5th Congress of the European Academy of Neurology

Oslo, Norway, June 29 - July 2, 2019

Teaching Course 15

Eye movements and vestibular function in critical care, emergency, and ambulatory neurology (Level 2)

Eye movements in cognitive and neurodegenerative disorders

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Eye movements in cognitive and neurodegenerative disorders

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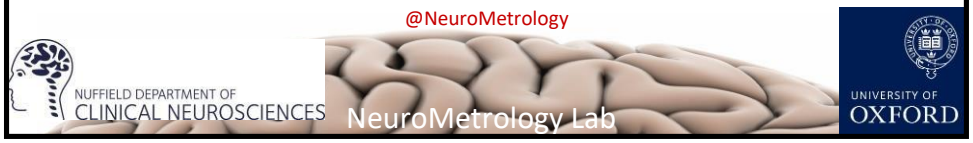


Conflict of Interest

In relation to this presentation and manuscript:

❑ the Author has no conflict of interest in relation to this manuscript.

ean congress Oslo 2019 5 years ean

Outline

- Parkinson's disease (PD)
- Surgical PD (deep brain stimulation)
- Progressive Supranuclear Pasly (PSP)
- Cerebellar Ataxia

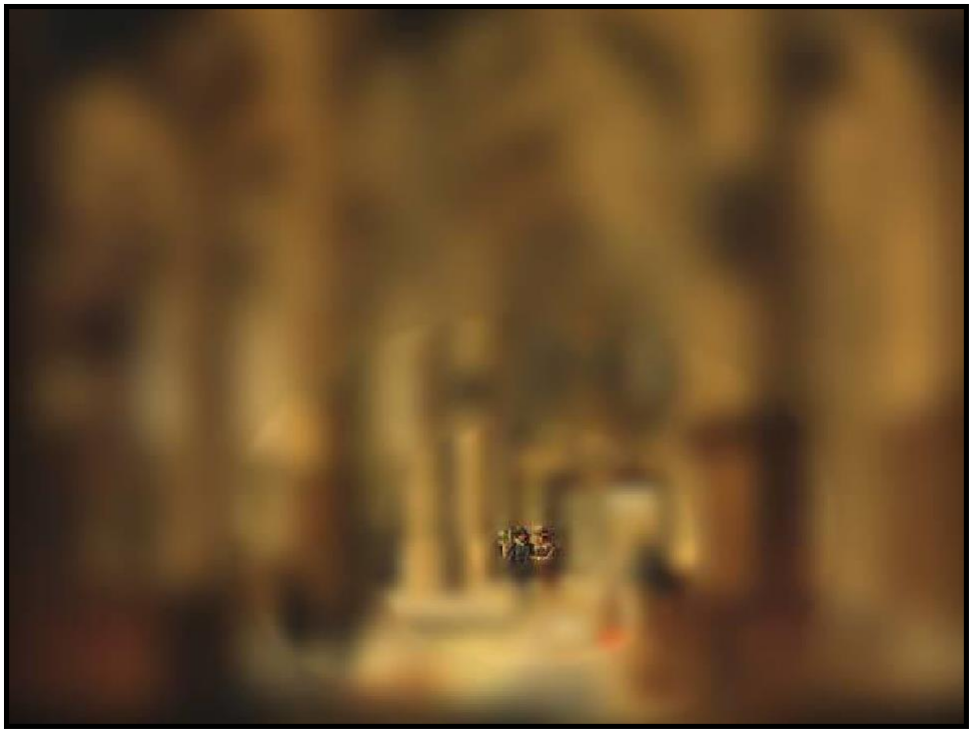
Sir Charles Sherrington

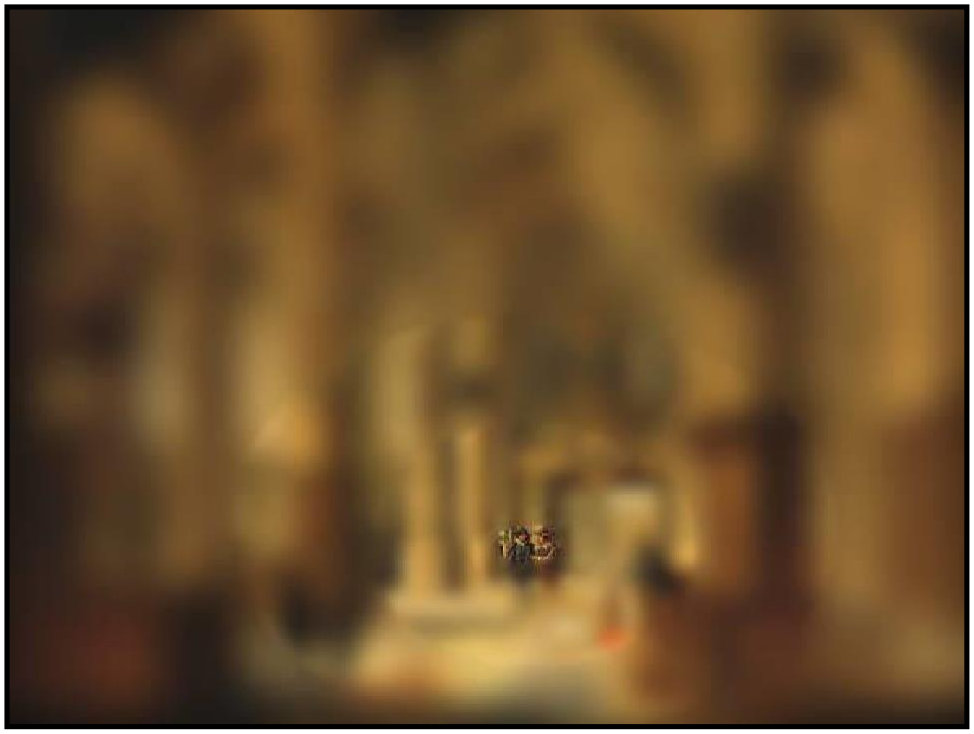
Professor of Physiology, Oxford; Nobel Prize for Medicine

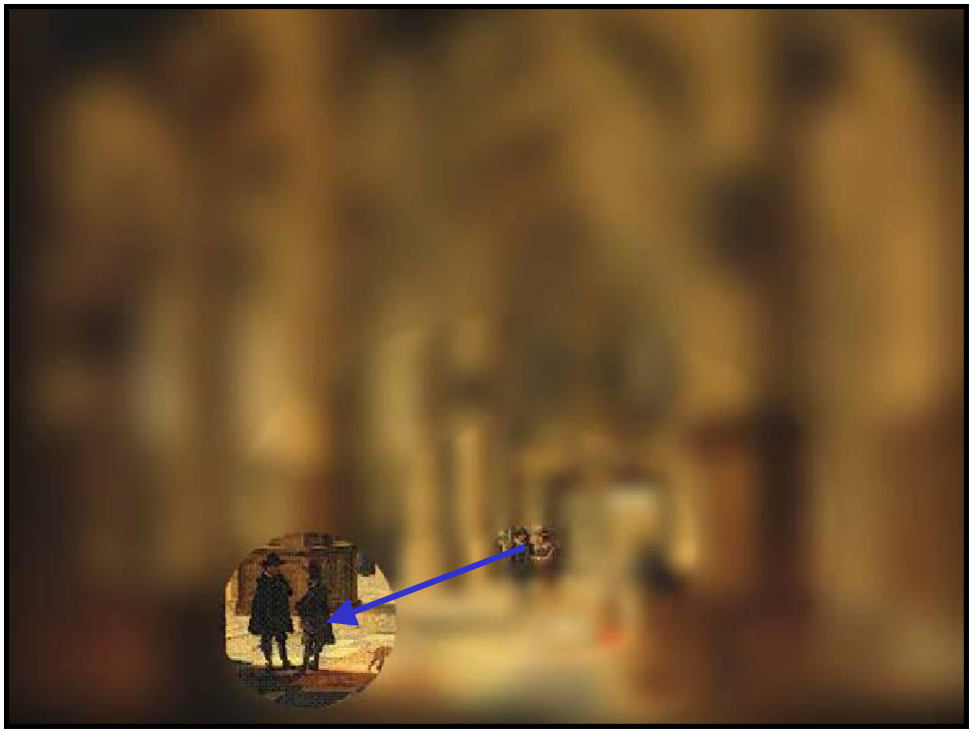
Man on his Nature (1938)

