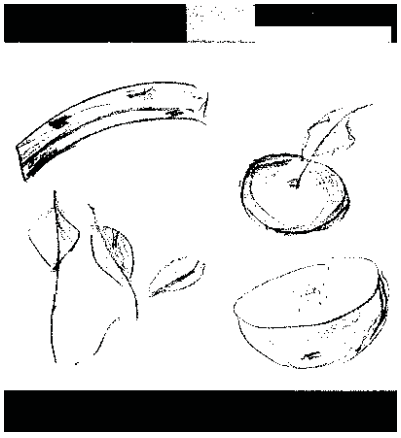




- Functional imaging provides one level of proof for a colour centre
- We can extend this proof by observing the deficits which occur when this area has been damaged

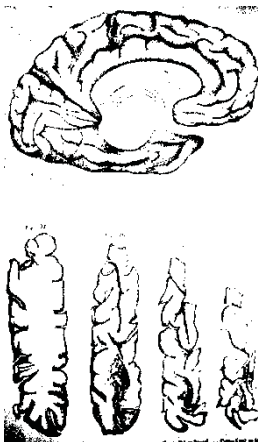


VIDEO

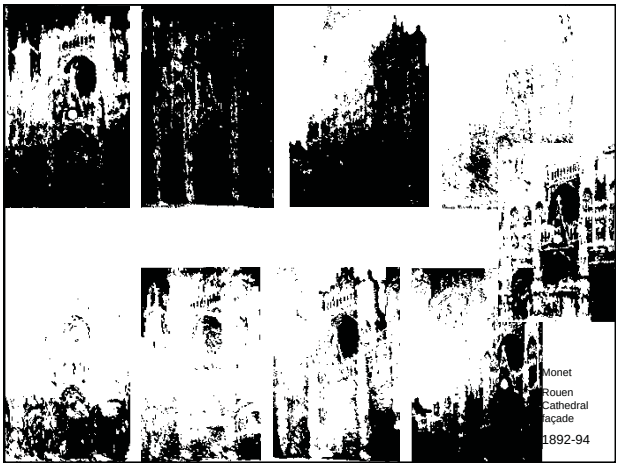


ACHROMATOPSIA

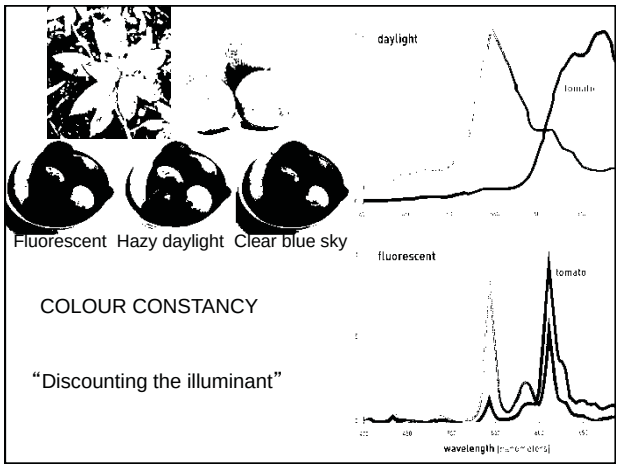
- An acquired disorder of colour perception with preservation of the vision of form, motion and depth.



Verrey
1888



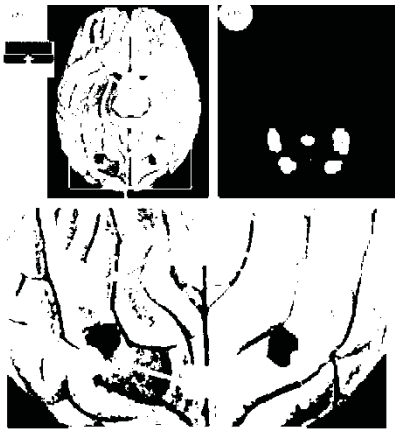
Monet
Rouen Cathedral façade
1892-94



Fluorescent Hazy daylight Clear blue sky

COLOUR CONSTANCY

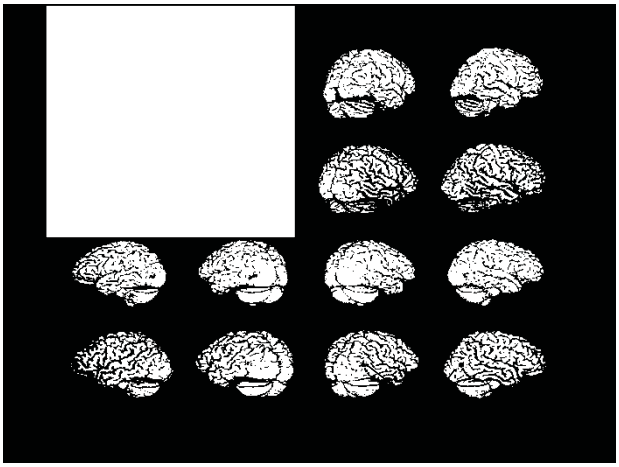
"Discounting the illuminant"

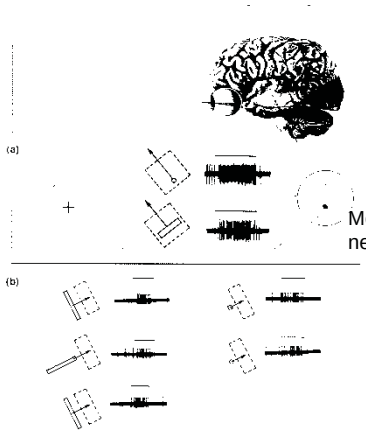


Bartels & Zeki (2000)

MOVEMENT

Seurat, Circus
1890-91





Movement sensiti
neurons

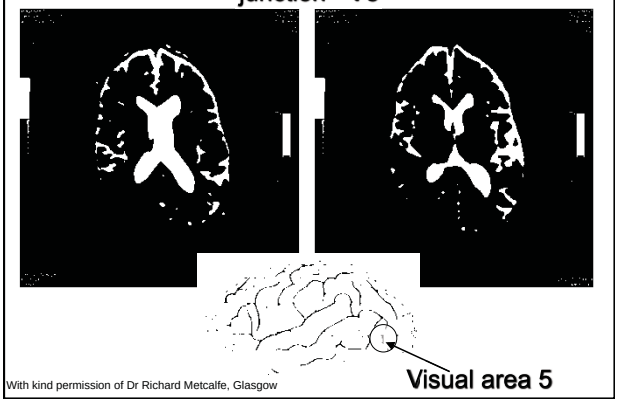
AKINETOPSIA

- A defect in the perception of visual motion

VIDEO

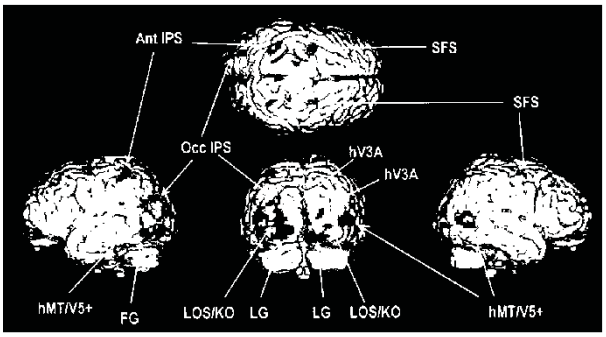
With kind permission of Dr Richard Metcalfe, Glasgow

Bilateral lesions (arrows) at occipito-temporal junction - V5

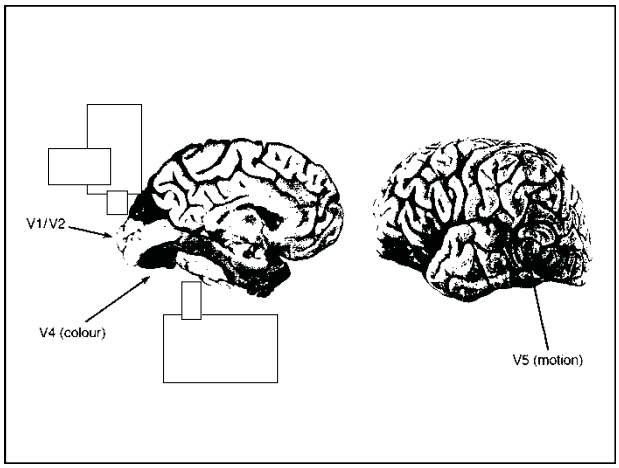


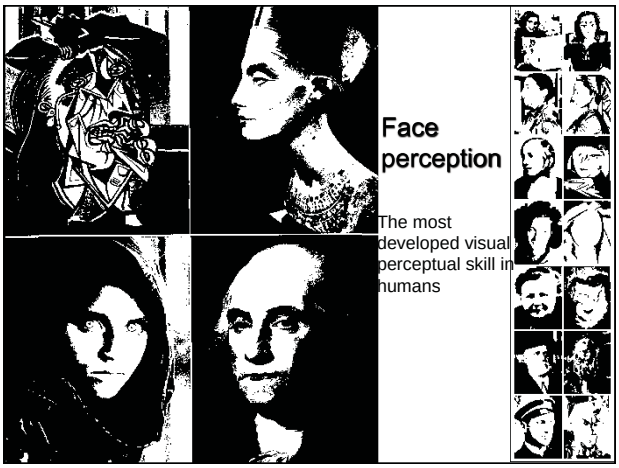
With kind permission of Dr Richard Metcalfe, Glasgow

The motion visual brain



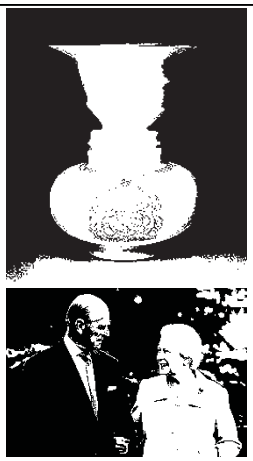
Sunaert et al (1999)





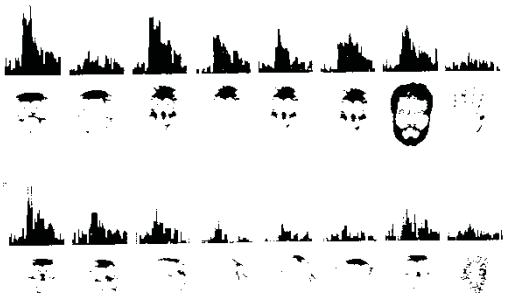
Face perception

The most developed visual perceptual skill in humans



Face Perception

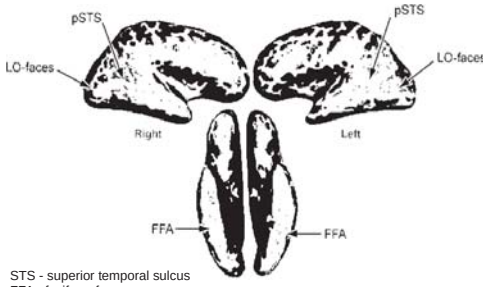
- Plays critical role in social interactions
- Visual appearances of faces provide information:
  - on identity and background of another person
  - enables influences about mood, level of interest and interactions
  - directs ones own attention to objects and events that others are looking at
- enhances comprehension of speech



Face-selective neurons

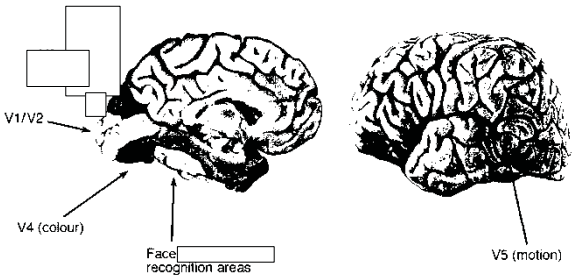
Perrett DI et al 1985

The Visual Brain

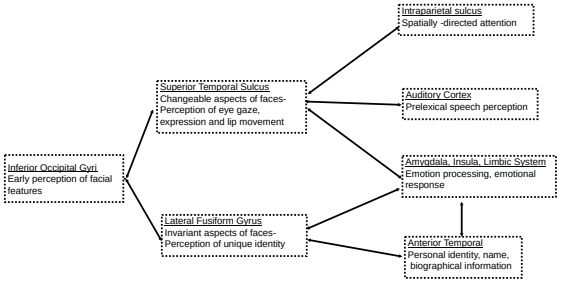


STS - superior temporal sulcus
FFA - fusiform face area
LO - lateral occipital area

Tsao, Livingstone 2008

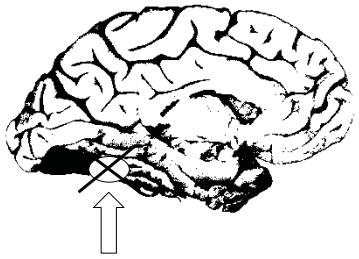


A model of the distributed human neural system for face perception (Haxby et al 2000)



Core System:
Visual analysis

Extended System:
Further processing in concert with other neural systems



VIDEO

PROSOPAGNOSIA

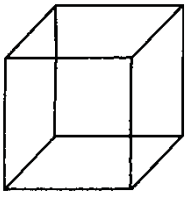
(prosopon - face ; agnosia - non-knowledge)

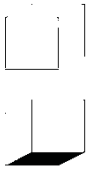
A neurological disorder characterised by an inability to recognise previously known faces and to learn new ones.

