

Posterior cortical atrophy

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Learning objectives

- Understand the definition of Posterior cortical atrophy (PCA)
- Appreciate typical clinical presentation of PCA
- Be familiar with signs associated with dorsal and ventral visual stream damage
- Understand the terms visual disorientation, Bálint's syndrome and constructional apraxia
- Become acquainted about the difference between apperceptive and associative agnosia
- Appreciate neuroimaging findings in PCA
- Be aware of the differential diagnosis and red flag features which suggest alternative diagnoses

Posterior cortical atrophy (PCA)

A syndrome that's easy to miss and often diagnosed late, many years after symptom onset

- ▶ **Progressive disorder of higher-order visual perception**
- ▶ **Usually of insidious onset, with prominent visual symptoms occurring early**
- ▶ **Marked atrophy of occipital, parietal and temporal regions on brain imaging**
- ▶ **Most frequently associated with Alzheimer pathology and therefore sometimes inappropriately termed 'visual variant' AD**

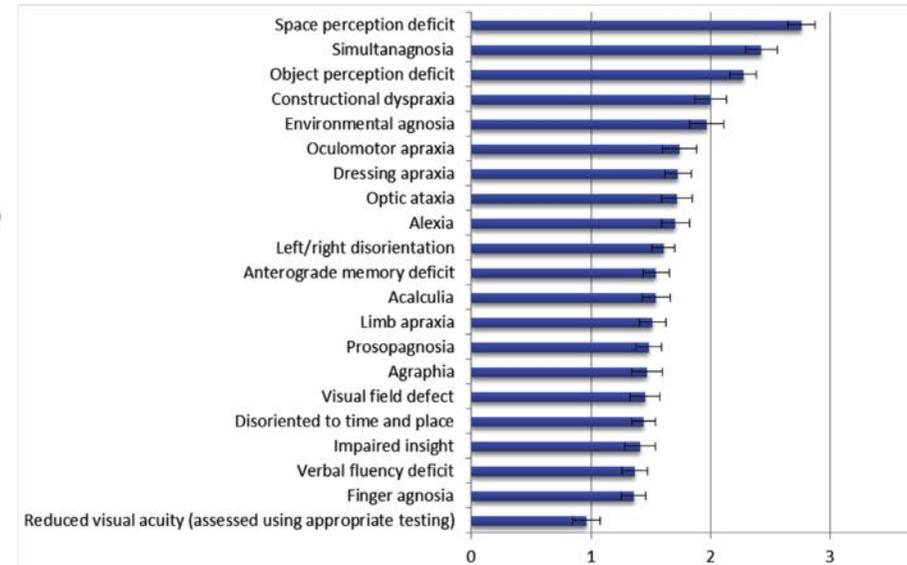
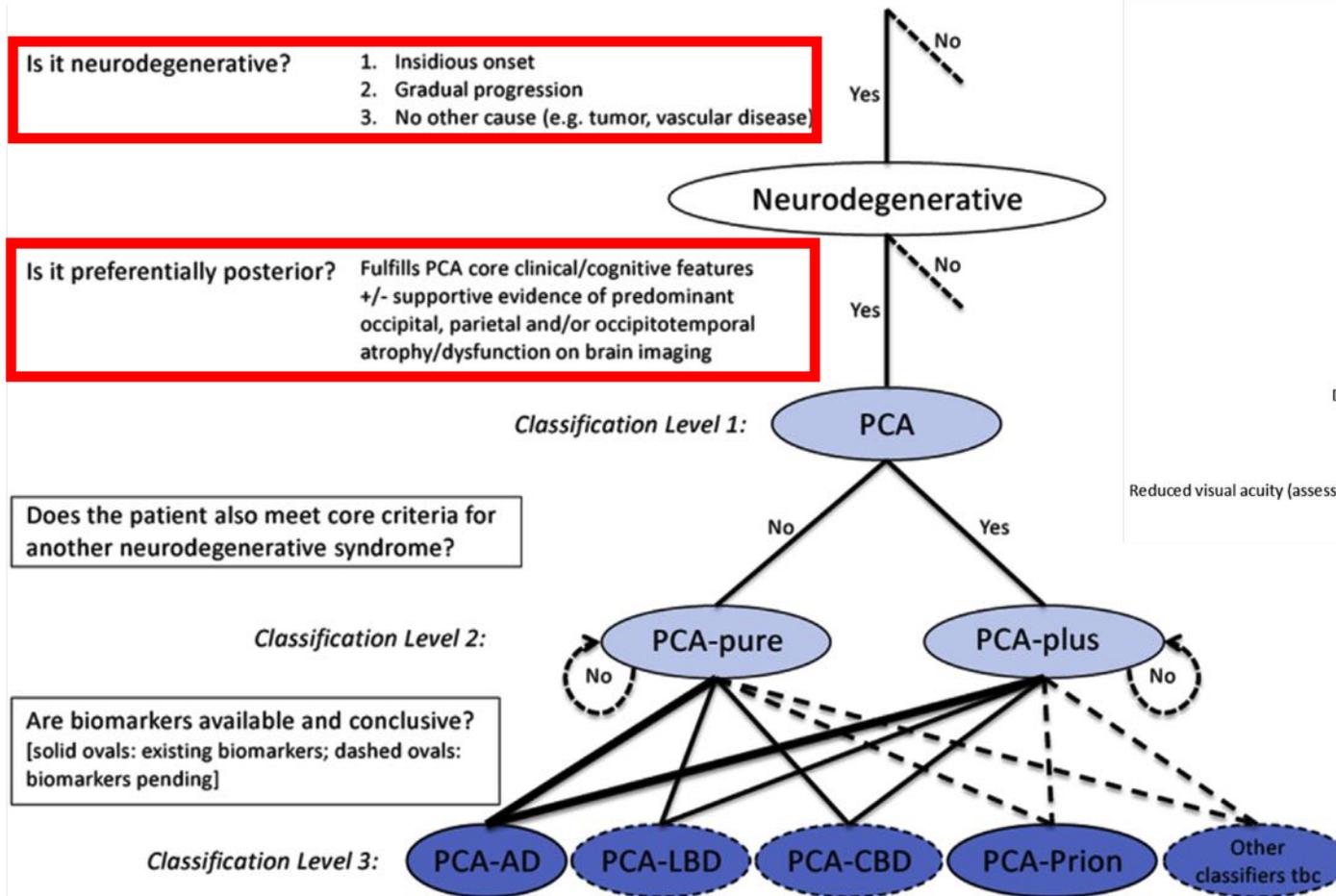
- ▶ **But there is an important differential diagnosis to consider**
- ▶ *Associated features can assist to discriminate non-AD causes from AD*