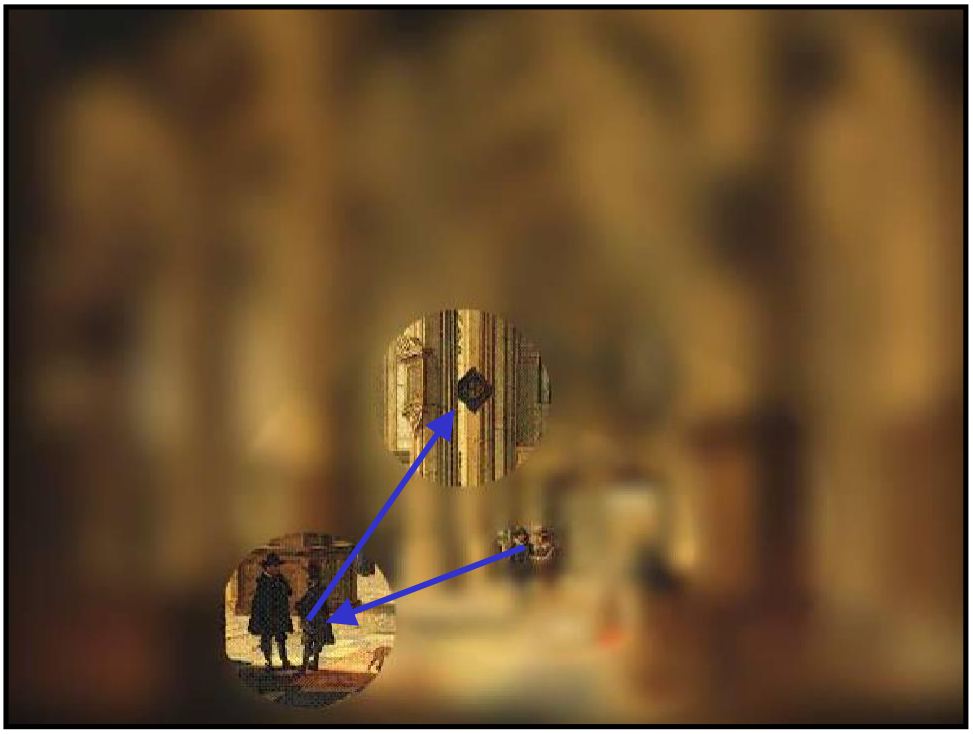
An act which may seem simple even to banality is the directing of the gaze. Yet its factors engage the roof-brain far and wide …

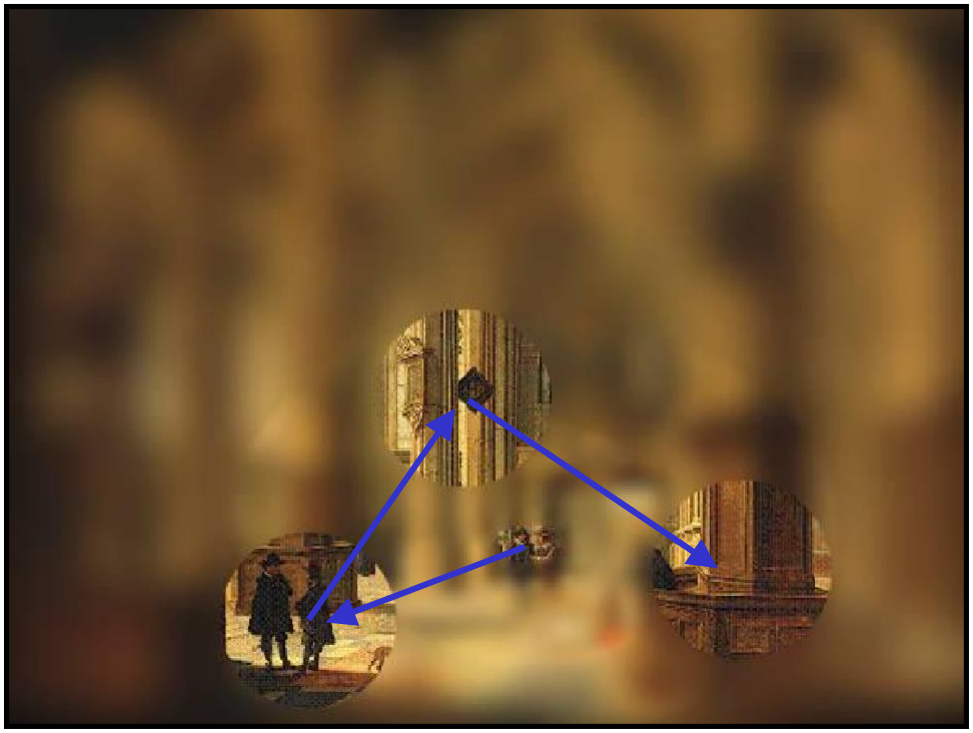
How do we look at a visual scene?