OBJECT RECOGNITION

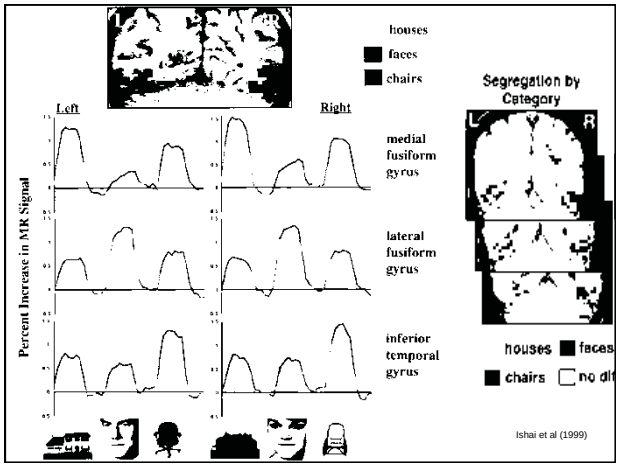
Cezanne Still life with commode (1887-87)

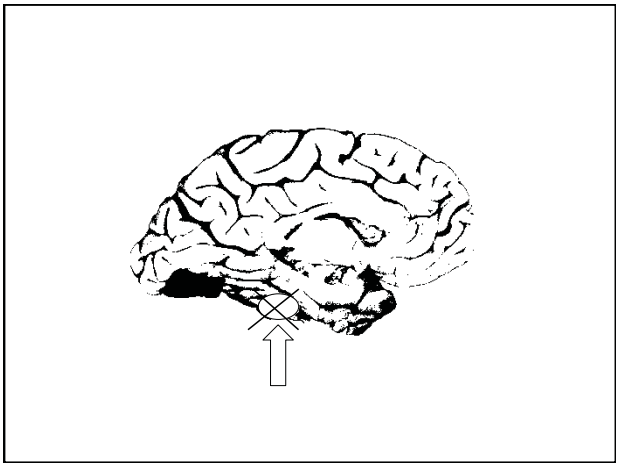
Necker cube - a multi-stable illusion





LA Necker - a Swiss crystalographer who in 1832 observing rhomboid crystals under a microscope observed that they appeared to flip to appear quite different





VISUAL AGNOSIA

An inability to recognise visualised objects

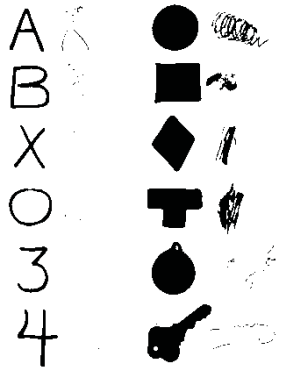
- Apperceptive
- Associative

VISUAL AGNOSIA - APPERCEPTIVE

A

A failure to recognise visual objects due to distortion of the stimulus at sensory- perceptual levels

VISUAL AGNOSIA - APPERCEPTIVE



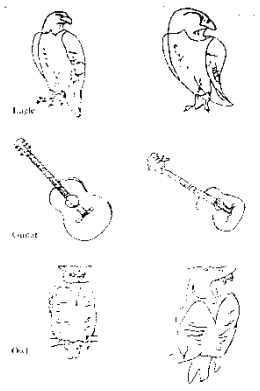
VISUAL AGNOSIA - APPERCEPTIVE

- A failure to recognise visual objects due to distortion of the stimulus at sensory- perceptual levels
- Cannot name, copy or recognise visually presented objects. Fails constructional tests
- Correctly identify colour, direction, motion and dimensions
- Causation - diffuse brain disorders eg. hypoxia

VISUAL AGNOSIA - ASSOCIATIVE

An inability to recognise visualised objects
"a normal percept stripped of its meaning" (Teuber)

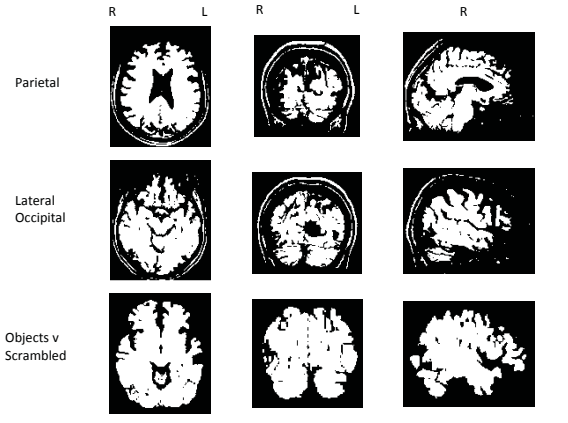
HJA - 63 yr old company executive. Following a appendicectomy has a small stroke, due to a clot from his heart resulting an irregular heart rhythm

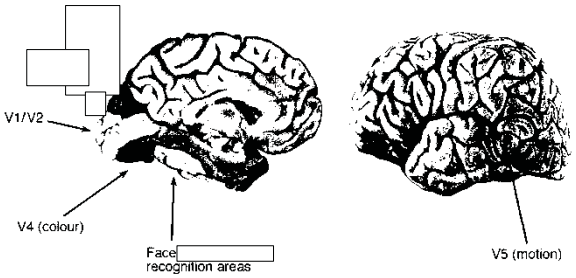


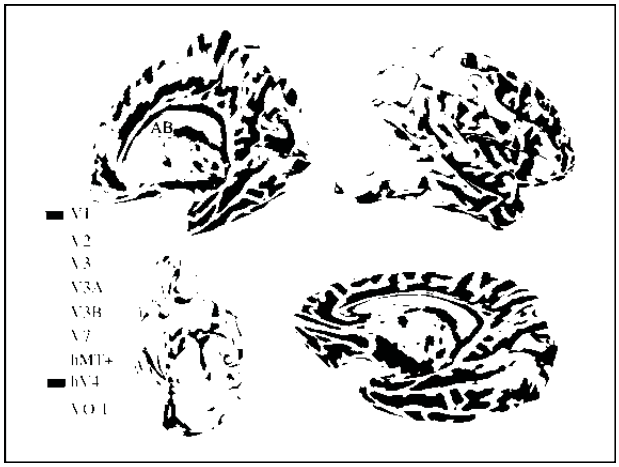
c. d.

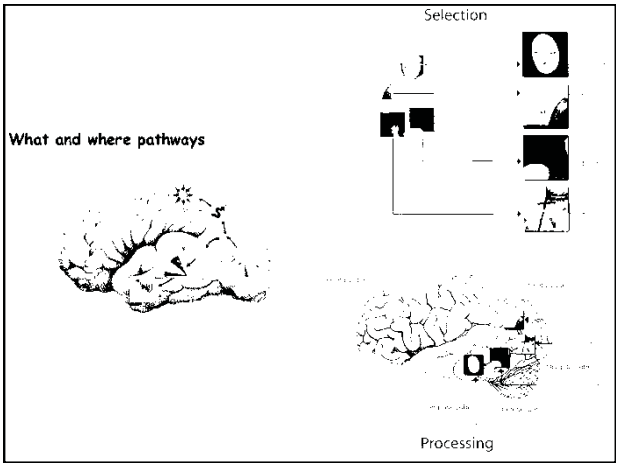
• Pepperpot - "a stand containing 3 separate pans; the top pan has a design on its lid; the second pan has a slightly smaller diameter than the top pan…"

• Onion - "I'm completely lost at the moment. You don't put it on. It has sharp bits at the bottom like a fork. It could be a necklace of sorts"









VISUAL ILLUSIONS AND HALLUCINATIONS - DEFINITIONS

- **Visual illusions** - a misperception of a stimulus that is present in the external environment
- **Hallucinations** - visual sensations perceived and possessing the compelling sense of reality of a true perception occurring without external stimulation of the eye
- **Charles Bonnet syndrome** - complex formed visual hallucinations associated with visual loss

Incidence of illusions and hallucinations in 112 patients with retrochiasmal lesions (Kolmel 1993)

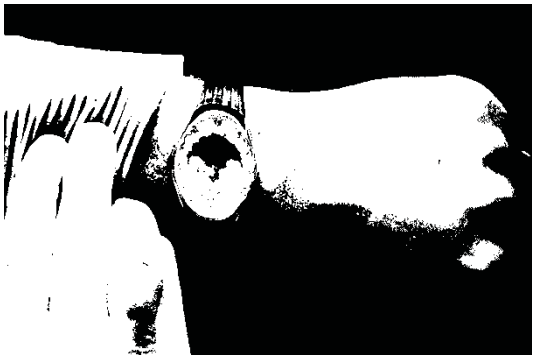
Photopsias	85 (31%)
Complex hallucinations	32 (12%)
Monocular diplopia	11 (4%)
Palinopsia	19 (7%)
Other	10 (4%)

Pathological visual illusions

Disorder	Visual illusion
Axis	Tilted or inverted
Distance	Pelopsia/teopsia
Size	Macropsia/micropsia
Shape	Metamorphopsia
Motion	Slow motion or elapsed time
Number of images	Diplopia/polyopia
Extinction	Perseveration
Memory	Déjà vu/jamais vu
Hemifield transposition	Visual allesthesia

Pathological visual illusions

Disorder	Visual illusion
Axis	Tilted or inverted
Distance	Pelopsia/teopsia
Size	Macropsia/micropsia
Shape	**Metamorphopsia**
Motion	Slow motion or elapsed time
Number of images	Diplopia/polyopia
Extinction	Perseveration
Memory	Déjà vu/jamais vu
Hemifield transposition	Visual allesthesia



TYPES OF VISUAL DISORDER AND CORRESPONDING VISUAL ILLUSION

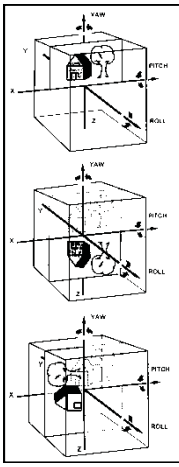
Disorder	Visual illusion
Axis	Tilted or inverted
Distance	Pelopsia/teopsia
Size	**Macropsia/micropsia**
Shape	Metamorphopsia
Motion	Slow motion or elapsed time
Number of images	Diplopia/polyopia
Extinction	Perseveration
Memory	Déjà vu/jamais vu
Hemifield transposition	Visual allesthesia

TYPES OF VISUAL DISORDER AND CORRESPONDING VISUAL ILLUSION

Disorder	Visual illusion
Axis	Tilted or inverted
Distance	Pelopsia/teopsia
Size	Macropsia/micropsia
Shape	Metamorphopsia
Motion	Slow motion or elapsed time
Number of images	**Diplopia/polyopia**
Extinction	Perseveration
Memory	Déjà vu/jamais vu
Hemifield transposition	Visual allesthesia

TYPES OF VISUAL DISORDER AND CORRESPONDING VISUAL ILLUSION

Disorder	Visual illusion
Axis	**Tilted or inverted**
Distance	Pelopsia/teopsia
Size	Macropsia/micropsia
Shape	Metamorphopsia
Motion	Slow motion or elapsed time
Number of images	Diplopia/polyopia
Extinction	Perseveration
Memory	Déjà vu/jamais vu
Hemifield transposition	Visual allesthesia



Transient upside-down inversion of vision

• a transient mismatch of the visual and vestibular 3-D map coordinates that occur in 90º and 180º steps as the erroneous result of the attempted cortical match.

• associated with:
- vestibulocerebellar lesions
- cortical lesions (parietal-occipital, frontal)

PATHOLOGICAL VISUAL ILLUSIONS - AETIOLOGY

- Macular oedema/scarring
- Drugs
- Epilepsy
- Migraine
- Focal cortical lesions
- Multiple sclerosis
- Conversion disorder

VISUAL HALLUCINATIONS

- Hallucinations - visual sensations perceived and possessing the compelling sense of reality of a true perception occurring without external stimulation of the eye
- Charles Bonnet syndrome - complex formed visual hallucinations associated with visual loss

Prevalence

- Under-reported
- In patients with visual impairment; complex 11-15%; elementary 41-59%

Age distribution

- Mean age of onset 75-83 yrs

VISUAL HALLUCINATIONS - TYPES

SIMPLE (elementary)

Photopsia (light flashes)

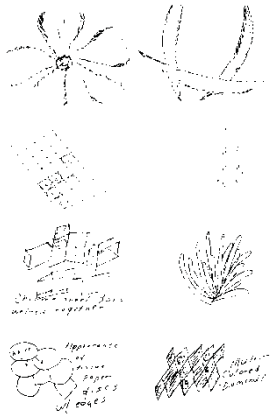
Phosphenes (blue lights)

Scintillations (zig-zag)

Geometric forms

Checkerboard forms

Positive scotomas



VISUAL HALLUCINATIONS - TYPES

COMPLEX (formed)

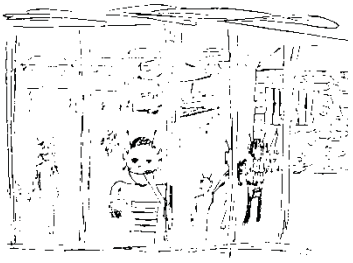
People

Objects

Scene and landscape

Animals (zoopsia)

Peduncular hallucinations



VISUAL HALLUCINATIONS - AETIOLOGY

Ophthalmologic
- Ocular pathology - senile macular degeneration
- Vitreoretinal tug
- Vitreous detachment
- Retinitis pigmentosa
- Inflammatory/para-neoplastic chorio-retinopathies
- Ocular hypoperfusion
- Optic neuritis
- Sensory deprivation or prolonged darkness

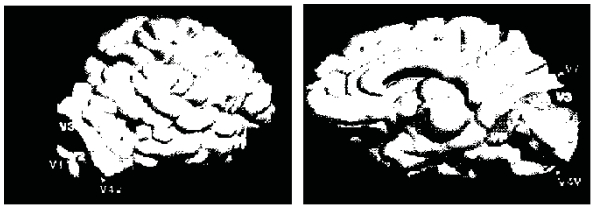
Neurological
- Migraine
- Parkinson's disease
- Dementia (Lewy body, AD)
- Posterior cerebral infarctions (Anton's syndrome)
- Epilepsy
- Peduncular hallucinosis
- Narcolepsy (hypnogogic, hypnopompic)
- Delerium; drug intoxications eg cocaine, LSD and withdrawal states

Psychiatric
- Major depression
- Mania
- Schizophrenia
- Post-traumatic stress disorder
- Anxiety
- Substance dependence (stimulants, cocaine, hallucinogenic drugs - LSD, marijuana)
- Alcohol intoxication / withdrawal (delerium tremens)

VISUAL HALLUCINATIONS - PATHOPHYSIOLOGY

- Deafferentation of cortical visual areas (perceptual release)
- Sensory deprivation eg ocular masking
- Sleep deprivation
- Ictal activity
- Social isolation
- Posterior cerebral hypoperfusion

The Attentive Brain & Eye Fields

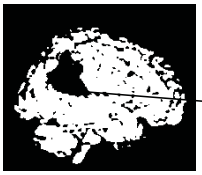


How the brain selects information and guides the eyes

UNILATERAL HEMI-NEGLECT

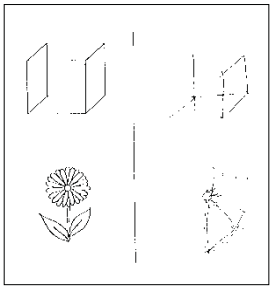
VIDEO

Unilateral neglect or inattention is an impairment in the ability to orient toward, perceive or act on stimuli from one side,despite preserved primary motor sensory functions



Right inferior parietal lobe

Copying (or painting) tasks
may reveal leftward omissions



NEGLECT AFTER STROKE

- Is common and long-lasting after right hemisphere stroke
- Up to 70% rt hem patients may show some signs acutely
- Many patients (approx. 2/3) recover
- Poor prognosis for independent function in those who don't
- No established treatments
- Therefore a need to understand underlying mechanisms
- Most investigators have focused on spatial deficits, consistent with classical views of anatomy of the syndrome

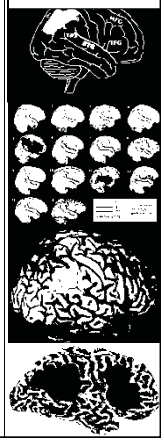
Anatomy of neglect

- Has been controversial recently (STG claim – Karnath)

Superior temporal gyrus

- Our study points to a critical role of right parietal lobe, consistent with classical reports
- Focal lesions of right inferior frontal lobe may also lead to neglect

Mort et al. *Brain* (2003)

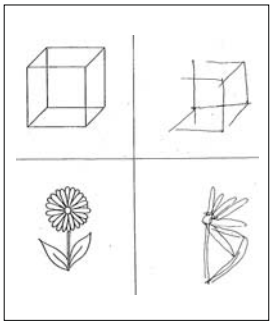


Space exploration in neglect reveals leftward deficit

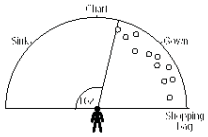
Tracking eye movements of neglect patients as they view natural scenes

Bays et al.