Case History | Patient JN

Middle aged man with visual symptoms

- 59 year old right-handed man with a progressive history
- 7 years ago: Frustrated with difficulty reading. “Letters jumbled”
- Seen by several opticians & ophthalmologists: no cause found
- 5 years ago at daughter’s wedding: Daughter realized he was afraid of treading on her gown
- Wouldn’t eat at wedding for fear of making a mess
- Prior to admission: Hit by a car moving slowly while crossing the road
- No visual hallucinations
- **Examination** | Simultagnosia. Bilateral neglect. Ocular apraxia. Optic ataxia – with both arms in both visual fields. Constructional apraxia. No Parkinsonism. Occasional myoclonic jerks

2017 Consensus | Diagnosis and classification



Core cognitive / clinical signs

▶ Dorsal visual stream signs

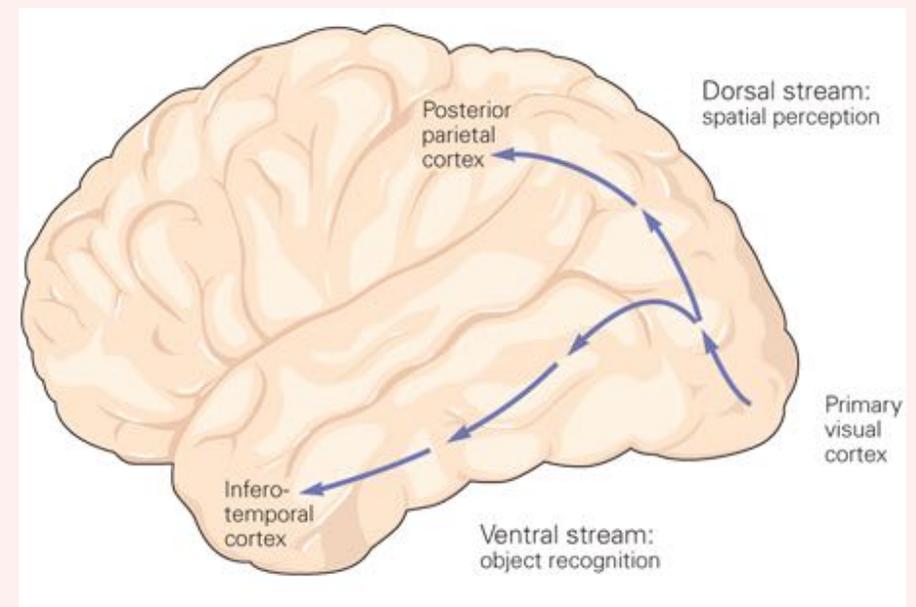
Deficits of visual space perception including

- Visual disorientation / mislocalization
- Bálint's syndrome
- Constructional apraxia

▶ Ventral visual stream signs

Deficits of form perception including

- Visual apperceptive agnosia
- Visual associative agnosia



Visual disorientation after bilateral parietal injury

First described by Gordon Holmes (1918) in patients he assessed on the Western Front

Holmes' cases of bilateral parietal injury (in his case from gunshot wounds):

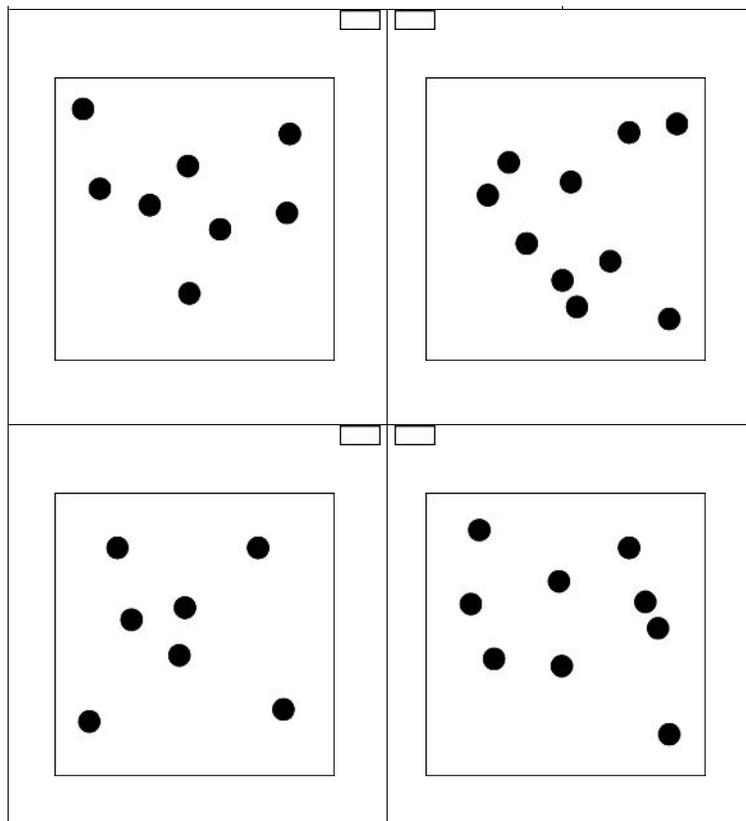
- When asked to touch an object in front of them they would grope hopelessly
 - Patients could not count coins set in front of them
 - They encountered difficulty in seeing more than one item at a time
 - Bumped into objects as they tried to walk through the ward
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- ▶ **Holmes emphasized this syndrome as a disorder of visual space perception**
 - ▶ **Referred to it as visual disorientation – essentially mislocalization of objects in space**