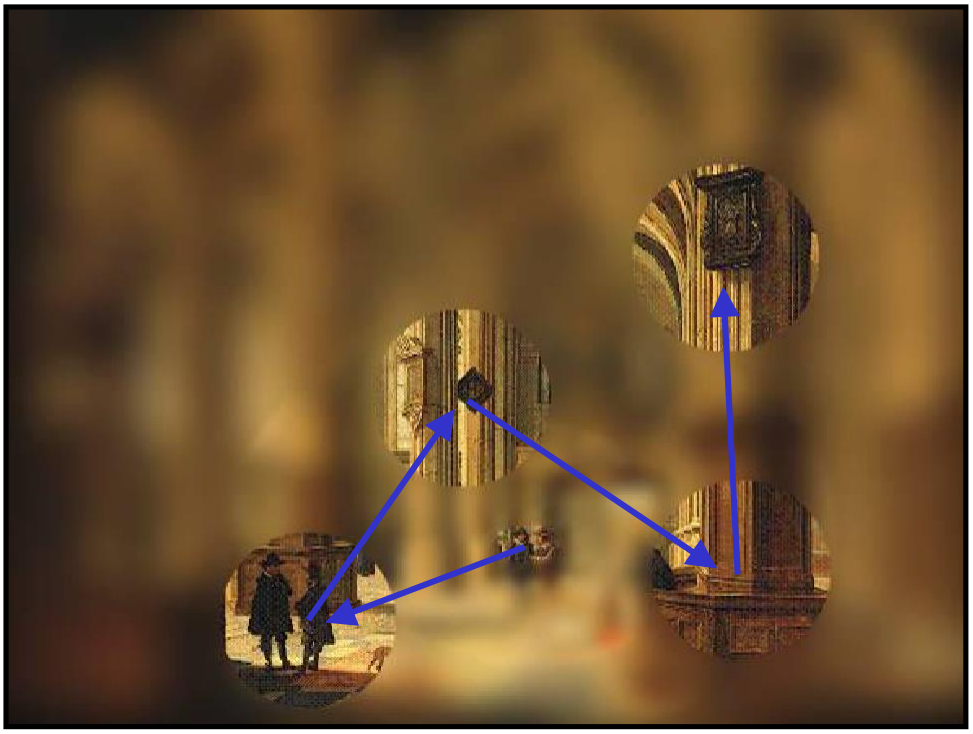


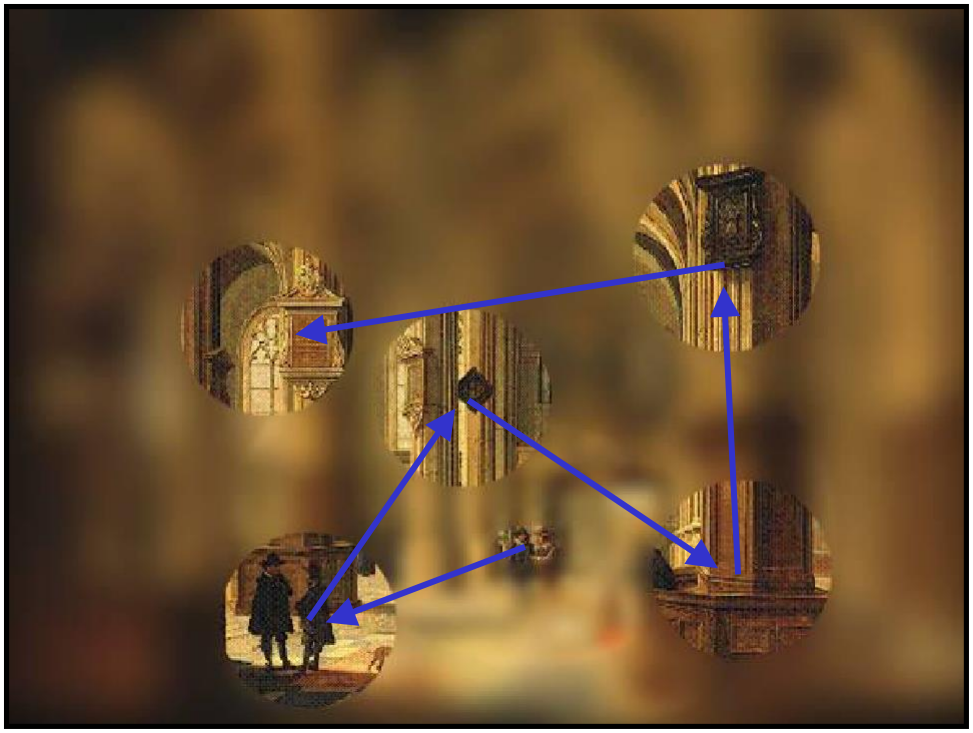


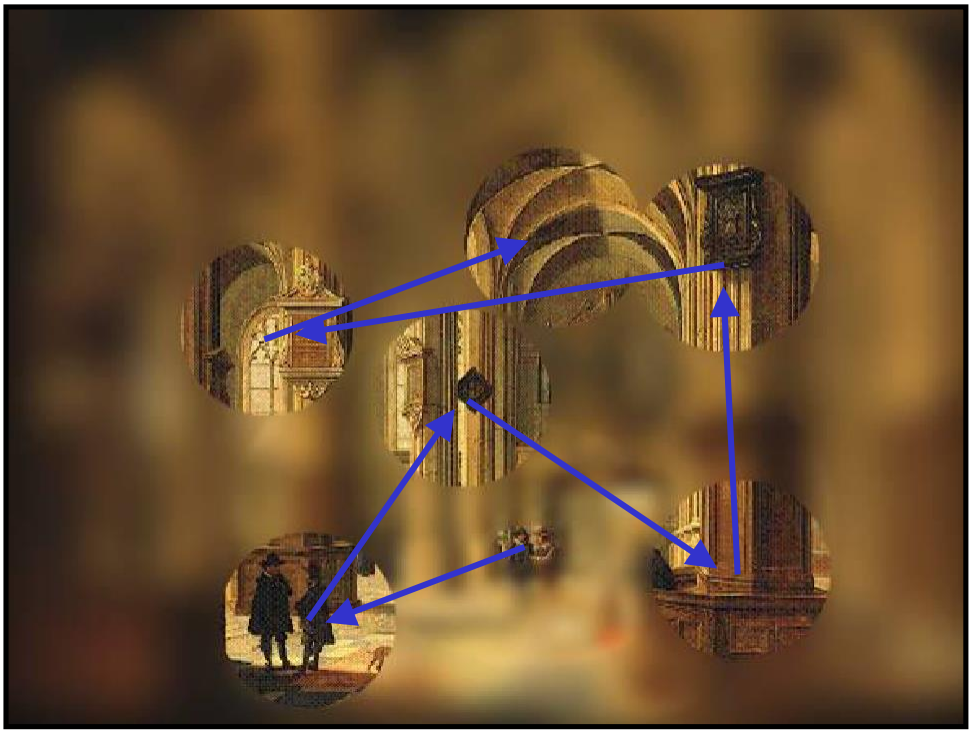


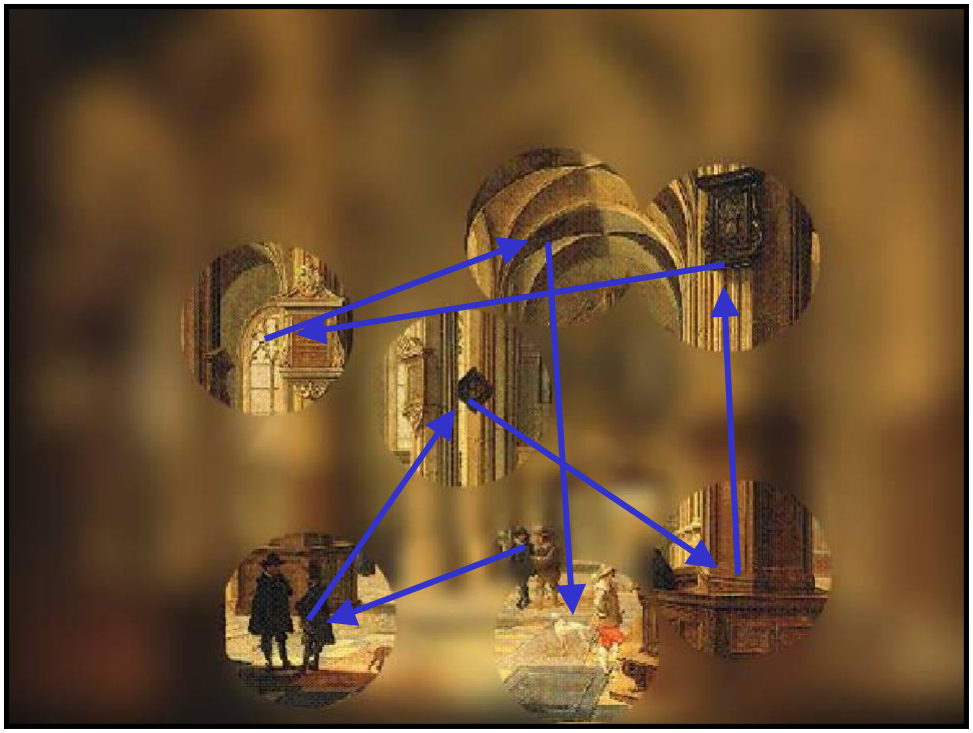


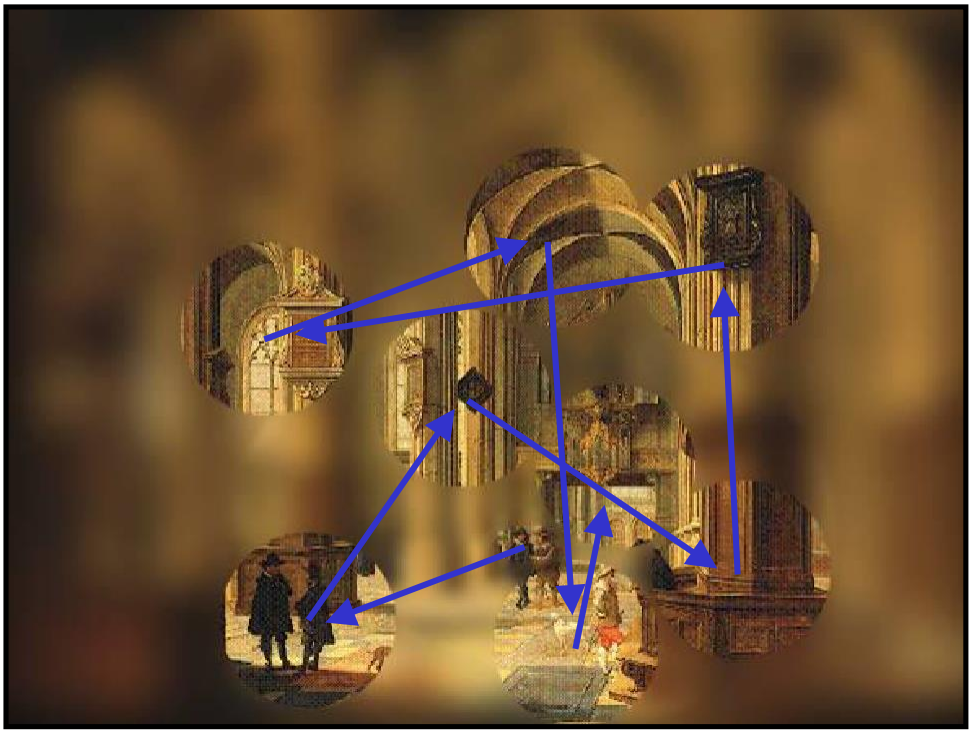


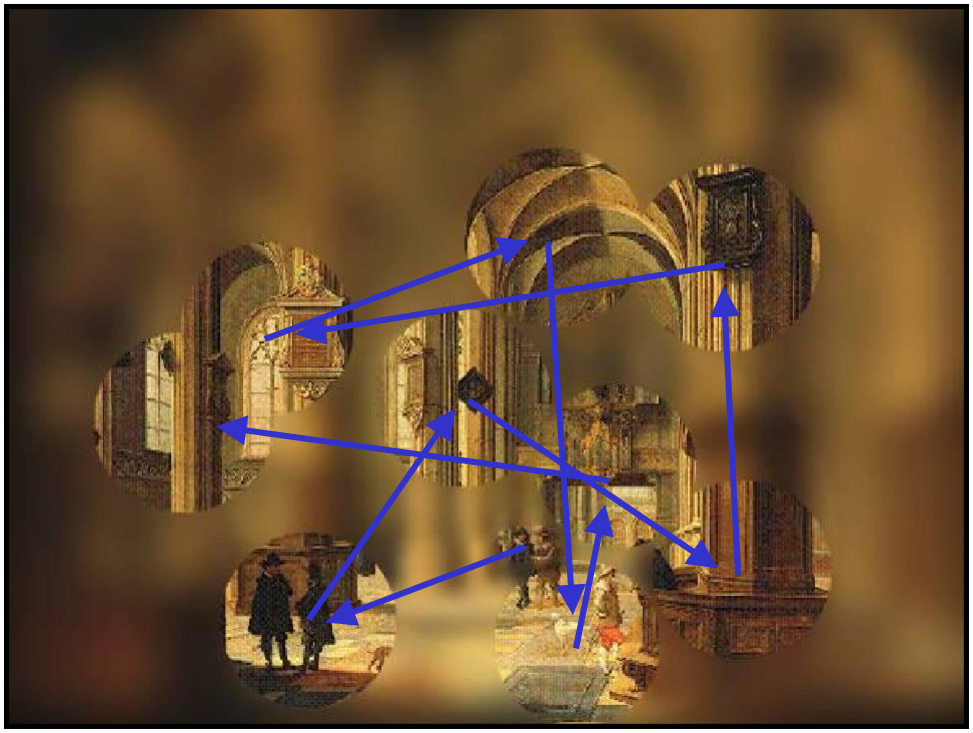


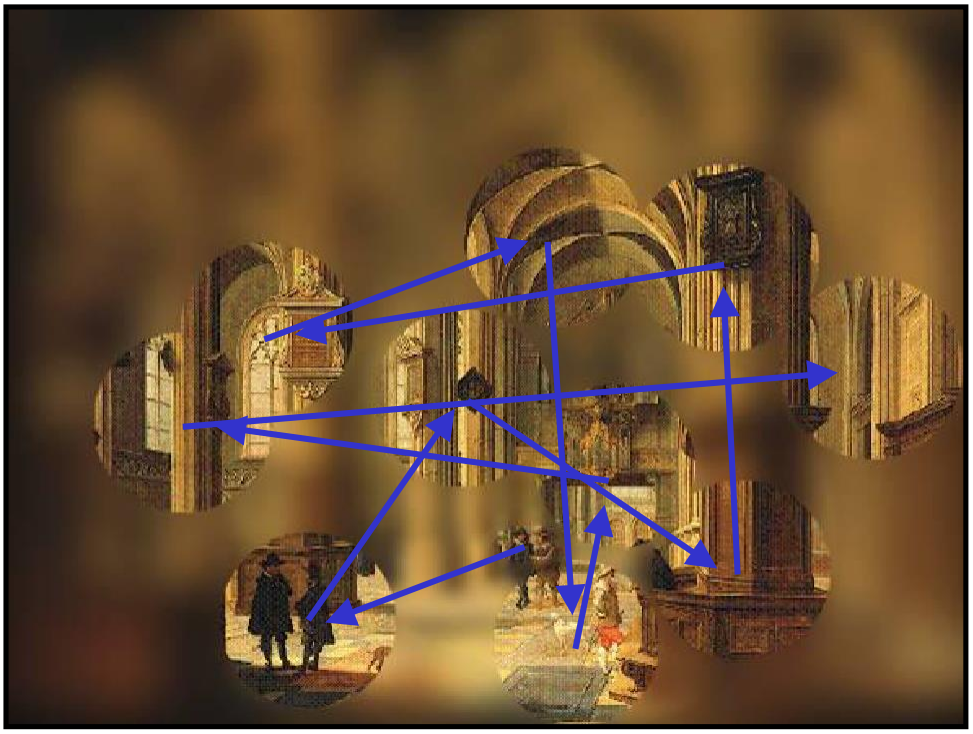


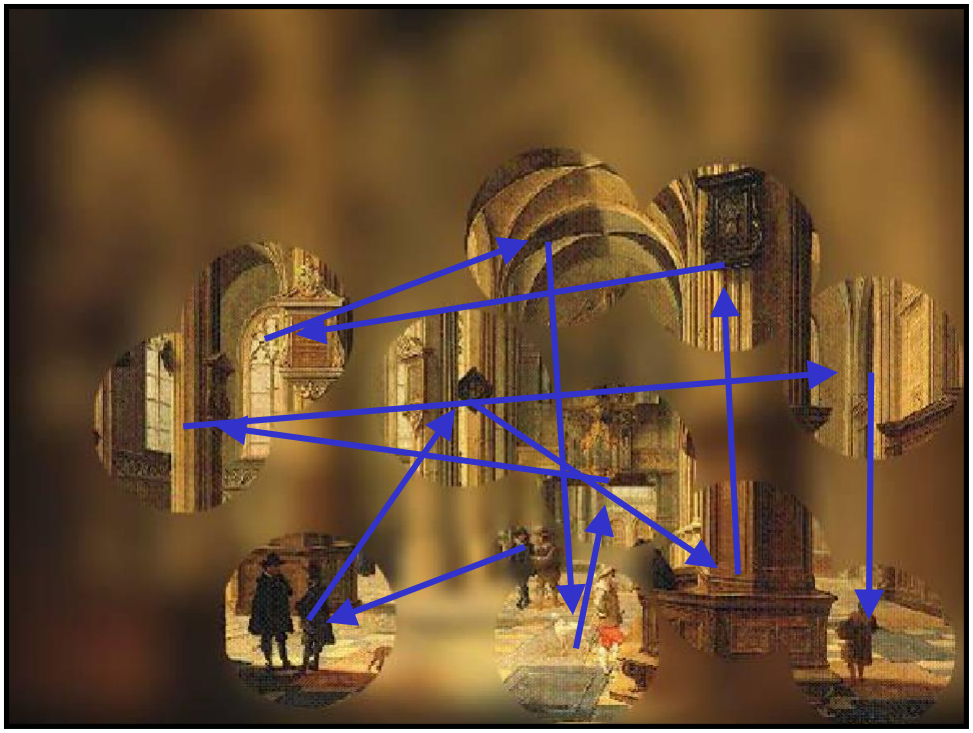












History of Parkinson's Disease

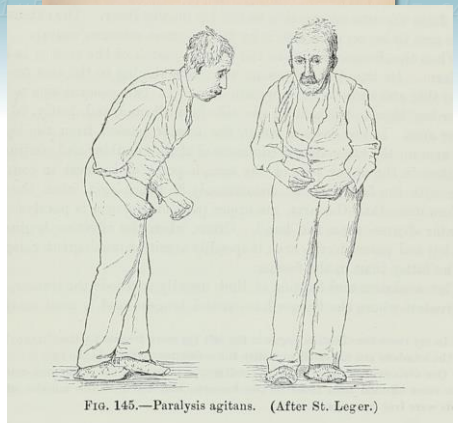


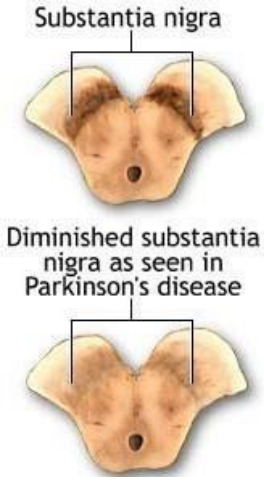
Fig. 145.—Paralysis agitans. (After St. Leger.)

With permission from the Bodleian libraries

- Descriptions date back to 1817
- Used to be known paralysis agitans – the "shaking palsy"
- The 19th century neurologist Jean-Martin Charcot began calling it "Parkinson's disease"
