Nothing to disclose
Dementia

Dementia is a general term for a decline in mental ability severe enough to interfere with daily life.

Dementia is not a specific disease. It's an overall term that describes a wide range of symptoms.

Alzheimer’s disease is the most common form of dementia, accounting for 60-80%.

Vascular dementia, after a stroke, is the second most common form of dementia.
While symptoms of dementia can vary greatly, at least two of the following core mental functions must be significantly impaired to be considered dementia:

Memory
Communication and language
Ability to focus and pay attention
Reasoning and judgment
Visual perception
Dementia

Many people have memory loss issues — this does not mean they have Alzheimer's or another dementia.

People with dementia may have problems with:

-- short-term memory
-- keeping track of a purse or wallet
-- paying bills
-- planning and preparing meals
-- remembering appointments
-- traveling out of the neighborhood.

Many dementias are progressive, meaning symptoms start out slowly and gradually get worse.
Dementia: Types

Dementia with Lewy bodies
Frontotemporal dementia
Posterior Cortical Atrophy
Parkinson’s disease dementia
Vascular Dementia
Anatomical relationship to function

Based on observation of patients with deficits and post mortem examination

Brodman’s areas
Organization of Visual Functions

Wernicke (1874) and Lissauer (1890)

First model of sequential organization of visual functions

Theory based on anatomical separation of:
- Primary center of sensation
- Secondary center of imagination
Holmes and Lister (1916)

Explored possibility that specialized areas could be distributed over two visual pathways

Distinction between visual agnosias
The visual system: Seeing

Conceptually two components

Central

- Anatomically = macula/fovea
- Cones are highest density in fovea (20 degrees)
  - Mediates color vision, high spatial frequency resolution
  - Functions optimally in conditions of light adaptation

Peripheral

- Rods are more abundant in periphery
- 20 degrees from the fovea Rods are in highest conc
  - Mediates motion detection, low spatial frequency
  - Functions best in dim illumination
The dualistic approach to vision

The ‘where’ system
- Magnocellular pathway
- Perceptual processing
- Memorization of spatial relationships
- Dorsal stream

The ‘what’ system
- Parvocellular pathway
- Object identification
- Ventral stream
The dualistic approach to vision

Dorsal or “where” stream
- Spatial processing
- Location
- Movement
- Spatial transformations
- Spatial relations

Ventral or “what” stream
- Object processing
- Color
- Texture
- Pictorial detail
- Shape
- Size
Dorsal Stream

Links primary visual cortex (V1), through the middle temporal area, to the posterior parietal lobe
Ventral Stream

Links primary visual cortex (V1), through area V4, to the inferotemporal region
Visual impairments of the Primary visual cortex

‘Blindsight’

‘Cortically blind’

- Loss of conscious vision in part of their visual field due to primary visual cortex lesion
- Able to produce accurate visuomotor responses to visual stimuli under forced choice situations/automatic responses
Visual impairments of the Primary visual cortex:

Deafferentation of the ventral pathway from retinal inputs

Dorsal pathway should still receive retinal information via subcortical routes

Retinal projections to the optic tectum and pulvinar reach the parietal cortex

Confirms the role of the parietal cortex in the automatic visuomotor transformation
Afferent visual impairments

ANTON SYNDROME

Cortical blindness

Patients denied any visual problems

Claim that they can see

No demonstrable visual behavior

Most common with bilateral occipital lobe infarctions
Afferent visual impairments

HEMISPATIAL NEGLECT

Do not see objects in areas of known visual function

Double simultaneous stimulation

Confrontation visual fields

Damage to the right hemisphere
  ◦ Posterior parietal cortex
  ◦ Frontal eye fields
  ◦ Cingulate gyrus
Dissociation of the visual processing mechanisms

Visual agnosias
- Apperceptive
- Associative
- Alexia
- Prosopagnosia
- Simultagnosia
- Unilateral spatial neglect
- Optic ataxia
- Spatial disorientation
Visual Agnosia