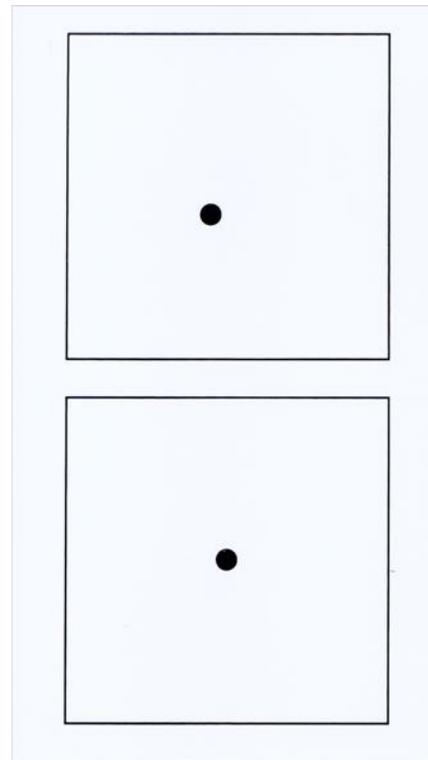
Holmes (1918)

Dot counting | Position discrimination | Number location

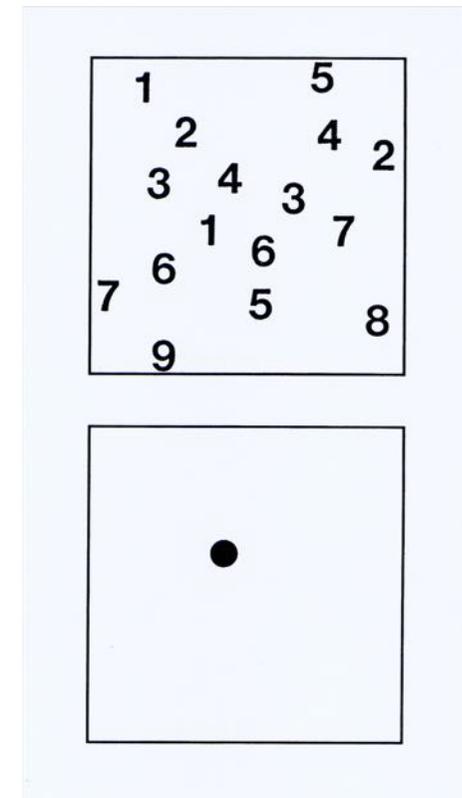
All still used as simple bedside tests of visuospatial ability, e.g. in Addenbrooke's Cognitive Examination



How many dots in each frame?



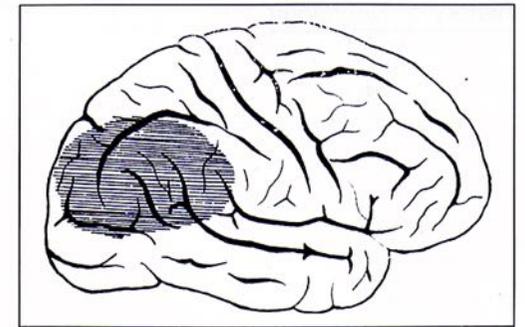
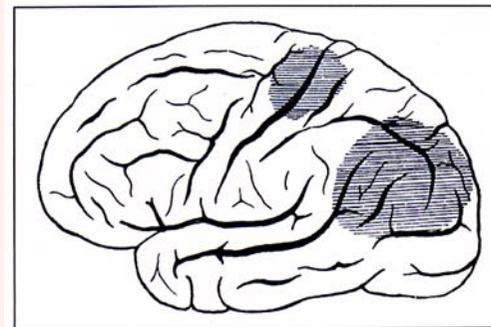
Which dot is central? Which number corresponds to dot position?