- 100 years later doctors realised that patients were losing brain cells
- In 1960 it was discovered that levels of the brain chemical dopamine were much lower in PD patients than in healthy controls.

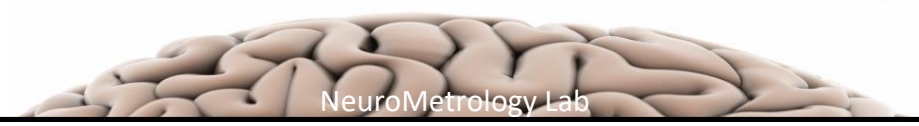
What causes PD?

- Death of nerve cells in an area of the brain called the *substantia nigra*
- In a few people due to faulty genes
- In a few more there is an identifiable environmental factor e.g. Chemical exposure
- But in most cases the cause is unknown



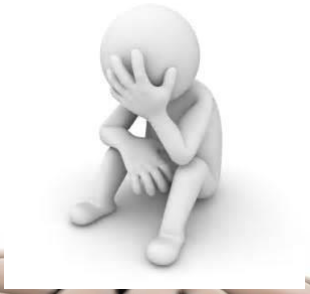
Motor symptoms of Parkinson's

- Progressive and disabling symptoms including
  - Slowing of movements
  - Tremor
  - Stiffness/rigidity of limbs