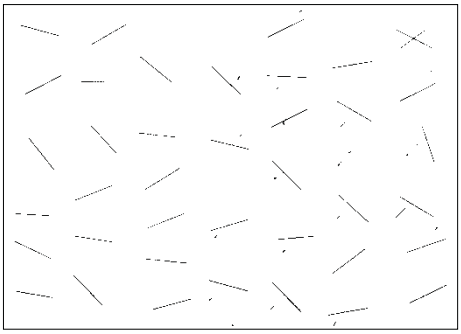
Copying or painting tasks
may reveal leftward neglect



Reporting items in a room
Only items towards the right may be described



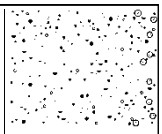
Cancellation (search) task
reveals failure to find items to left



NEGLECT AFTER STROKE

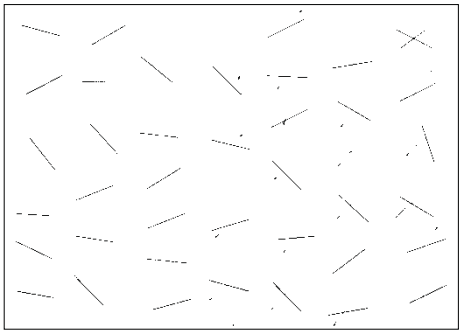
- These types of finding have understandably focused attention on spatial mechanisms and parietal cortex
- And at first glance, consistent with classical role of parietal cortex in visual processing

DEFICITS IN REPRESENTING LEFT SPACE CAN'T EXPLAIN SEVERAL ASPECTS OF NEGLECT

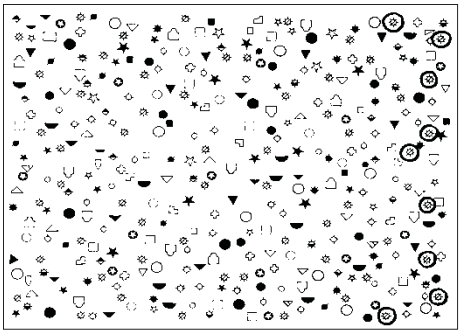


1 The severity of neglect is modulated by the clutter in the visual scene.

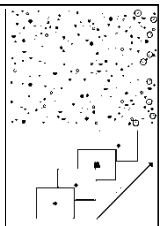
Cancellation task
reveals neglect of half sheet



Same patient on same day
Neglect modulated by competing stimuli (distractors)



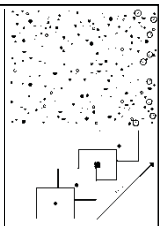
DEFICITS IN REPRESENTING LEFT SPACE CAN'T EXPLAIN SEVERAL ASPECTS OF NEGLECT



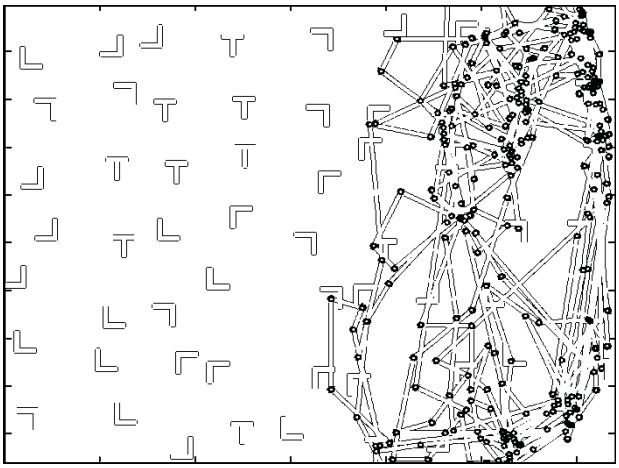
1. The severity of neglect is modulated by the clutter in the visual scene.
2. Patients with right parietal lesions also have impaired detection on their supposedly good *right side*.

.

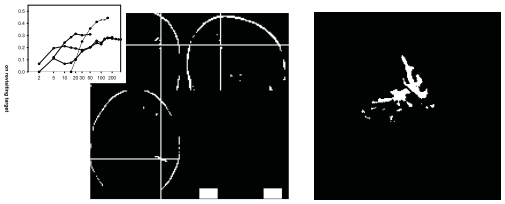
DEFICITS IN REPRESENTING LEFT SPACE CAN'T EXPLAIN SEVERAL ASPECTS OF NEGLECT



1. The severity of neglect is modulated by the clutter in the visual scene.
2. Patients with right parietal lesions also have impaired detection on their supposedly good *right side*.
3. Many neglect patients revisit locations *on the right*, failing to keep track of where they have looked before.



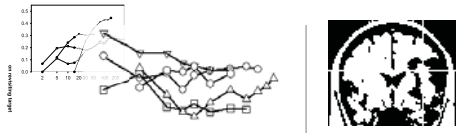
Lesion site associated with impaired tracking of spatial locations in patients with posterior lesions



Role for intraparietal sulcus in updating spatial locations across saccades?

Mannan et al (2005) *J Cog Neurosci*

Frontal neglect patients with high re-click rates in neglect – more perseverative

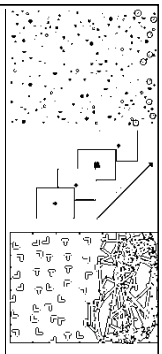


Inferior frontal lobe

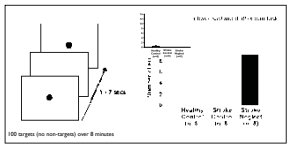
Mannan et al (2005) *J Cog Neurosci*

DEFICITS IN REPRESENTING LEFT SPACE CAN'T EXPLAIN SEVERAL ASPECTS OF NEGLECT

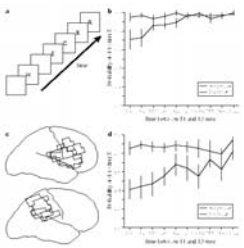
1. The severity of neglect is modulated by the clutter in the visual scene.
2. Patients with right parietal lesions also have impaired detection on their supposedly good right side.
3. Many neglect patients revisit locations *on the right*, failing to keep track of where they have looked before.
4. Neglect patients show deficits on non-spatial tasks



Non-spatial sustained attention and selective attention are also impaired in patients with spatial neglect



Impaired vigilance for central visual stimuli



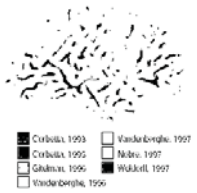
Abnormal 'attentional blink' indicative of reduced visual processing capacity

Malhotra, Coulthard et al *(in prep)*

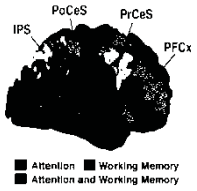
Husain *et al* (1997) *Nature*

A framework to understand spatial and non-spatial deficits

Superior parietal and frontal regions – the dorsal system



Corbetta & Shulman (2002)



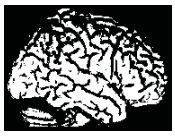
Corbetta et al (2000)

are activated in covert shifts of spatial attention and memory tasks in functional imaging studies

Goal-directed attention

A framework to understand spatial and non-spatial deficits

Inferior parietal and frontal regions – the ventral system



- Sustained attention

- Salience detection (oddball paradigm)

- Selective attention at fixation / attentional capacity

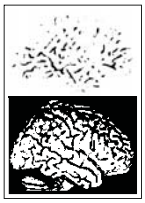
are activated in non-spatial attention tasks in functional imaging studies

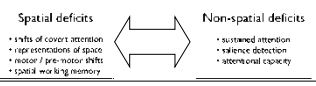
Stimulus-directed attention

Husain & Rorden (2003) *Nat Rev Neurosci*

Parietal cortex has both spatial and non-spatial functions

Different neglect patients have different combinations of cognitive/ behavioural deficits

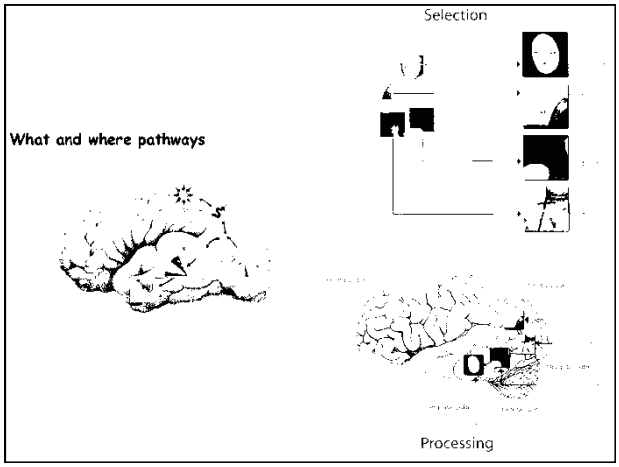




Non-spatial mechanisms may interact with spatial ones to define the severity and extent of neglect.

Treatment and rehabilitation of hemispatial neglect

- Scanning therapy and hemianopic patching
- Inducing shifts in spatial representations
- Prism adaptation
- Treating non-spatially lateralised deficits


Selection
What and where pathways
Processing

What the eyes say about the brain: Diagnosing central disorders of eye movement

Tuesday November 15th 2011, 09:00-12:30
Teaching Course [TC26]: Neuro-Ophthalmology

Tim Anderson
Christchurch, New Zealand

Schema

Typical eye movement signs and their brain disorders

Brain disorders and their typical eye movements

I. Brainstem and cerebellum
II. Subcortical: thalamus and basal ganglia structural disorders
III. Movement disorders (basal ganglia emphasis)
IV. Focal and structural cerebral disorders
V. The dementias

Eye movements serve to let us look at the aspects of the visual world that interest us and keep them stable in our vision

- **Gaze-shifting eye movements**
  Saccades
  Smooth Pursuit
  (Vergence)
- **Gaze-holding/stabilising movements**
  Central fixation
  Eccentric gaze
  OKN
  Vestibulo-ocular reflex (VOR)



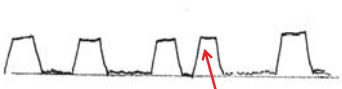


Video

I. Brainstem and Cerebellum

Fixation instability

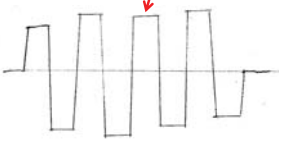
- **Square-wave jerks**
  - < 9/min in normal subjects
  - ↑ ↑ in Friedreich's , PSP
  - ↑ MSA > PD



Inter-saccadic interval, 200ms

Video

- **Macrosaccadic Oscillations**
  - eyes cross midline
  - cerebellar disorders

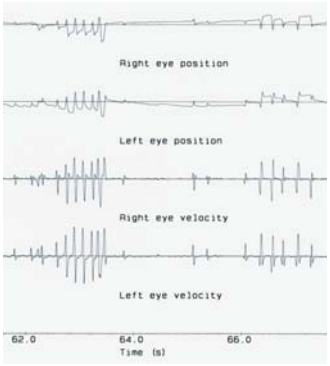


Video

Fixation instability

- **Ocular Flutter**
  - bursts of back-to-back saccades
  - no inter-saccadic interval
  - cerebellar/brainstem disease
  - encephalitis, paraneoplastic

No inter-saccadic interval



Video

- **Opsoclonus**
  - "saccadomania"
  - omnidirectional
  - back-to-back saccades
  - cerebellar/brainstem disease
  - encephalitis, paraneoplastic

Video

Fixation instability

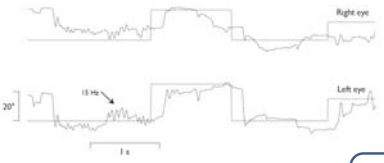
- **Upbeat nystagmus (UBN)**
  - brainstem, non localising
  - common in Wernicke's

Video

- **Downbeat nystagmus (DBN)**
  - cerebellar degenerations
  - Arnold Chiari
  - Drugs (e.g. lithium)

Video

- **Voluntary nystagmus**
  - usually present with oscillopsia or blurred vision
  - pendular, back-to-back saccades
  - 5 – 28Hz (mean 16Hz)
  - often initiated by convergence



Video

Fixation instability

- **pendular nystagmus**
  - various
  - visual failure
  - demyelinating disorders
  - oculopalatal tremor, Whipple's

Video

- **PAN (periodic alternating nystagmus)**
  - horizontal, reversing every 90-120 s
  - cerebellar disorders
    - Arnold Chiari, degenerations, masses
  - CJD
  - Visual failure