Bálint's syndrome: simultagnosia, ocular apraxia, optic ataxia

Bálint put greater emphasis than Holmes on inattention and visually guided misreaching

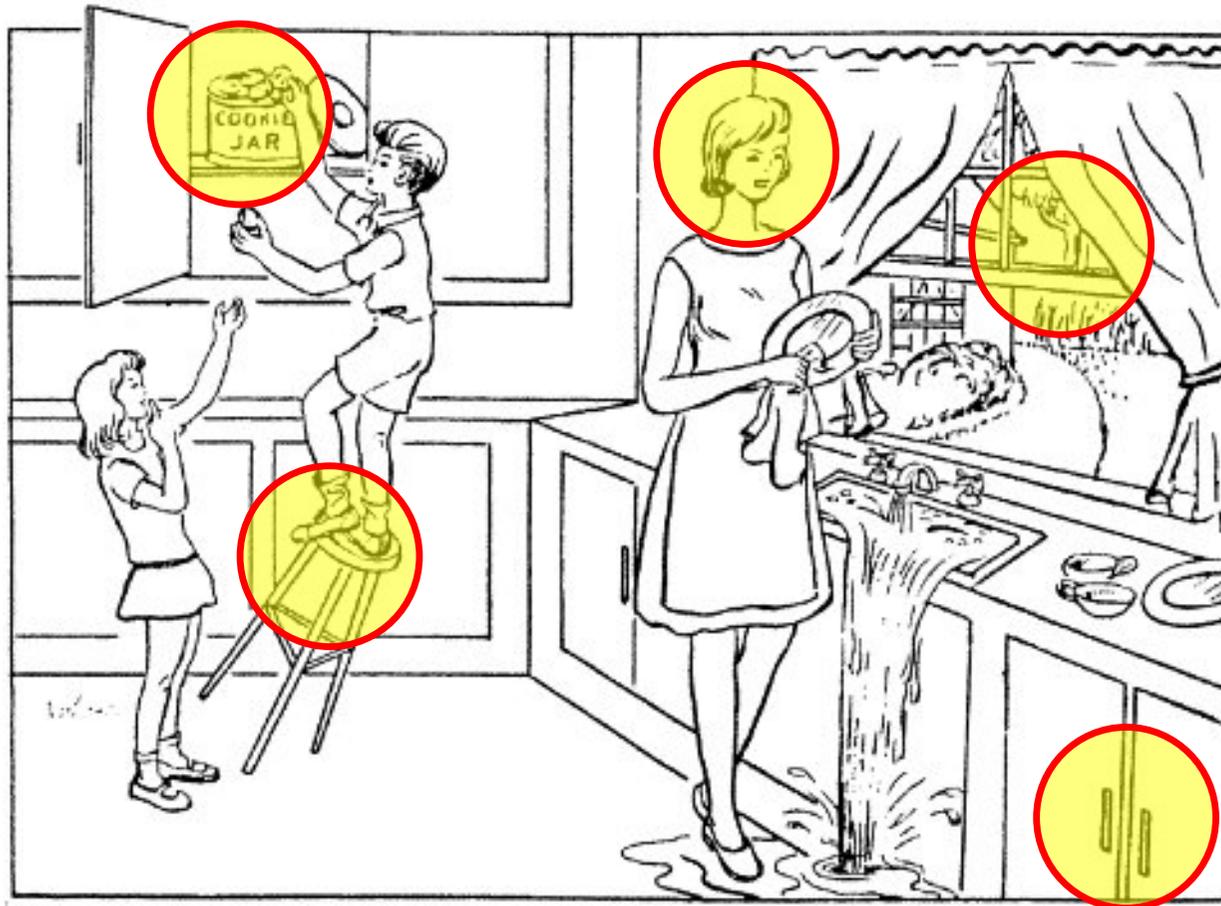
- Patient could no longer judge where things were. Felt unsafe to cross roads.
- Could report only one item at a time (**simultagnosia**)
- Looked straight ahead, unaware of objects on either side (bilateral inattention)
- Bálint called it “psychic paralysis of gaze” (**ocular apraxia**)
- Misreached to visual objects (**optic ataxia**)
- Post-mortem: large bilateral posterior strokes