  - Instability
  - Loss of facial expression



Non motor symptoms of Parkinson's

- Loss of sense of smell
- Sleep disturbance
- Constipation
- Urinary problems
- Depression
- Anxiety
- Cognitive problems



NeuroMetrology Lab

Idiopathic Parkinson's Disease

- Fixation disrupted by square wave jerks (horizontal small saccadic intrusions)

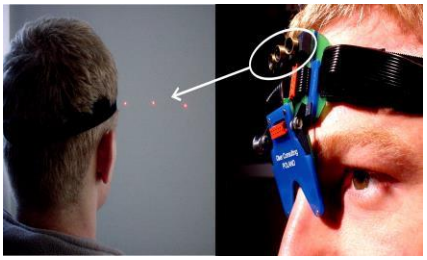
- Hypometria of horizontal saccades

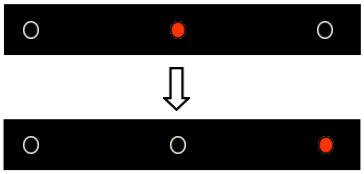
- Impaired smooth pursuit
- Preserved vestibulo-ocular reflex
- Slower in advanced disease …..but can we detect changes at the very early stages of PD?

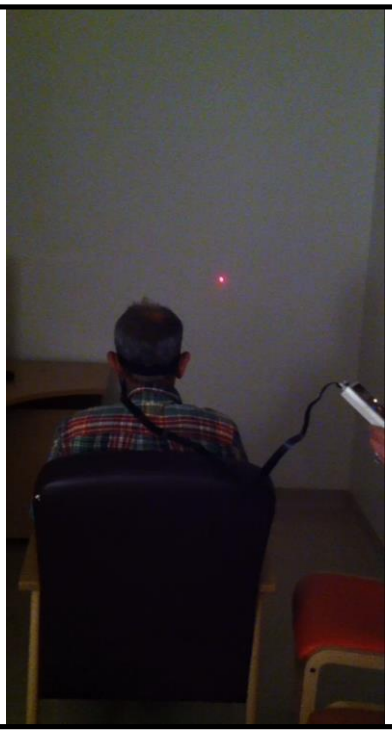
Video courtesy from the Neurology of Eye Movements Leigh and Zee