‘mind blindness’ Lissauer 1890

‘Agnosia’ Freud 1891

Unable to perceive and/or recognize visual objects

not blind since they clearly respond to visual stimuli
Case:
47 yo man found comatose and low BP

RHH c macular sparing
Normal memory, language and intelligence
Could not name objects nor group them
Could not demonstrate or describe the use of
PET – specific storage of functional knowledge of objects
Middle portion of temporal lobe
Category specific deficits
Associative agnosia

‘normal precept stripped of meaning’
‘psychic blindness’

Normal perception of the object, although object recognition is impaired
Neural mechanisms for object recognition

Sequential processing of information

V1- prestriate cortex – inferotemporal cortex – superior temporal sulcus

Processed serially from simpler to complex

Eg V1 & V2 extract oriented edges and contours

V4 responds shape or color

Inferotemporal cells respond to 2D or 3D
Case: Mr. S
Carbon monoxide overexposure

Unable to name visually presented objects
Could name objects place in hands
VF intact
Unable to copy simple objects
Able to describe objects from memory
Alexia
Prosopagnosia
Lesion – bilateral occipito-temporal junction sparing the calcarine sulcus

Fig. 3.4 Inability to copy block letters, numbers or simple two-dimensional shapes in a patient with apperceptive agnosia. (From Benson and Greenberg 1969 with permission from the American Medical Association.)
Apperceptive agnosia

Visual form agnosia
- Object agnosia
- Alexia
- prosopagnosia

Benson and Greenberg (1969)

‘Identification of shape or form is the only precondition for identifying an object, a letter or a face. Other visual attributes, like color or brightness, are not essential for object identification’
Neural mechanisms for object recognition

One exception to single cell discharge

15% of elaborate anterior inferotemporal (STS) respond to the sight of a face, parts of a face, hand, and certain hand actions
Prosopagnosia

Impaired ability to recognize familiar faces or to learn to recognize new faces

Debate: perception vs memory

Prosopagnosia triad:
- VF deficits: LHH
- Hemiachromotopsia
- Topographagnosia

Inferior temporo-occipital cortex
- Lingual and fusiform gyri
- Lesions typically bilateral
Alexia

Loss of efficient reading for comprehension

Slow laborious letter by letter reading to complete global alexia

Left medial and inferior temporo-occipital region

Left angular gyrus
  ◦ Stores visual representation of words

Associated findings:
  ◦ RHH
  ◦ Dyschromotopsia
  ◦ Anomia
Alexia without agraphia

Loss of efficient reading for comprehension

Slow laborious letter by letter reading to complete global alexia

Left medial and inferior temporo-occipital region

Left angular gyrus
  ◦ Stores visual representation of words

Associated findings:
  ◦ RHH
  ◦ Dyschromatopsia
  ◦ Anomia
Cerebral achromatopsia

Colors look dull to complete colorless
- Vertebrobasilar ischemia
- HSV encephilitis
- Cerebral mets
- Focal recurrent seizures
- Dementia

Ventromedial sector of Occipital lobe
Middle third of the Lingual gyrus and fusiform gyri
White matter immediately behind posterior tip of the lateral ventricle
Bilateral hemispheric capacity to perceive color
Hemiachromatopsia
Cerebral akinetopsia

Complete loss of movement perception
Requires bilateral lesions
Lateral temporo-occipital cortex
  ◦ Conjunction of the inferior temporal sulcus and the lateral occipital sulcus
Subtle symptoms – unilateral
Object motion guides
  ◦ Limb reaching movements
  ◦ Smooth pursuits
  ◦ Influencing saccadic accuracy
Self motion
  ◦ Distinguish self vs object motion
  ◦ Complements VOR
Smooth pursuits and OKN
Dorsal simultagnosia

Patient accurately perceives the individual elements or details of a complex picture, but cannot appreciate the overall meaning of the picture

Bilateral or unilateral parieto-occipital damage

Posterior cortical atrophy, CBG degeneration, AD

Balint (1909) – as part of a syndrome

Disorder of visual attention i.e. inability to disengage attention from current location
Simultagnosia: case
Cookie theft picture
Simultanagnosia in Dementia

Patients from the Aging and Alzheimer’s Clinic
- Probable Alzheimer’s disease
- mild cognitive impairment
- frontotemporal dementia
- Lewy body disease
- corticobasal ganglionic degeneration

Mini-Mental Status Examination (MMSE)

Clinical Dementia Rating

VA at least 20/60 in the better eye.