Video

Fixation instability

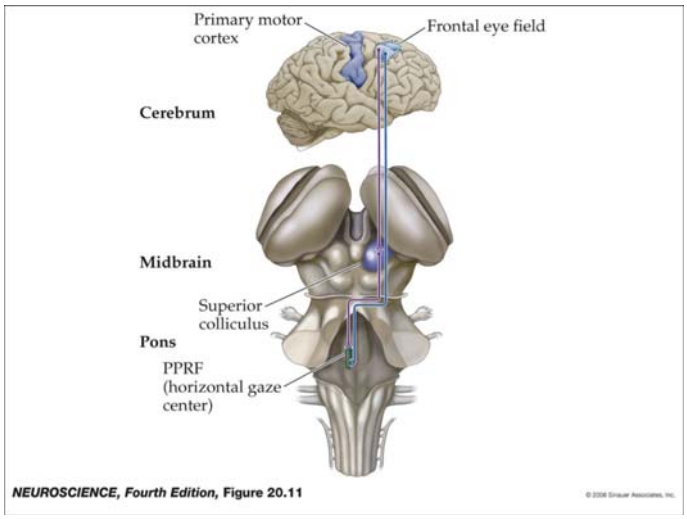
- **Gaze-evoked nystagmus**
  - (gaze-paretic nystagmus)
  - Drugs
  - Cerebellar disease
  - Vestibular
    - ↑ with gaze in fast phase direction

Video

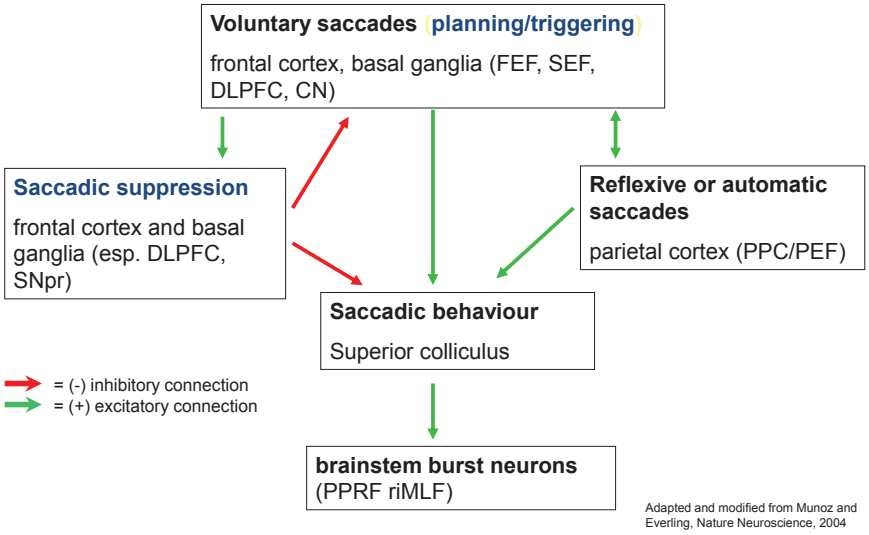
- **Rebound nystagmus**
  - cerebellar disease

Video

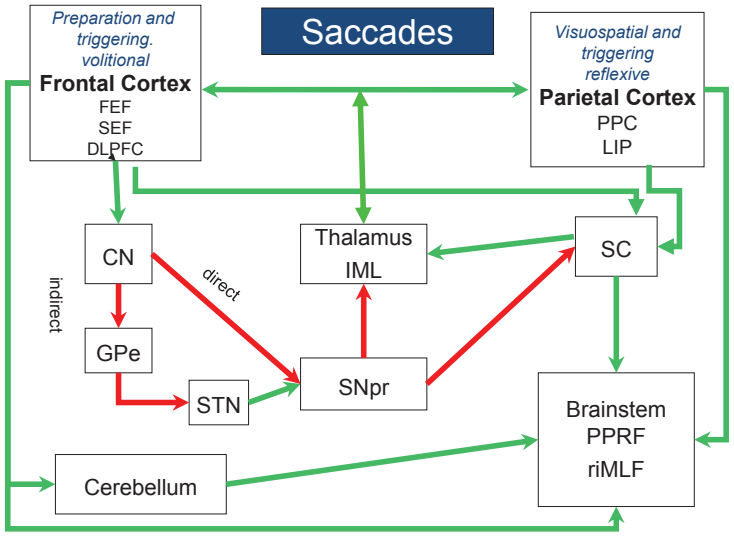
Saccades



Saccade production is the result of interplay between cortical and subcortical excitatory and inhibitory influences



Adapted and modified from Munoz and Everling, Nature Neuroscience, 2004

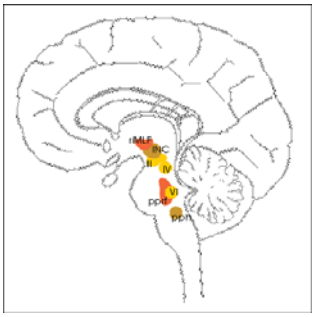


= (-) inhibitory connection
= (+) excitatory connection

Adapted and modified:from Munoz, Prog Brain Res 2002; and Leigh and Kennard, Brain 2004

Saccades: brainstem and cerebellum

- Saccades are generated by burst neurons
  - PPRF (horizontal)
    pons
  - riMLF (vertical)
    midbrain
- Disorders
  - ✓ Velocity (speed)
  - ✓ Amplitude (metrics, accuracy)
  - ✓ Latency (reaction time)



www.uni-tuebingen.de/uni/knl/Vilis/originof.htm

Slow saccades

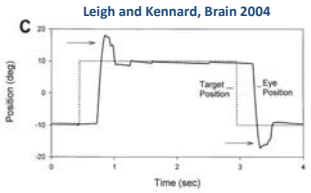
"the globe can be see throughout the saccade"

- SCA 2
- PSP
- HD
- (Gaucher's - horizontal)

Video

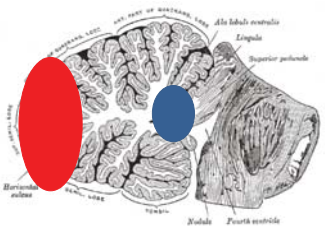
Impaired metrics of saccades

- Hypermetria
  - Lesions of cerebellum (fastigial nuclei)
  - Contrapulsion



Video

- Hypometria
  - Lesions of cerebellum (dorsal vermis) and brainstem
  - Lateropulsion (Wallenberg's syndrome)

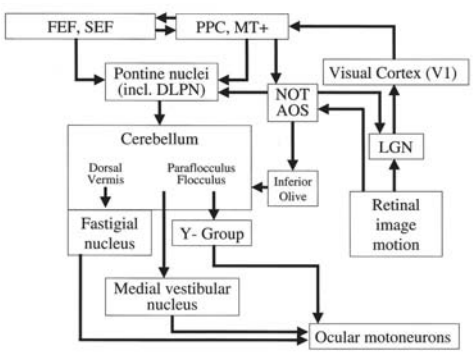


Video

Smooth Pursuit (SP)

- Smooth pursuit pathway widely distributed
- Sensitive but not specific
- Abnormalities generally non-localising
- ↓↓ SP in cerebellar disease
- ↓ drugs, elderly

Video



The Neurology of Eye Movements by R. J. Leigh and D. S. Zee, 3rd edition, 1999, (p. 165) © 1999 Oxford University Press

Vestibulo-ocular reflex (VOR)

Rapid impulsive head turn

Slow side-to-side head movements

- Peripheral disorders (most common)
- Central disorders (less common)
  - Brainstem
  - Cerebellar disease

Video

A patient with Arnold-Chiari malformation

gaze –evoked nystagmus
(incl. DBN)

saccadic hypermetria

impaired smooth pursuit

+ one other sign

Video

II. Subcortical: thalamus and basal ganglia structural disorders

Thalamic lesions

- conjugate gaze deviation – "wrong way eyes"
  - i.e. deviated to opposite side of lesion
- forced/tonic downward deviation
  - upgaze palsy
  - ± convergence and meiosis ("thalamic esotropia")
- sometimes impaired horizontal gaze

Video

thalamic haemorrhage

III. Movement disorders (basal ganglia emphasis)

Movement disorders (basal ganglia emphasis)

- Parkinson's disease (PD)
- Multiple System Atrophy (MSA)
- Progressive Supranuclear Palsy (PSP)
- Corticobasal syndrome (CBS)
- Huntington's disease (HD)

Parkinson's disease (PD)

The examination is frequently completely normal but mild abnormalities may be present

Clinical Signs

Impaired convergence

Smooth pursuit is normal or mildly impaired

mild hypometria of self generated saccades

Esp. Upwards saccades

Video

Stell and Bronstein, 1994, Sereno and Holzman 1996, Chan et al 2004, Amador et al 2006, Hood et al 2006, Lueck et. al., 1990, 1992, van Stockum 2008.

MSA – Oculomotor Features

Two main phenotypes: MSA-C and MSA-P

- Mild or moderate ↑SWJ's
- mild vertical supranuclear gaze palsy (SNGP) in a minority.
- Gaze evoked nystagmus may be present in those with no extraocular evidence of cerebellar dysfunction.
- Mild-moderate impairment of smooth pursuit and VORs in most

Anderson et al. *Movement Disorders* 2008

MSA – Oculomotor Features

- Mild-moderate hypometria of saccades in most
  - velocities are clinically normal.
- Positional downbeat nystagmus (pDBN) in over 30%
  - can be present in absence of other cerebellar signs
  - can habituate

Video

- Perverted head shaking nystagmus (pHSN)
  - vertical nystagmus on horizontal head oscillation
  - 30% of MSA-P

Video

Anderson et al. *Movement Disorders* 2008, Lee et al., *Movement Disorders* 2009

PSP (RS) – eye movements

1. **Eye opening/closing apraxia**
2. ↓↓blinking
3. **↑↑ SWJ's**
4. **SNGP (supranuclear gaze palsy)**
   - Gaze restriction, especially vertically
   - **up > down**[1]
   - overcome with SP or VOR
   - Complete palsy often late feature
5. Smooth pursuit impaired ++

Videos

[1]Chen et al., Frontiers in Neurology, Dec 2010, Volume 1, Article 147

PSP (RS) – eye movements

6. **Vertical > horizontal saccade slowing (occurs early)**
7. Hypometria of saccades (V > H) ++
8. OKN → may show deviation of the eyes in the direction of the slow phase

Videos

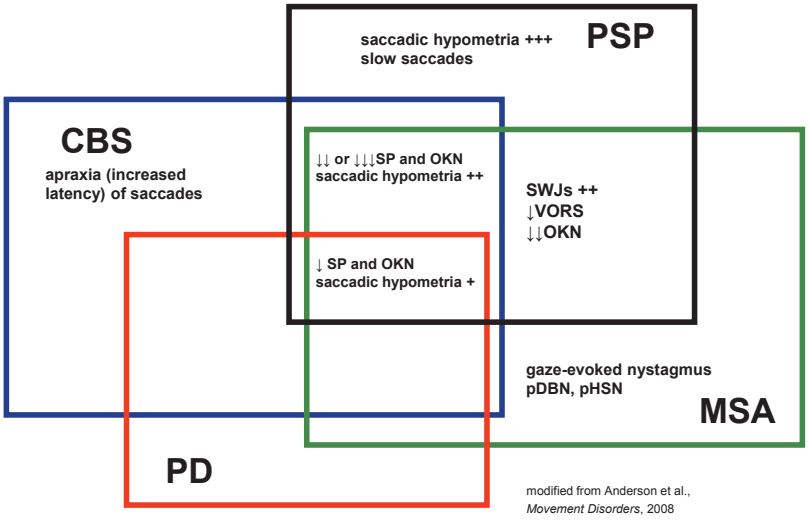
Rivaud-Pechoux, S. et al. Neurology 2000;54:1029-32, Vidailhet M et al. Ann Neurol 1994;35:420-26

CBS – Corticobasal syndrome

- **The distinguishing feature is apraxia of saccades**
  - **i.e. marked delay in saccade latency**
  - **ipsilateral to manual apraxia**
- Saccades can be mild-moderately hypometric
- Normal saccadic velocity
- Smooth pursuit may be mildly impaired

Video

Oculomotor hallmarks of the Parkinsonian syndromes



modified from Anderson et al., *Movement Disorders*, 2008

Huntington's Disease (HD)

Clinical oculomotor features

- Apraxia of saccades
- Distractibilty and impersistence of gaze
- Slow saccades (usually vert > horiz)

Video

Video

- Hypometria of saccades
- Mild-moderate impairment of smooth pursuit

Huntington's Disease (HD)

Westphal (early onset) variant

- Akinetic rigid phenotype
- Slow saccades are prominent

Video

Clinically *slow saccades* in movement disorders

- PSP
- HD
- SCA2

Video

- Lytico-Bodig
- Guadaloupean Parkinsonism
- Neimann-Pick type C
- Wilson's disease
- Manganism
- PKAN
- Whipple's disease
- CJD
- Gaucher's disease (esp. horizontal)

SNGP's in movement disorders

Most common

- PSP
- CBS

Next most common

- MSA
- DLB
- HD
- Niemann-Pick type C
- SCA3, SCA2
- Neuroacanthocytosis

Video

Uncommon disorders

- Lytico-Bodig
- Guadaloupean Parkinsonism
- Wilson's disease
- Manganism
- PKAN
- Whipple's disease
- CJD
- Gaucher's disease

IV. Focal and structural cerebral disorders

Acute Hemispheric Lesions[1]

- Conjugate eye deviation
  - ipsilateral to the lesion (almost always)
    - mostly large infarcts
    - especially posterior
    - especially right sided
      - BG and temporo-parietal regions (inf. parietal lobule) especially[1]
      - Usually associated with spatial neglect
  - rarely contralateral (and usually haemorrhage)
    - esp. thalamic haemorrhage
  - usually transient (< 1 week)

[1]Singer, O. C. et al. Stroke 2006;37:2726-2732

Unilateral Hemispheric Lesions[1]

- ipsilateral conjugate eye deviation (temporary)
- cerebral nystagmus
  - fast phase to side towards lesion side (ophthalmoscopy)
- impaired smooth pursuit and OKN towards lesion side[1] Video
- hypometric contralateral saccades[1]
  - ± slowed
  - ± ↑ latency Video
- "Cogan's spasticity of conjugate gaze"
  - with forced eye closure, eyes deviate to side opposite the lesion
  - especially parieto-occipital lesions

[1]Leigh and Zee, The Neurology of Eye Movements, 4th ed., OUP, 2006, Chapter 12

Acute conjugate ocular deviation

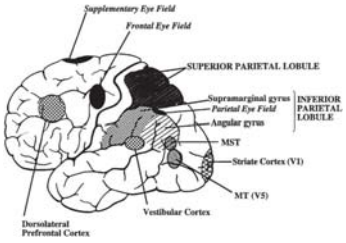
- **Upwards gaze deviation**
  - hypoxic-ischaemic episode (non-localising)
  - drugs/oculogyric crises
- **Downwards gaze deviation**
  - thalamic haemorrhage
  - dorsal midbrain compression (hydrocephalus, tumour, haemorrhage