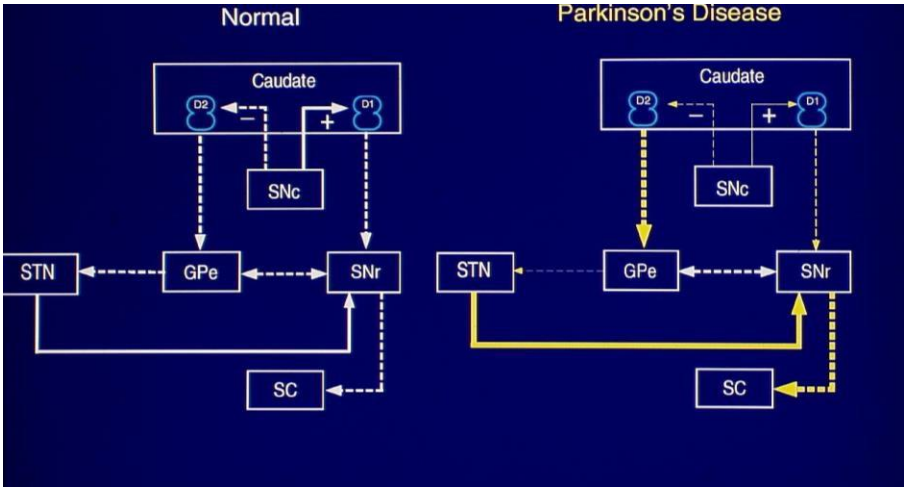
The saccadometer

- Micro-miniaturised head-mounted infrared oculometer
- Non-invasive
- Accurately measures hundreds of saccades in minutes
- Self – calibrating to establish correct gain
- No need to restrain head

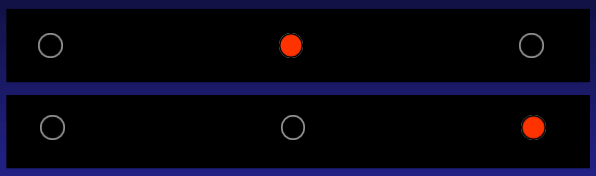






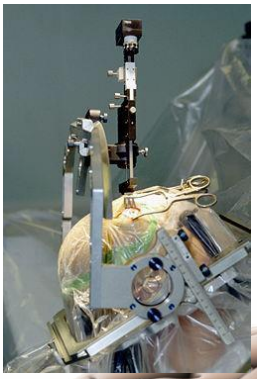


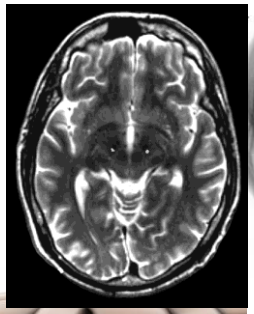
Evoked saccades - step task

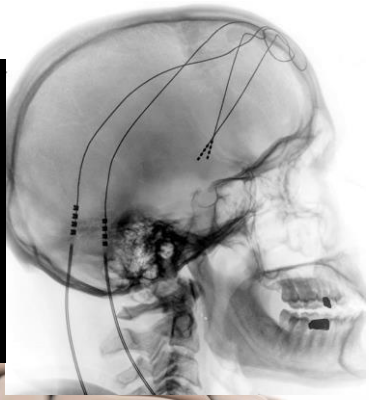


Deep brain stimulation

- Electrical stimulation of specific deep brain areas can relieve symptoms







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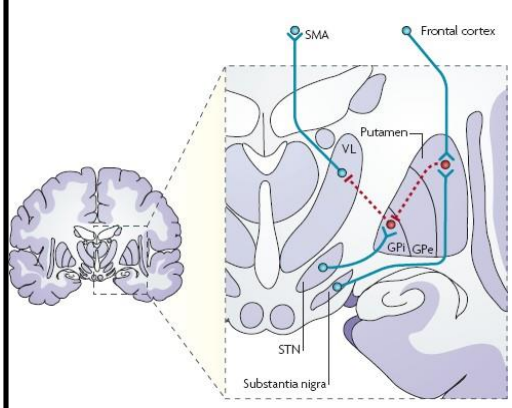
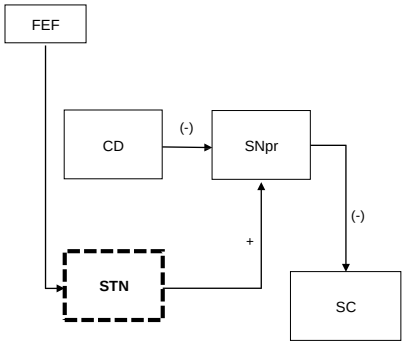




Left figure: Adapted by permission from Macmillan Publishers Ltd, Nature Reviews Neuroscience, *Kringelbach et al. "Translational principles of deep brain stimulation", 8:8(623-635).*

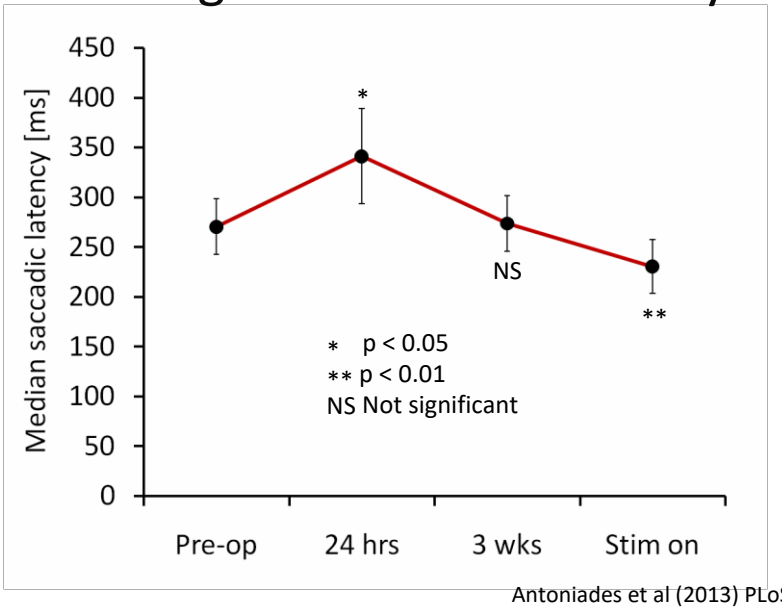
Video courtesy from BBC 2018

Saccadometry in DBS

- 10 PD patients from a multidisciplinary movement disorder clinic
- 3 female, 7 male
- Bilateral STN DBS
- Saccadometry performed:
  1. Pre-implantation
  2. Within 24 hrs post-implantation
  3. 3 weeks later prior to switch-on
  4. 3 weeks later after switch-on

Antoniades et al (2013) PLoS One

Changes in Median Latency



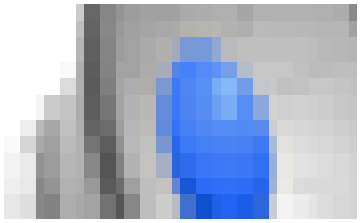
Antoniades et al (2013) PLoS One

Changes in Median Latency

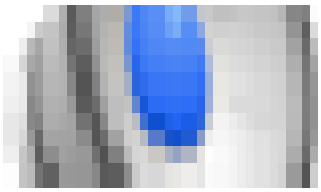
- Qualitative difference between oculomotor effects of lead insertion (temporary 'lesion') and stimulation
- Mechanism of DBS uncertain – this demonstrates it is not simply producing a blockade as many had previously thought