Simultanagnosia was determined if the patient could not see the Ishihara control (IC) plate or the American Optical Hardy Rand Rittler control (AC) plates with both eyes open.

They were also shown two diagrams of a large number or letter constructed from smaller numbers and letters termed the 3/4 diagram and the A/M diagram.
Simultanagnosia in Dementia

The mean MMSE score was 23.4

Average age patients was 72.5

Simultanagnosia by AC testing had either probable AD or Lewy body disease
  - Mean MMSE was 20.3

Simultanagnosia by IC
  - Mean MMSE was 14.5

Study suggests simultanagnosia is not an early finding in dementing illness

AC plates may assist in the diagnosis of some forms of dementia or lend information regarding severity of disease
The Clinical Spectrum of Posterior Cortical Atrophy
(IRB00010075)

WILLIAM L HILLS, MD, OD
ASSOCIATE PROFESSOR
SEPTEMBER 15, 2016
Nothing to disclose

- Jennifer Olds, MD (Lowe)
- Victoria Palek, MD
- Judith EA Warner, MD
- Samuel Passi, MD
- Wayne Cornblath, MD (Univ of Michigan)
- Roger Turbin, MD (Rutgers Newark Campus)
- David Katz, MD (Georgetown Univ and Howard Univ)
- Andrew Lee, MD (Houston Methodist Hospital)
- Marilyn Kay, MD (Univ of Wisc)
- Ben Frishberg, MD (The Neurology Center)
Posterior cortical atrophy (PCA)

- Progressive neurodegenerative condition
- Selective decline in higher order visual processing
- Dysfunction of the parietal, occipital, and occipito-temporal regions
- First described by Benson in 1988 in patients with marked parieto-occipital atrophy
- Histopathologic studies subsequently identified AD as most common pathology
  - Visual variant of Alzheimer’s disease
  - Biparietal AD

Posterior cortical atrophy

- Prevalence and Incidence relatively unknown
  - Estimated to be 5% of Alzheimer’s population (Snowden et al)
  - Increasingly prevalent disease with today’s aging population, yet rare condition
  - Difficult to define due to a lack of clear diagnostic criteria, a general lack of awareness…

- Underdiagnosed, misdiagnosed or significantly delayed diagnosis
Posterior cortical atrophy

- Clinical presentation is heralded by subjective vision loss, yet a normal ophthalmic examination
- Earlier age of onset – 50’s – mid 60’s (range 40 – 80)
- Gender though to be equal, however, some studies suggest women are affected more
- Neuro-psychological deficits
- Visual spatial impairments
- Alexia
- Balint’s syndrome
- Gertmann’s syndrome
- Working memory deficits
Posterior cortical atrophy

**BALINT’S SYNDROME**
- Oculomotor apraxia
- Optic ataxia
- Simultanagnosia

**GERTMANN’S SYNDROME**
- Acalculia
- Agraphia
- Finger agnosia
- Left/right disorientation
Posterior cortical atrophy

**BASIC VISUAL PROCESSING**
- Form
- Motion
- Color
- Point localization

**IQ TESTING**
- Performance IQ is often up to 30–40 points lower than verbal IQ scores
- Performance on cognitive tasks with any significant visual component (e.g. visual memory recall, Trail Making, Stroop test) are vulnerable to impairment and isinterpretation
Incomplete Left Homonymous Hemianopsia
March 2012

Progressive Left Homonymous Hemianopsia
July 2012
Posterior cortical atrophy

- Poor visuospatial skills on neuropsychological testing
- Occipito-parietal hypometabolism on PET imaging
- CSF analysis detected reduced $\text{AB}_{1-42}$ Tau Index and elevated phosphorylated-tau
Posterior Cortical Atrophy

Jennifer Lowe, MS4; Julie Falardeau, MD2; Robert Egan, MD3; and William L. Hills, MD2

Posterior cortical atrophy (PCA) is a rare progressive neurodegenerative disease with prominent cortical visual dysfunction, first described by Benson in 1988. Studies have shown visual field defects, on formal testing, increased phosphorylated-tau protein in the CSF, and hypometabolism in the parieto-occipital regions on PET imaging. We describe one patient with PCA whose symptoms are classic but whose progression has been atypically slow. To further investigate this disease entity, we retrospectively reviewed 9 additional charts and report the commonalities in all 10 cases.