Bálint (1917)

Simultagnosia

Reporting elements of a picture piecemeal and not grasping the contents of the entire scene



Patient JN

"There's a woman.....by a window.....a cookie jar and a stool...oh yes and a cupboard."

Boston cookie theft picture

Bilateral neglect, ocular apraxia

Patient explores limited area of space, gaze fixating centrally and inattentive of peripheral stimuli



Patient JN

Eye tracking during report of a scene

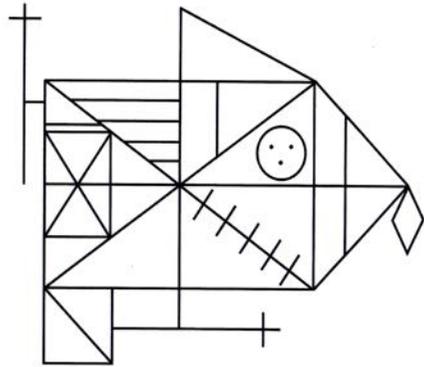
Optic ataxia

Misreaching to peripheral visual targets (get the patient to fixate centrally, e.g. your nose)

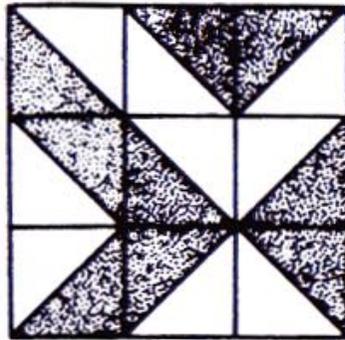


Constructional apraxia

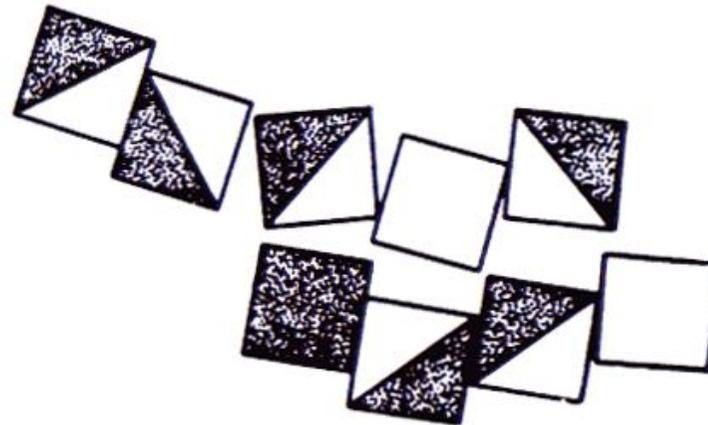
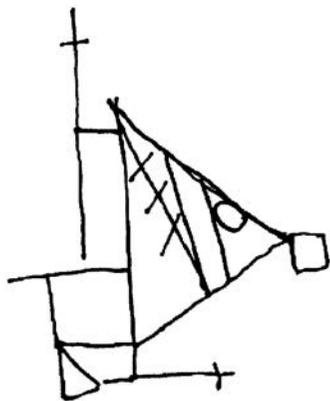
Difficulty copying a figure or block design