Antoniades et al (2013) PLoS One

OFF stimulation post-op STN DBS



ON stimulation post-op STN DBS



Eye movement consortium

Vision Research 84 (2013) 1–5

Contents lists available at SciVerse ScienceDirect

Vision Research

journal homepage: www.elsevier.com/locate/visres

An internationally standardised antisaccade protocol

Chrystalina Antoniades[a,b], Ulrich Ettinger[c], Bertrand Gaymard[d], Iain Gilchrist[e], Arni Kristjánsson[f], Christopher Kennard[b], R. John Leigh[g], Imran Noorani[a], Pierre Pouget[d], Nikolaos Smyrnis[h], Adam Tarnowski[i], David S. Zee[j], R.H.S. Carpenter[a,*]

BRIEF REPORT

Antisaccades and Executive Dysfunction in Early Drug-Naive Parkinson's Disease: The Discovery Study

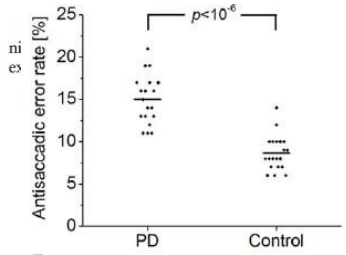
Chrystalina A. Antoniades, PhD,[1]* Nele Demeyere, PhD,[2] Christopher Kennard, PhD,[1] Glyn W. Humphreys, PhD,[2] and Michele T. Hu, PhD[1,3]

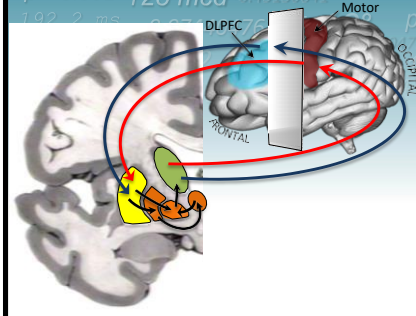
[1]Nuffield Department of Clinical Neurosciences, John Radcliffe Hospital, University of Oxford, United Kingdom [2]Department of Experimental Psychology, University of Oxford, South Parks Road, Oxford, United Kingdom [3]Oxford Parkinson's Disease Centre, Department of Physiology, Anatomy and Genetics, University of Oxford, South Parks Road, Oxford, United Kingdom

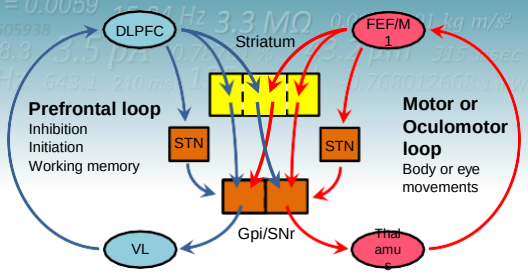
tasks, occurring independently of PD-related motor impairment. Patients exhibited higher antisaccadic error rates and switch costs in the task switching test, and performed significantly worse in the rule finding task.

Conclusions: Certain cognitive domains and saccadic parameters are already significantly impoverished in newly diagnosed Parkinson's patients, even before the initiation of medication. © 2015 International Parkinson and Movement Disorder Society

Key Words: Parkinson's disease; eye movements; antisaccades; executive function; task switching







The problem

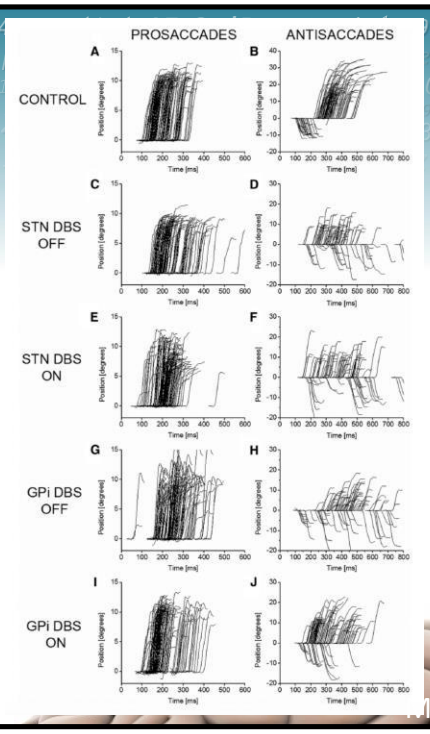
Parkinson's treatments address basic motor problems – tremor, stiffness, slowness – but not more complex motor problems where "higher" brain circuits have to instruct the lower level circuits what to do.

Behavioral/Cognitive

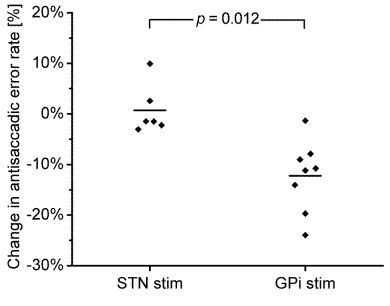
Pallidal Deep Brain Stimulation Improves Higher Control of the Oculomotor System in Parkinson's Disease

Chrystalina A. Antoniades,[1] Pedro Rebelo,[2] Christopher Kennard,[1] Tipu Z. Aziz,[1,2] Alexander L. Green,[1,2] and James J. FitzGerald[1,2]

[1]Nuffield Department of Clinical Neurosciences and [2]Nuffield Department of Surgical Sciences, University of Oxford, Oxford OX3 9DU, United Kingdom



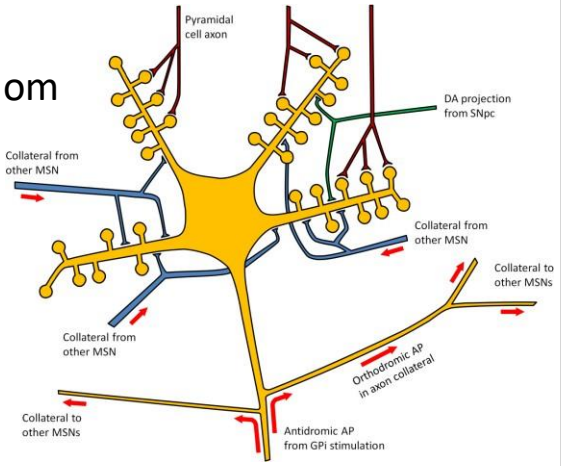
- Both STN DBS and GPi DBS reduce prosaccade latency
- Only GPi DBS reduces antisaccade errors



Metrology Lab

Hypothesis

- Striatal damping
- Reduction in random firing (=noise)
- Increase in SNR



The Journal of Neuroscience, September 23, 2015 • 35(38):13043–13052 • 13043

Progressive Supranuclear Palsy

Progressive Supranuclear Palsy

Steele, J. C. Richardson, J. C. Olszewski, J. 1964 Archives of Neurology

Progressive Supranuclear Palsy. a Heterogeneous Degeneration Involving the Brain Stem, Basal Ganglia and Cerebellum with Vertical Gaze and Pseudobulbar Palsy, Nuchal Dystonia and Dementia

CAUSES:

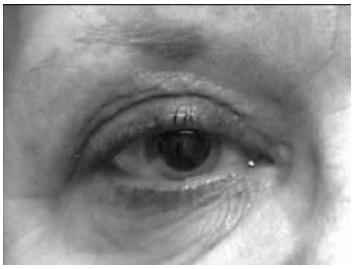
- Still largely unknown
- Underlying pathology identified
  - ✓ Accumulation of abnormal tau in parts of the brain that control movement, cognition and behaviour
- Tau – microtubule associated protein involved in Alzheimer's (AD), Frontotemporal Dementia (FTD), Dementia with Lewis Bodies (DLB), PSP, Corticobasal degeneration (CBD) and other tauopathies.