**PCA Key Points:**
- Visuoperceptual disturbances and Cortical visual dysfunction
- Progressive neurodegenerative disease
- Visual neglect is common
- Less memory impairment than Alzheimer’s
- Simultanagnosia
- Parieto-occipital atrophy
- Diminished metabolic activity in the posterior aspect of the brain on PET imaging

**Methods:** We reviewed the index subject's symptoms and findings on presentation and follow up. We reviewed 8 additional cases of PCA evaluated by Neuro-Ophthalmology. We analyzed the signs and symptoms in, as well as the demographics of, these cases to look for common themes at presentation.

**Results:** A 58 year old woman presents with a progressive 10 year history of difficulty processing spatial information, reading handwriting and recognizing faces. She described visual hallucinations, photophobia, poor depth perception, and visual recall. Poor visuospatial skills were found on neuropsychological testing and occipito-parietal hypometabolism on PET imaging (Figure 1). Visual field testing found progressive incomplete homonymous hemianopsia (Figures 2 and 3). CSF analysis detected reduced AB1-42, Tau Index and elevated phosphorylated-tau (Figure 4).

**Conclusion:** Posterior cortical atrophy is an uncommon atypical variant of Alzheimer’s disease, sometimes termed “Benson’s syndrome”. Patients commonly report difficulty reading despite normal visual acuities. Balint’s syndrome is common in PCA, yet difficult to detect at the bedside. Our observations and previous studies describe visual signs and symptoms attributable to the parieto-occipital cortex. More recently, CSF phosphorylated-tau has been utilized as a bio-marker. A decreased AT index and elevated phosphorylated Tau concentration can assist in differentiation from other forms of dementia. The most common symptoms were difficulty with reading and depth perception. Most common findings were simultanagnosia, decreased color vision, decreased stereopsis, abnormal Amsler’s grid and visual field defects. Posterior cortical atrophy should be considered in patients whose chief complaint is difficulty reading despite normal visual acuities. A systematic approach using clinical, laboratory, and radiographic data can aid in diagnosis of PCA. Complementary diagnostic studies can include MRI, PET, and CSF analysis. Early diagnosis is important to prevent unnecessary costly investigations, allow for appropriate therapeutic and psychosocial interventions and reduce the stress of an “unknown diagnosis.”

**Symptoms/Signs at Presentation**

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<th>Ms. MK</th>
<th>Mr. PR</th>
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**Methods:**

**Figure 1: MRI and PET**

**Figure 2: Incomplete Left Homonymous Hemianopsia**

**Figure 3: Progressive Left Homonymous Hemianopsia**

March 2012

July 2012

**Figure 4:**

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**Figure 4: ATI versus P-tau**

**Conclusion:**

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Visual dysfunction in posterior cortical atrophy. Individuals with posterior cortical atrophy have difficulty identifying objects and faces, particularly when they consist of many parts or are viewed from an unfamiliar (non-canonical) perspective. Eye-tracking studies contrasting scene perception in healthy individuals (A) and people with posterior cortical atrophy (B) suggest that patients have poor top-down guidance and control of oculomotor function. Circles represent fixation locations and circle size represents fixation duration. Patients with posterior cortical atrophy fixate prominent features initially (e.g., dome on pier), but subsequently fixate relatively uninformative aspects of the scene (e.g., sea or sky) and miss important contextual details (e.g., beachfront or near the end of the pier). Images from Tim Shakespeare and Sebastian Crutch (unpublished).

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