Video

post-AAA repair cerebral hypoxia/ischaemia

Epileptic ocular deviation and nystagmus

- the epileptic focus is most commonly in posterior hemisphere (parietal)
  - contralateral conjugate deviation ± nystagmus
    - PEF activation
  - rarely, ipsilateral conjugate deviation ± nystagmus
    - pursuit mechanisms activation
- frontal lobe foci can result in contraversive deviation ± nystagmus
    - FEF activation



Video

Diagram from Leigh and Kennard, Brain 2004

Coma and eye movements

- sustained conjugate deviations
  - as previously discussed
- intermittent conjugate deviation ± nystagmus
  - epileptic
- spontaneous (non-epileptic) eye movements

Coma: spontaneous (non-epileptic) eye movements

- Ocular bobbing
  - Rapid conjugate downwards, slow upwards
  - Pontine lesions, metabolic/toxic disorders
- Ocular dipping (inverse bobbing)
  - slow conjugate downwards deviation, fast return
  - non-localising
    - hypoxic-ischaemic
    - metabolic
- Ping-pong gaze
  - conjugate horiz alternating deviations
    - bilateral cerebral hemisphere insults/dysfunction
- Reverse bobbing and reverse dipping (converse bobbing)
  - non-localising
- Periodic alternating gaze deviation
  - conjugate horiz gaze deviations alternating every two minutes
    - hepatic encephalopathy, vegetative state, PAN in comatose patient

Video

ping pong and dipping

V. The dementias

The dementias

1. **The primarily posterior dementias**
   1. Alzheimer's disease (AD)
   2. Parkinson's disease dementia (PDD)
   3. Dementia with Lewy bodies (DLB)

Inability to shift attention and launch reflexive saccades

i.e. "fixation spasm"

2. **The primarily frontal dementias**

   Fronto-temporal lobar degeneration (FTLD)
   - Frontal/Behavioural Variant 40%
   - Semantic Dementia 40%
   - Progressive Nonfluent Aphasia 10%

Inability to suppress saccades/glances

i.e. "visual grasp"

Gaze impersistence, distractability and fixation spasm (esp. your face)

Summary

- Central eye movement disorders are usually conjugate
- They are highly sensitive to disease states but frequently asymptomatic
- Thus careful and orderly clinical oculomotor exam is key
- Can be excellent pointers to diagnosis but few are pathognomonic in themselves
- Diagnosis is usually clinched by the associated neurological features
- Spontaneous (fixation) eye movements, nystagmus, slow saccades, and SNGPs are particularly helpful oculomotor features

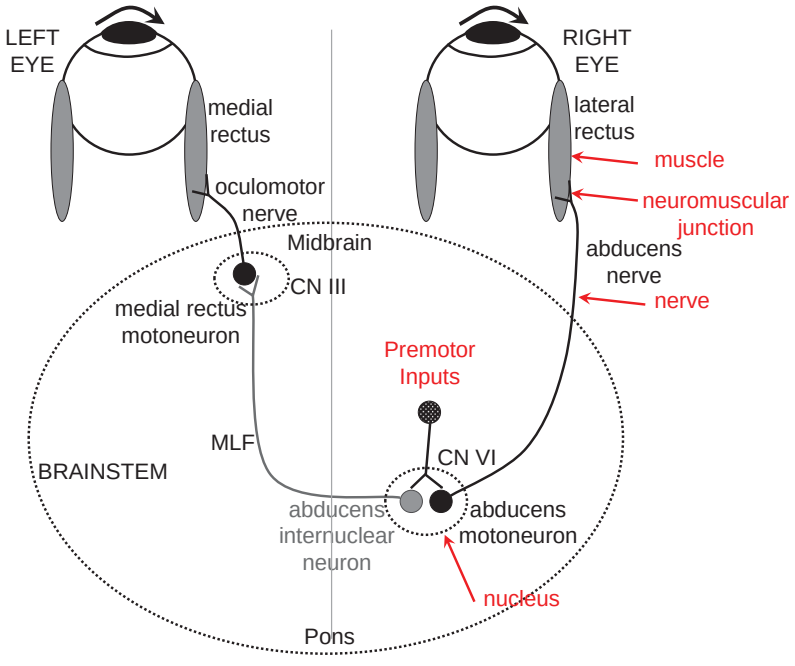
When the Eyes Don't Move Together: Diagnosing peripheral and central causes of diplopia

R. John Leigh, M.D.
Case Western Reserve University
Cleveland, Ohio

CASE WESTERN RESERVE UNIVERSITY EST. 1826

Prelude: A Conceptual Approach

For simplicity, first consider the anatomy underpinning horizontal gaze



A map for this talk

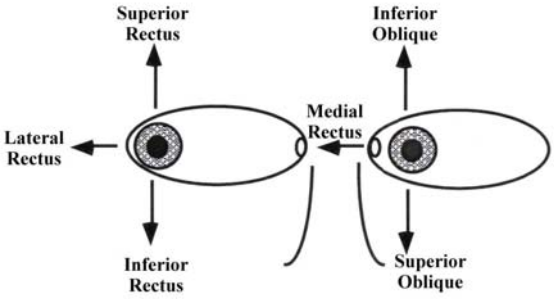
- Clinical evaluation
- Orbital disorders
- Disease affecting the extraocular muscles
- Disease of the neuromuscular junction
- Disease of the ocular motor nerves
- Brainstem causes of diplopia
- Spasm of convergence

Clinical Evaluation in Diplopia

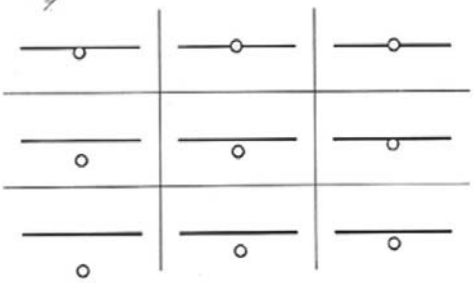
- First test visual acuity and fields; fundi, pupils, lids
- Cover one eye to determine if diplopia is binocular (disappears) or monocular (persists)
- Monocular diplopia is often due to refractive error or incipient cataract – improves with pinhole

Clinical Evaluation in Diplopia

- Determine if binocular diplopia is:
  - Horizontal, vertical, or both (diagonal)
  - Worse at far or near
  - Worse in one direction of gaze
- Test range of movements with each eye viewing monocularly (ductions)
- Test range of movement with both eyes viewing (versions):
  - Determine the direction of gaze in which diplopia is worst

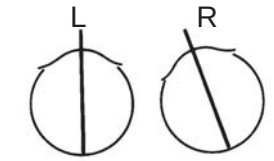


Subjective Tests (Maddox Rod)

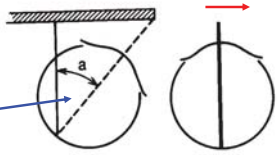


COVER TEST

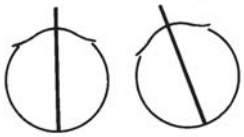
Consider right sixth nerve palsy → Right Esotropia



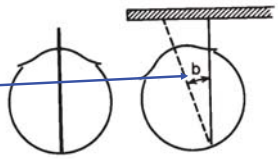
Cover left eye
Right eye makes "movement of redress"
Normal left eye under cover is turned far in – *Secondary Deviation* (a)



Remove Cover
Normal left eye takes up fixation

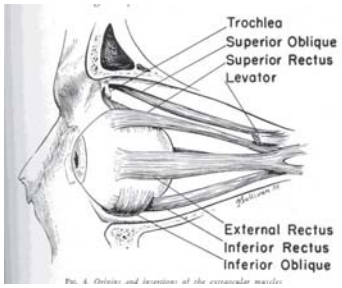


Cover right eye
Paretic right eye under cover is turned in – Primary *Deviation* (b)



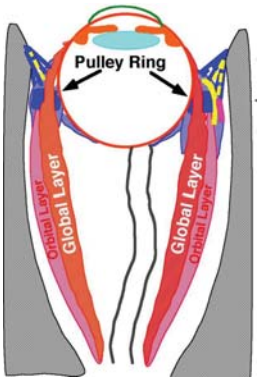
Orbital Anatomy

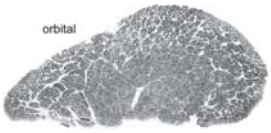
David G. Cogan



Joel Miller and Joseph Demer

Demer and Miller

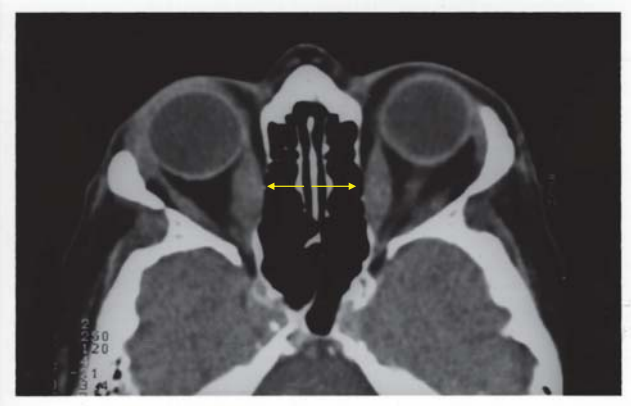




John Porter

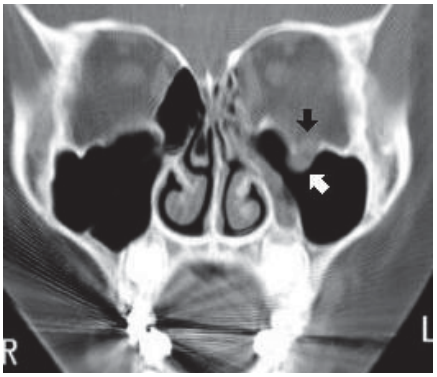
Orbital disease causing diplopia

Orbital disease causing diplopia



Thyroid and other infiltrates

Orbital disease causing diplopia

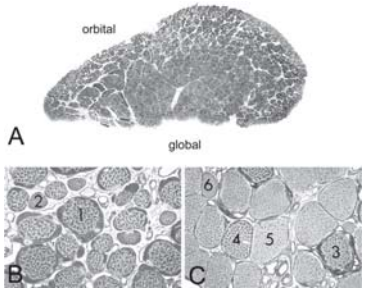


Trauma – blow-out fracture

Disease affecting the extraocular muscles

Disease of the extraocular muscles (EOM)

- Orbital and global layers
- Unique fiber types
- Susceptible to disorders of energy metabolism → mitochondrial myopathy
- Affected by nuclear genetic disorders, *e.g.,* of myosin
- *Rarely* causes diplopia
- *Sometimes* cause strabismus
- *Often* causes ptosis
- Progressively limit and slow eye movements



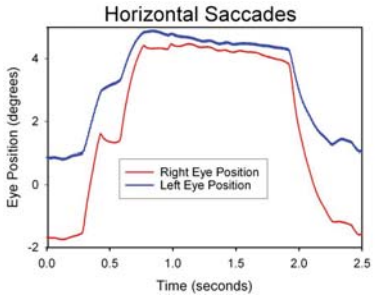
Courtesy: Dr. John D. Porter

Mitochondrial Myopathy

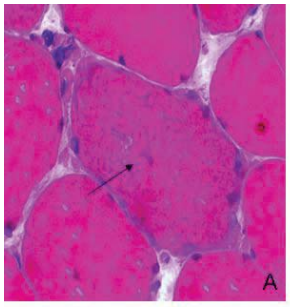
- A 67-year-old man presented to the neurology clinic
- Ptosis for 30-years, unilaterally → bilateral
- By 40's, retracted his upper eyelids with adhesive tape.
- By late 50's →difficulty moving eyes – so turned head
- Only fleeting diplopia, a few times each year
- Upper extremity weakness for the past 4 to 5 years
- Sensorineural hearing loss
- Ptosis in the patient's mother and maternal aunt; mother also developed hearing loss in middle age
- Cardiological evaluation -- normal

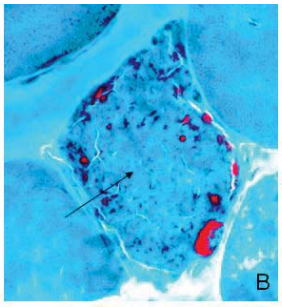
Chronic Progressive External Ophthalmoplegia (CPEO)

VIDEOS



- Ptosis
- Very limited horizontal range of movement
- Horizontal saccades very slow and disjunctive
- Vertical range larger (> 10 degrees)
- Vertical saccades slow but conjugate
- Head rotations did not increase range of eye movements



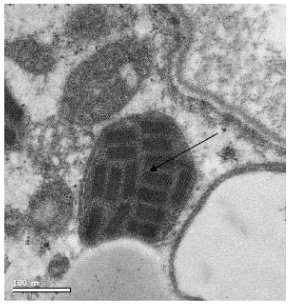


Deltoid Muscle Biopsy

Gomori trichrome, X40: Classic “ragged red fiber”

H&E, X40: Dystrophic myofibers containing subsarcolemmal accumulation of abnormal mitochondria

EM X50,000: Swollen dystrophic subsarcolemmal mitochondrion packed with paracrystalline inclusions



Southern blot → mitochondrial DNA deletion

Disease affecting the neuromuscular junction

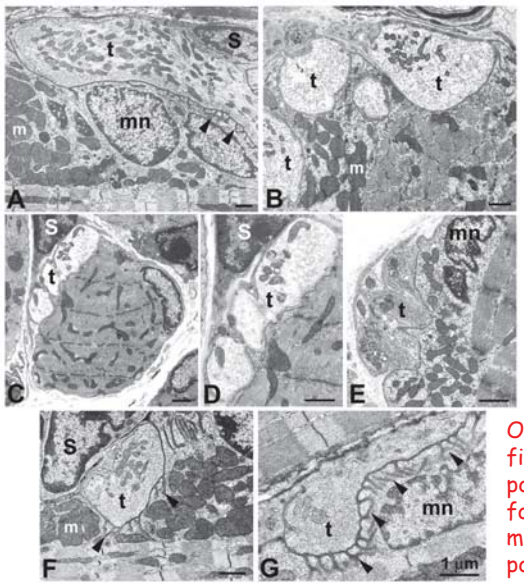
Myasthenia Gravis – Edrophonium Test

VIDEOS

Before edrophonium, patient attempts to make horizontal saccades → limited range but sometimes fast ("quiver movements")

After edrophonium, patient attempts to fixate on camera, but macrosaccadic oscillations (hypermetria) intrude