Progressive Supranuclear Palsy

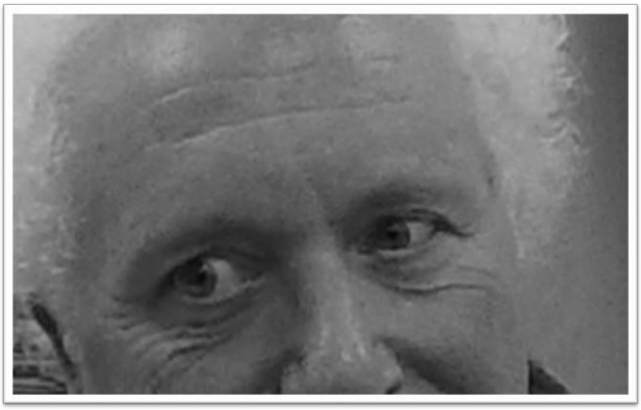
- About 5 – 7 per 100,000
- Mean age of onset is around 65 years old
- Prominent falling (often backwards)
- Involuntary eyelid closure
- Difficulty looking up and down (eventually left/right)
  - – Can experience double vision, difficulty reading
- Eye discomfort, blurred vision and lid apraxia

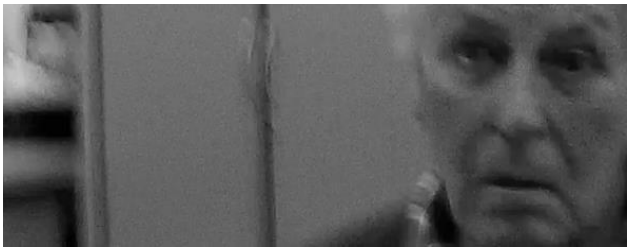
Progressive Supranuclear Palsy

- Vertical and eventually horizontal saccades are hypometric early in the disease and at the end become very slow
- Square wave jerks (horizontal small saccadic intrusions that aren't nystagmus)



Video courtesy from the Neurology of Eye Movements Leigh and Zee





Is Limited vertical gaze purely due to PSP? Ageing?

- Is paralysis of downgaze diagnostic for PSP?
- Upward range of voluntary movement becomes progressively limited in elderly individuals due to orbital factors
- PSP patients may show limited voluntary up-or downgaze
- Impaired voluntary downgaze overcome with head rotation is suggestive of PSP
- But slow vertical saccades are more reliable for diagnosis of PSP

Thank you to Prof John Leigh

Diagnostic potential of saccadometry in progressive supranuclear palsy

Chrystalina A Antoniades[1†], Thomas H Bak[4,5], RHS Carpenter[3], John R Hodges[2,4] & Roger A Barker[1,2]

Background: Progressive supranuclear palsy (PSP), an atypical parkinsonian syndrome characterized by extrapyramidal features, imbalance, supranuclear gaze paresis and dementia, can be difficult to diagnose, especially in the early stages. From the clinician's point of view, the main difficulty with this disorder is the inability to provide an accurate diagnosis, at least for the initial stages of the disease, where symptoms are often confused

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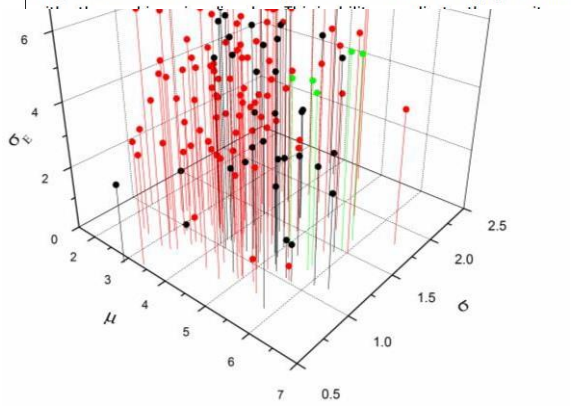
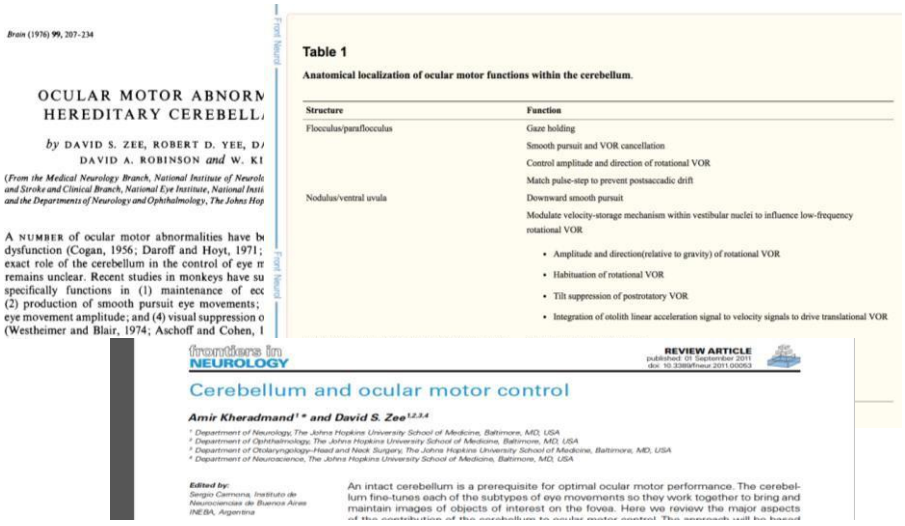


Antoniades et al (2007) *Biomarkers inMedicine* 1(4):487-490

Cerebellar ataxia



Brain (1976) 99, 207-234

OCULAR MOTOR ABNORM
HEREDITARY CEREBELL

by DAVID S. ZEE, ROBERT D. YEE, D
DAVID A. ROBINSON and W. KI

(From the Medical Neurology Branch, National Institute of Neurol
and Stroke and Clinical Branch, National Eye Institute, National Insti
and the Departments of Neurology and Ophthalmology, The Johns Hop

A NUMBER of ocular motor abnormalities have b
dysfunction (Cogan, 1956; Daroff and Hoyt, 1971;
exact role of the cerebellum in the control of eye m
remains unclear. Recent studies in monkeys have su
specifically functions in (1) maintenance of ecc
(2) production of smooth pursuit eye movements;
eye movement amplitude; and (4) visual suppression o
(Westheimer and Blair, 1974; Aschoff and Cohen,

Table 1

Anatomical localization of ocular motor functions within the cerebellum.

Structure	Function
Flocculus/paraflocculus	Gaze holding
	Smooth pursuit and VOR cancellation
	Control amplitude and direction of rotational VOR
	Match pulse-step to prevent postsaccadic drift
Nodulus/ventral uvula	Downward smooth pursuit
	Modulate velocity-storage mechanism within vestibular nuclei to influence low-frequency rotational VOR
	• Amplitude and direction(relative to gravity) of rotational VOR
	• Habituation of rotational VOR
	• Tilt suppression of postrotatory VOR
	• Integration of otolith linear acceleration signal to velocity signals to drive translational VOR

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REVIEW ARTICLE

Cerebellum and ocular motor control

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An intact cerebellum is a prerequisite for optimal ocular motor performance. The cerebellum fine-tunes each of the subtypes of eye movements so they work together to bring and maintain images of objects of interest on the fovea. Here we review the major aspects

Thank you

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