Most EOM endplates lack postjunctional folding → makes them susceptible to fatigue in MG by lowering safety factor



Orbital singly-innervated fibers. t= nerve terminal, m=mitochondria, mn=myonuclei, s=Schwann cell

Orbital (C,D) and global (E) multiply (innervated fibers

Only global pale fibers show post-junctional folding→ fast movements still possible

John D. Porter

Botulism

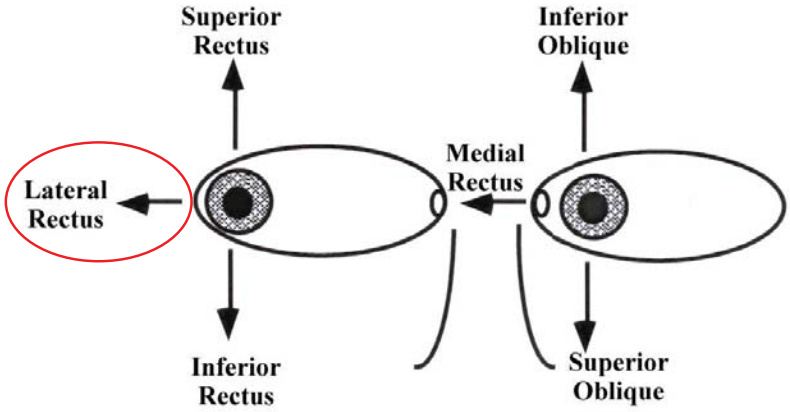
- 39-year-old man developed dysphagia, drooling, diplopia, and generalized weakness following a gastrointestinal illness
- Diagnosis made from stool cultures and nerve conduction studies
- Treated with trivalent antitoxin, and recovered in 7 weeks
- Video made on day 6 of illness, when he had sluggish pupillary responses, mild ptosis, and exotropia

VIDEOS

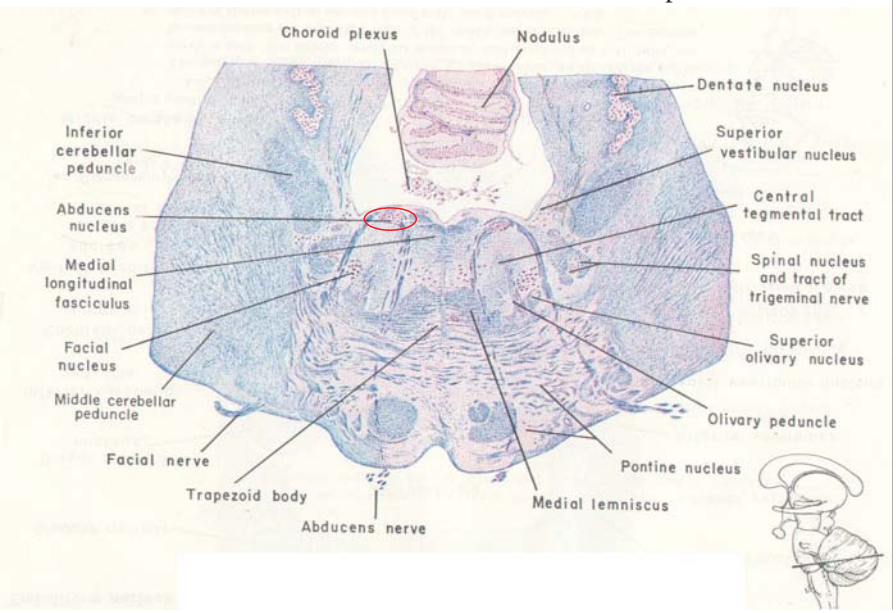
Stahl,J.S., Averbuch-Heller,L., Remler,B.F. & Leigh,R.J. *Neurology* **51**, 1093-1099 (1998)

Palsies of the abducens, trochlear and oculomotor nerves

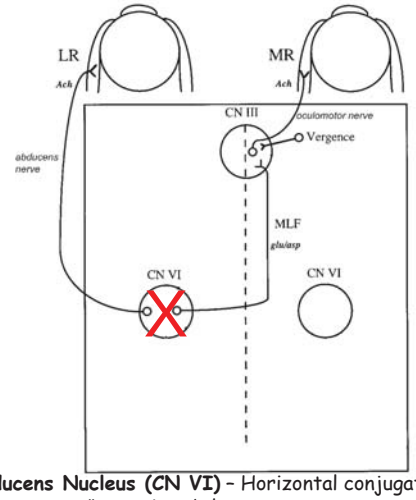
Abducens Nerve Palsy



Abducens nerve nucleus is in the pons



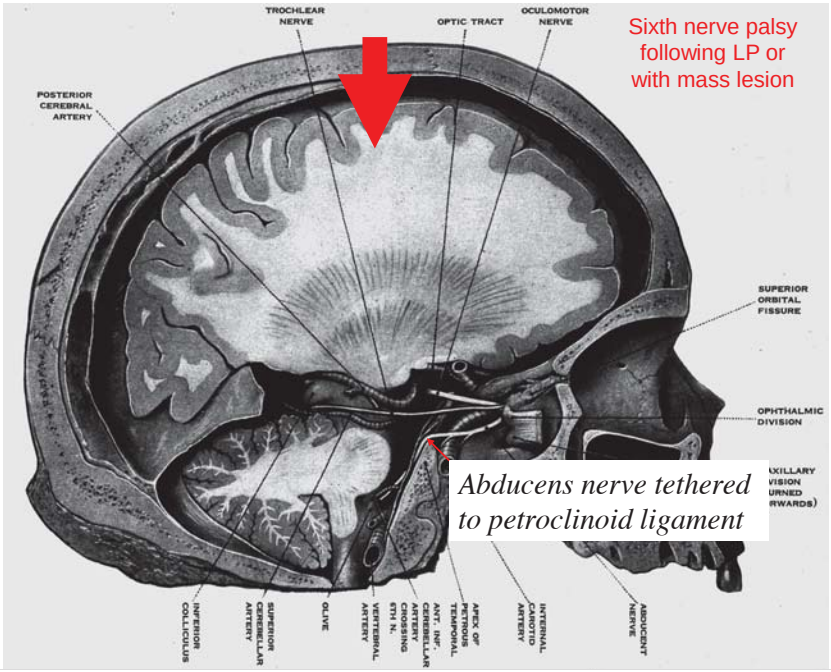
Horizontal Gaze Palsy



Abducens Nucleus (CN VI) – Horizontal conjugate "gaze center" contains abducens motoneurons and internuclear neurons. *Lesions of the abducens nucleus cause horizontal conjugate gaze palsy.*

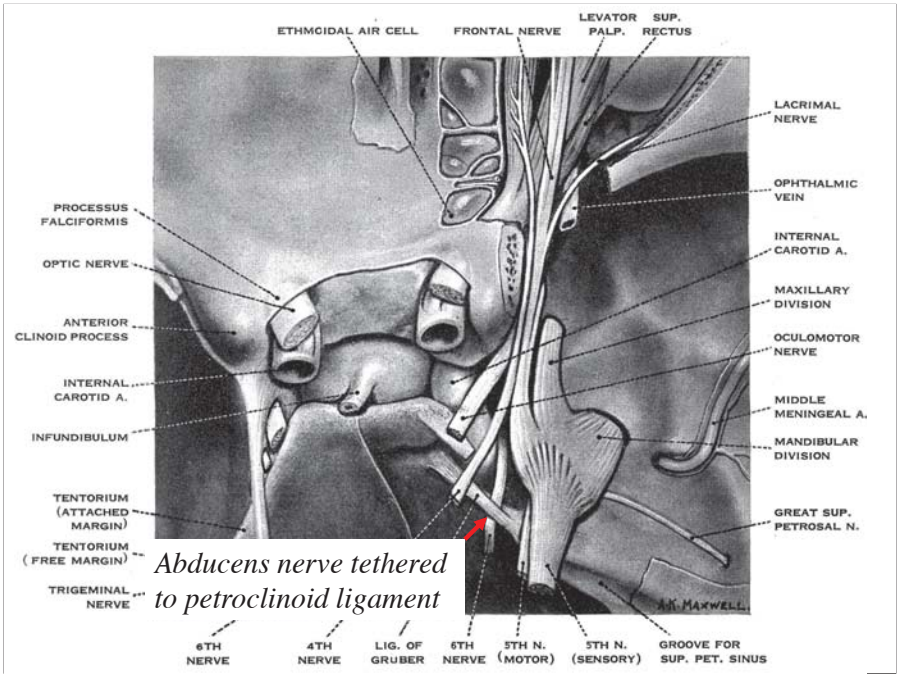
VIDEOS

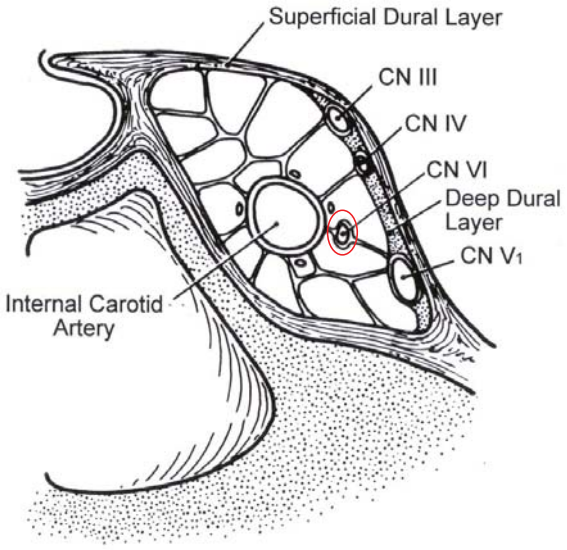
From Miller et al. J Neuroophthalmology 22:204-207, 2003, with Permission of Lippincott, Williams and Wilkins (http//:lww.com)



Sixth nerve palsy following LP or with mass lesion

Abducens nerve tethered to petroclinoid ligament





Sixth nerve palsy and Horner syndrome localizes to the cavernous sinus

Common causes of CN VI Palsy

- Nerve infarction (occlusion of vasa nervorum) in association with diabetes or hypertension
- Subarachnoid disease – meningitis, aneurysms
- Petrous bone disease (infection, tumor, trauma) can affect CN VI
- Associated with immunization or viral illness (in children versus pontine glioma)

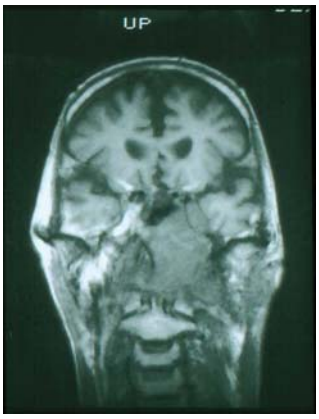
Common causes of CN VI Palsy

- Nerve infarction (occlusion of vasa nervorum) in association with diabetes or hypertension
- Subarachnoid disease – meningitis, aneurysms
- Petrous bone disease (infection, tumor, trauma) can affect CN VI
- Associated with immunization or viral illness (in children versus pontine glioma)

VIDEOS

Common causes of CN VI Palsy

Base of skull tumors and nasopharyngeal cancer may present with CN VI palsy and facial pain

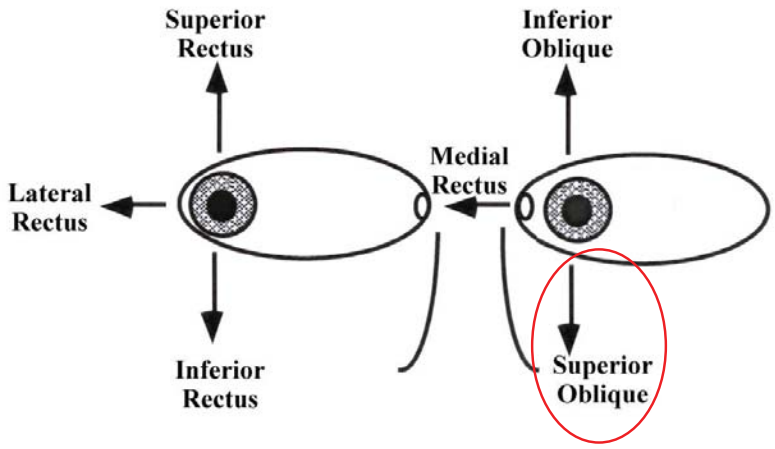


Abducens nerve palsy is not the only cause of abduction weakness

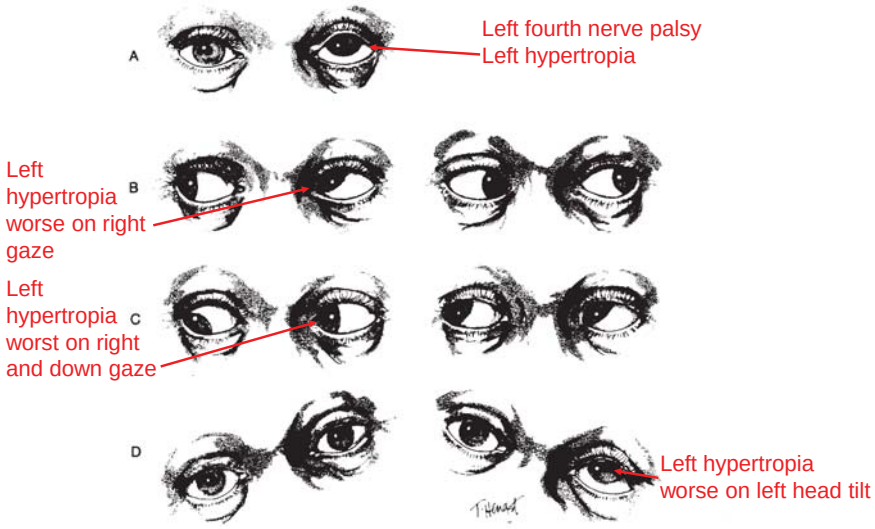
Dr. Daroff's List of "T" Suspects for Abduction Weakness

- Tricks – convergence spasm
- Trauma – muscle entrapment in the orbit
- Thyroid and other restrictive processes
- Tensilon – neuromuscular disease
- Thiamine – Wernicke's encephalopathy
- Tropia – longstanding misalignment due to mal-development of binocular vision

Trochlear Nerve Palsy



Bielschowsky Head-tilt Test



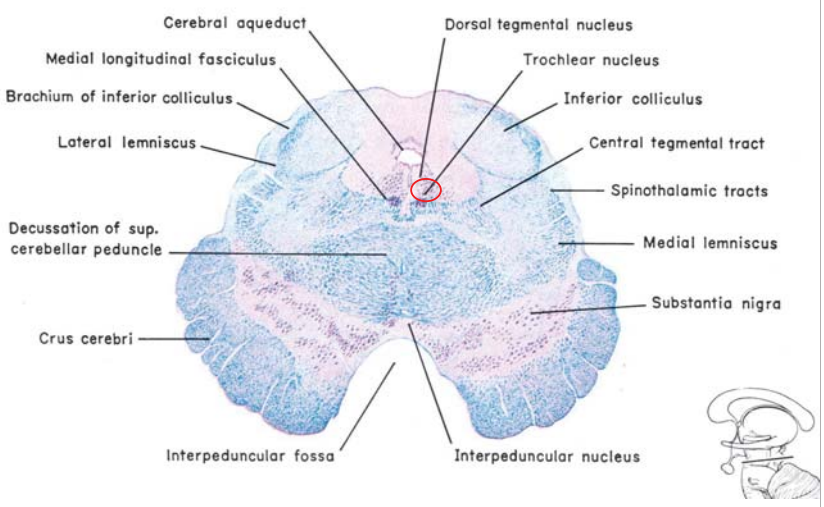
Left Trochlear Nerve Palsy

Hyperphoria decreases | Left hyperphoria | Hyperphoria increases

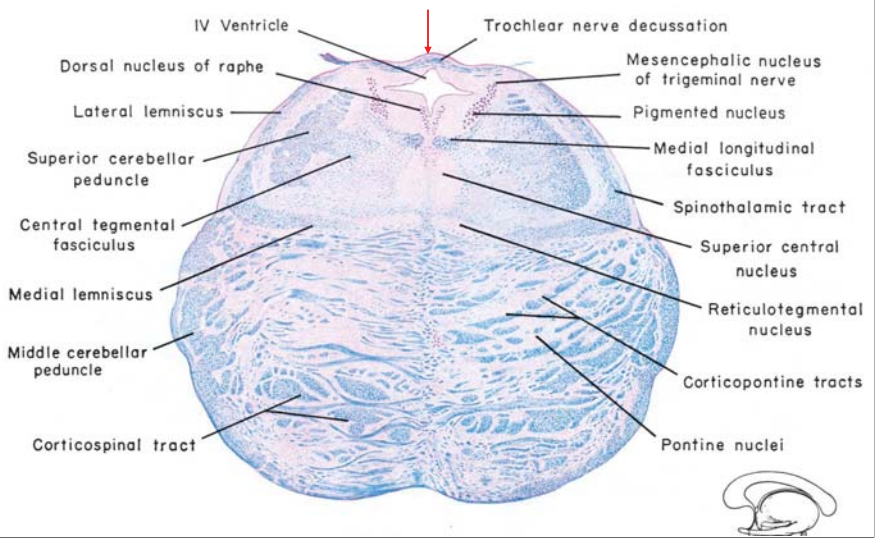
VIDEOS

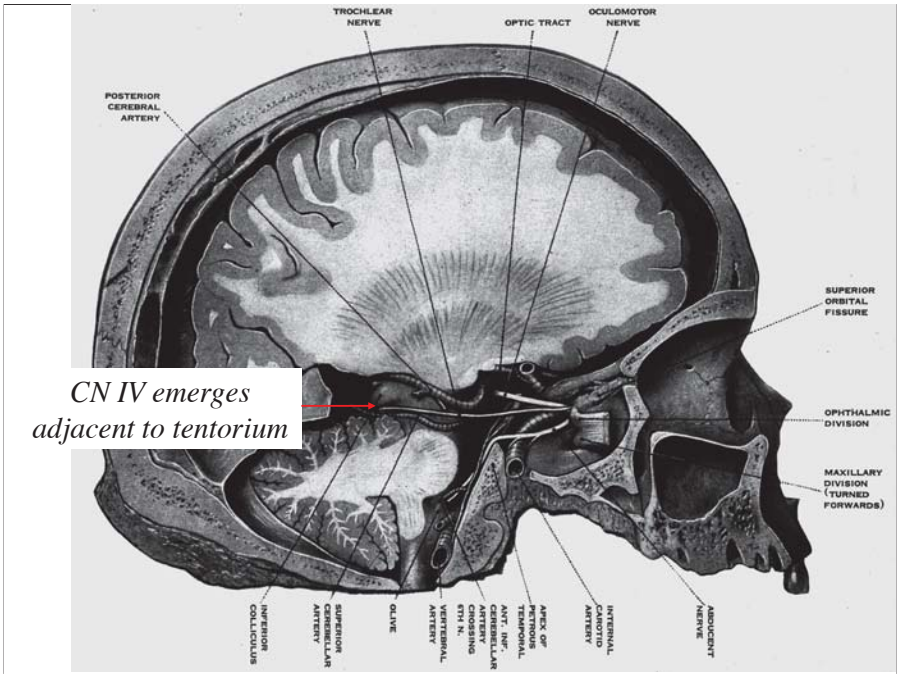
Trochlear nerve palsy in a hypertensive 55-year-old man

The trochlear nerve nucleus lies in the lower midbrain



CN IV rootlets emerge from the *dorsal* surface of the isthmus





CN IV emerges adjacent to tentorium

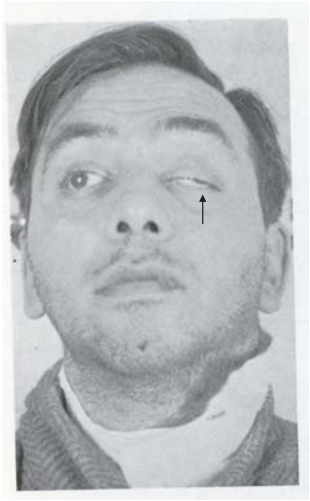
Common causes of CN IV palsy

- Trauma (compression by free tentorial edge as nerve emerges from dorsum of midbrain)
- Following craniotomy (due to long course of the nerve in the skull)
- Nerve infarction in association with diabetes and hypertension

Oculomotor Nerve Palsy

Appearance of complete left CNIII palsy

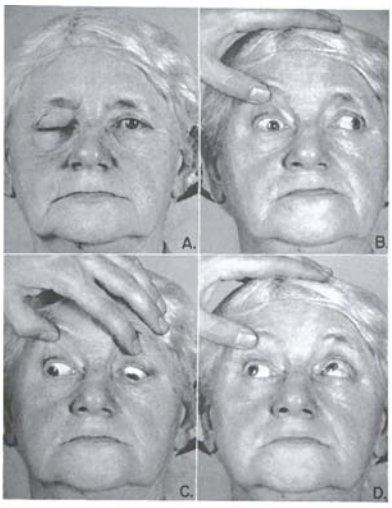
David G. Cogan

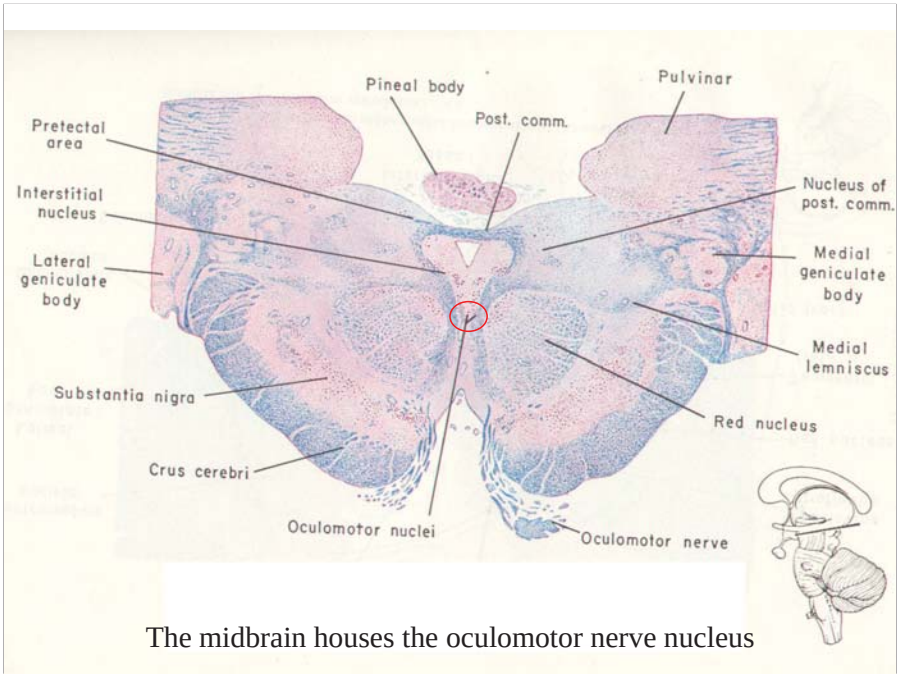


Resting position of the affected eye – *down and out*

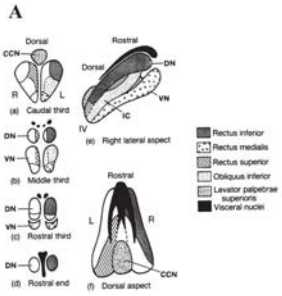
Appearance of complete right CNIII palsy

David G. Cogan





The midbrain houses the oculomotor nerve nucleus



Nuclear CN III

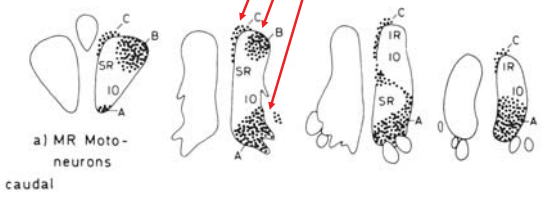
Ptosis is bilateral

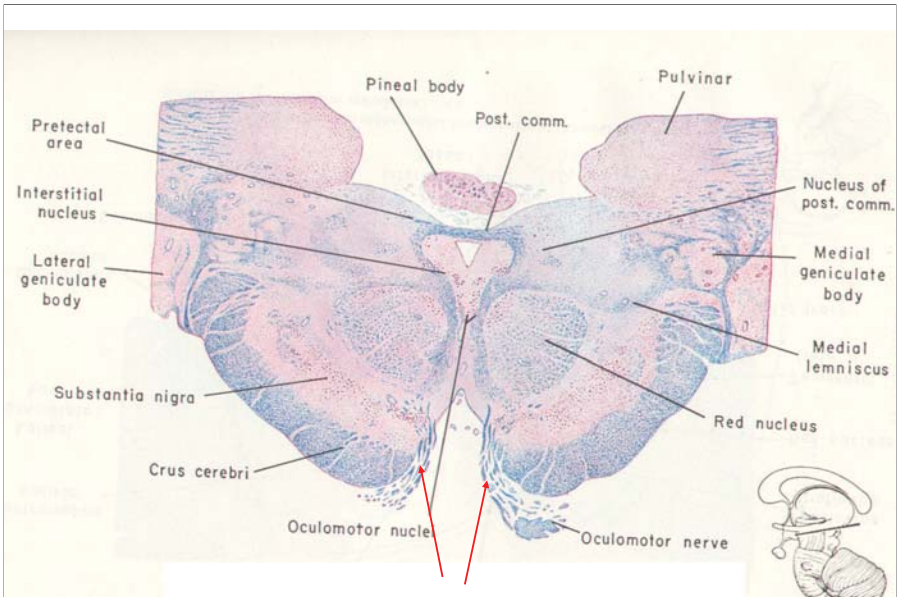
Superior rectus weakness is bilateral

Isolated weakness of other muscles is possible

Isolated medial rectus paresis is unlikely

Jean Büttner-Ennever's revision: More than one group of medial rectus motoneurons (A,B,C)





The oculomotor nerve fascicles emerge from the medial side of the cerebral peduncles

Partial CN III palsy +

VIDEOS

- 54-year-old man presented with right ptosis and diplopia
- Main limitation of movement: elevation of right eye
- Adduction and infraduction were spared
- Note large secondary deviation of left eye under cover

Partial CN III palsy +

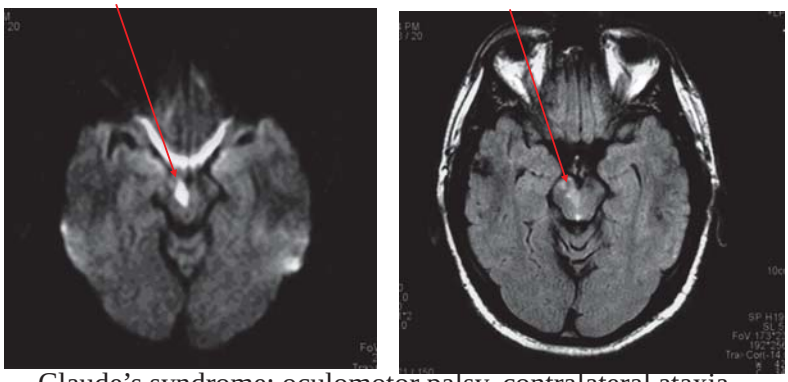
VIDEOS

Pupil spared

…plus left hemiataxia

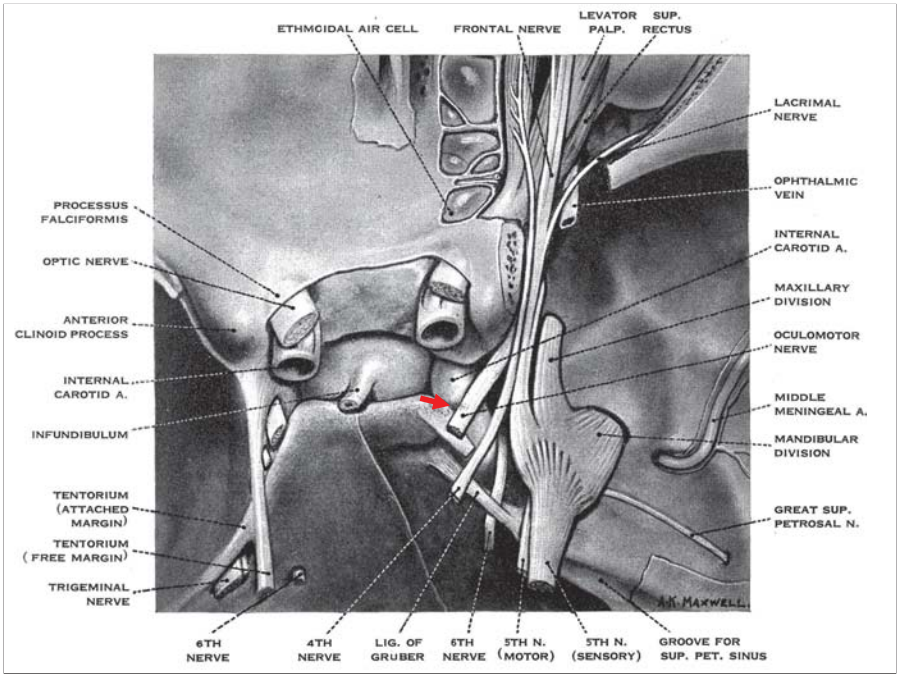
Claude's Syndrome

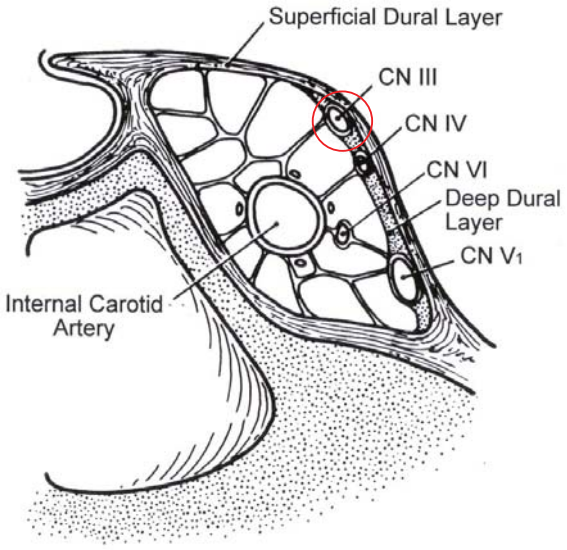
Signal change on DWI and T1 MRI consistent with infarction affecting right oculomotor nerve fascicle and superior cerebellar peduncle



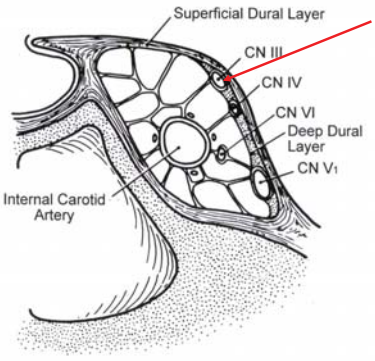
Claude's syndrome: oculomotor palsy, contralateral ataxia

Superior division of CNIII may be selectively affected





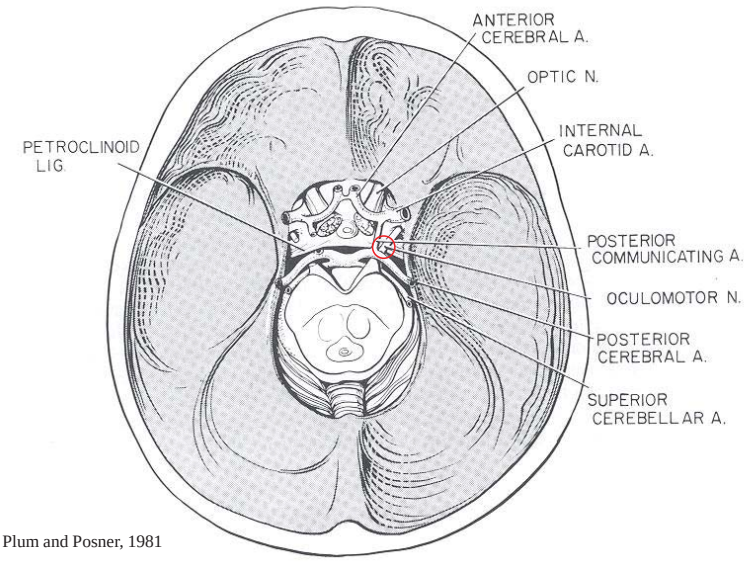
Pituitary apoplexy causing CNIII palsy



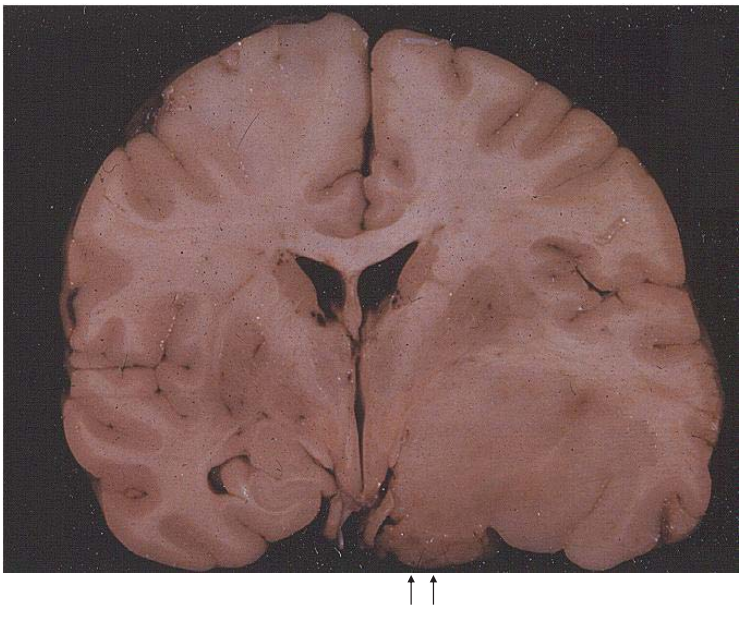
VIDEOS

Common causes of CN III palsy

- Nerve infarction in association with diabetes or hypertension (“pupil spared”)
- Compression by aneurysm (“pupil involved”)
- Involvement in its subarachnoid course by meningitis or tumor
- Compression by herniating temporal lobe…



Plum and Posner, 1981



Neuropathy Affecting Multiple Ocular Motor Nerves

The New England Journal of Medicine

Copyright, 1956, by the Massachusetts Medical Society

Volume 255 257-65 JULY 12, 1956 Number 2

AN UNUSUAL VARIANT OF ACUTE IDIOPATHIC POLYNEURITIS (SYNDROME OF OPHTHALMOPLEGIA, ATAXIA AND AREFLEXIA)*

MILLER FISHER, M.D.†

BOSTON

THE purpose of this communication is to report 3 cases of an acute neurologic illness characterized among other features by total external ophthalmoplegia, severe ataxia and loss of the tendon reflexes. The

for 3 days. On the 1st day of illness, a slight transient dizziness had been noted - not a rotational feeling, but an unsteady sensation in the head. Later in the day there was a feeling of malaise, and the chest felt as if it were tightening up "like an ordinary cold." About 4 p.m., on trying to climb a stepladder, he noted that the unsteady

VIDEOS

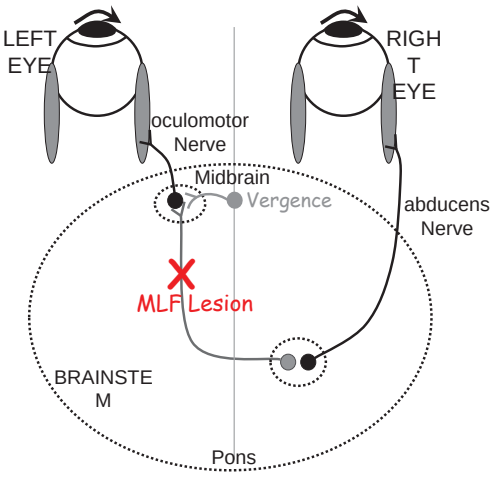
Brainstem Causes of Diplopia

INO and 1 ½ syndrome

Midbrain vergence disorders

Skew deviation

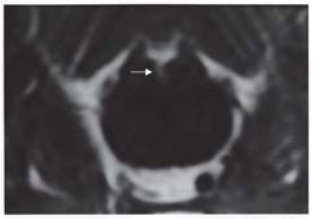
Left MLF Nucleus Lesion → Left INO



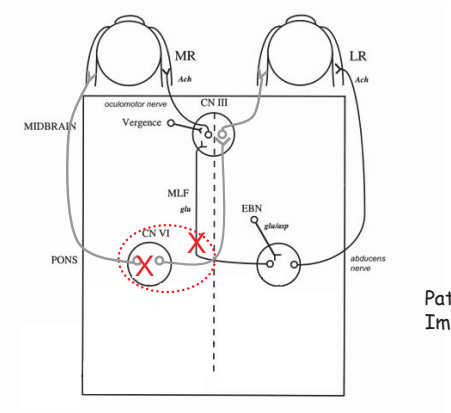
Ipsilateral adducting movements abolished

Vergence spared

VIDEOS



One-and-a-half syndrome



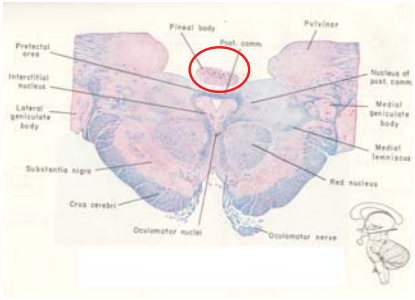
VIDEOS

Video courtesy R. B. Daroff

Patient with MS. Impaired left conjugate gaze. Impaired left adduction. Preserved convergence

Pineal Tumor and Vergence: Convergence-retraction nystagmus

VIDEOS



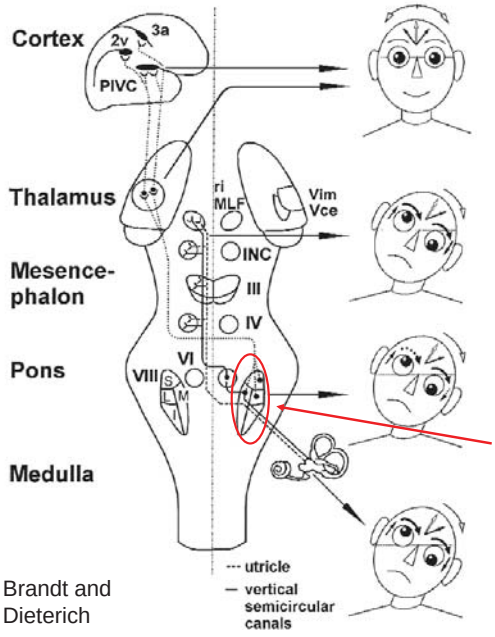
Videos courtesy Dr. Robert L. Tomsak

Skew Deviation and Ocular Tilt Reaction

Imbalance of Otolithic Inputs

Inner ear (otoliths) or CN VIII
Lateral medulla
INO
Midbrain – interstitial nucleus of Cajal

Negative Bielschowsky Head-Tilt Test

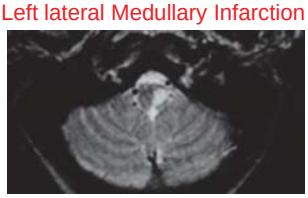


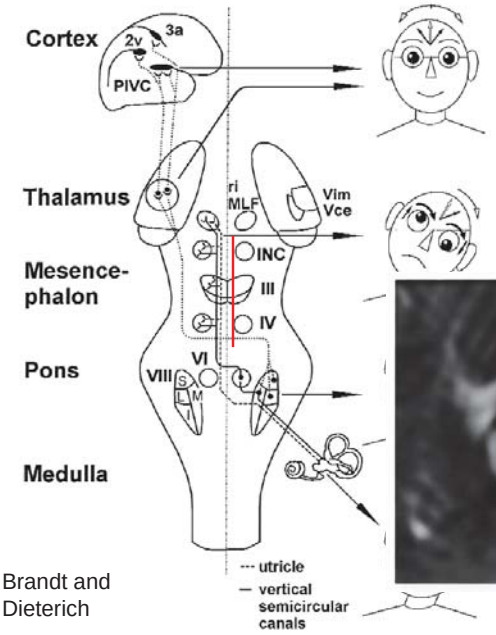
Brandt and Dieterich

VIDEOS

Eye down on side of lesion

Left lateral Medullary Infarction

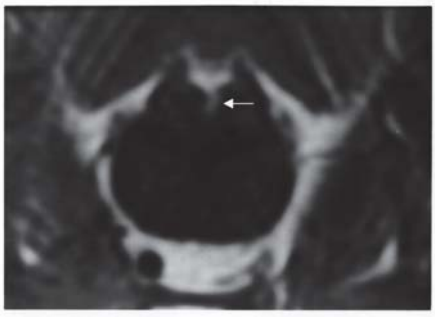




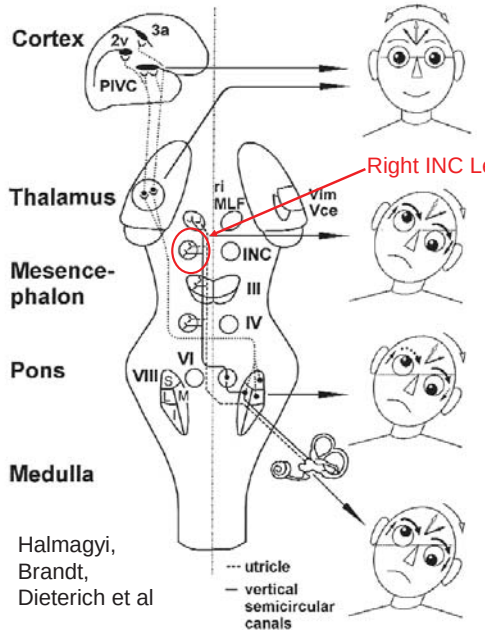
Brandt and Dieterich

VIDEOS

Eye up on side of lesion

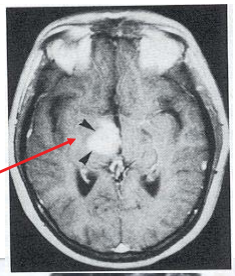


Left INO



Halmagyi, Brandt, Dieterich et al

Right INC Lesion



Eye up on side of lesion

Spasm of Convergence

Voluntary convergence when asked to make conjugate movements

Appearance is of variable abduction weakness

Constriction of pupil occurring with vergence

VIDEOS

SUMMARY

- Disorders of the tissues of the orbit, especially thyroid disease, can cause diplopia
- Disease of the extraocular muscles limits eye movements and causes ptosis, but does not usually cause prominent diplopia
- Ocular myasthenia is unique in causing limited range but rapid movements
- Diagnosis of ocular motor nerve palsies is helped by consideration of the nerves' anatomical courses
- Brainstem lesions may cause INO or skew deviation, due to interruption of ascending pathways
- Midbrain lesions may cause abnormal vergence with saccades
- Psychogenic spasm of convergence – watch the pupil!