Rey-Osterreith Figure

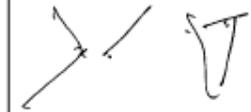
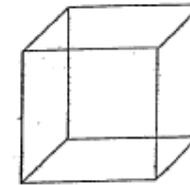
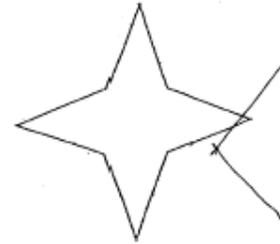


Block construction



Line drawings

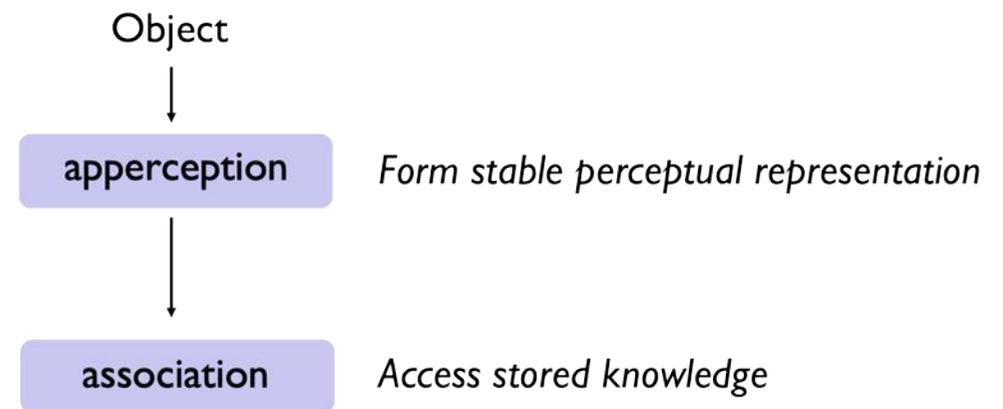
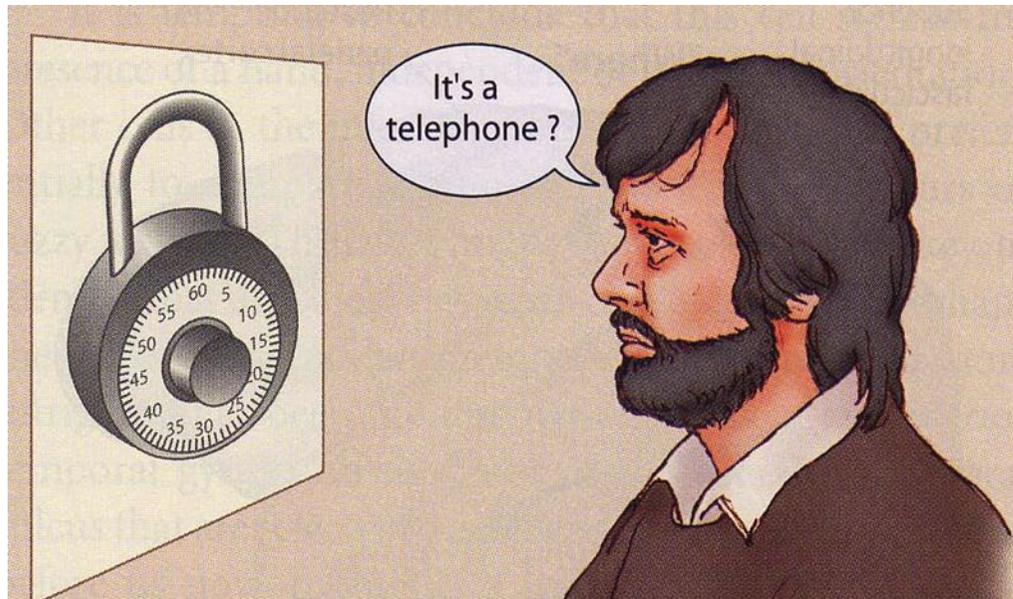
Patient JN's copies



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Visual object agnosia & Lissauer's two-stage framework

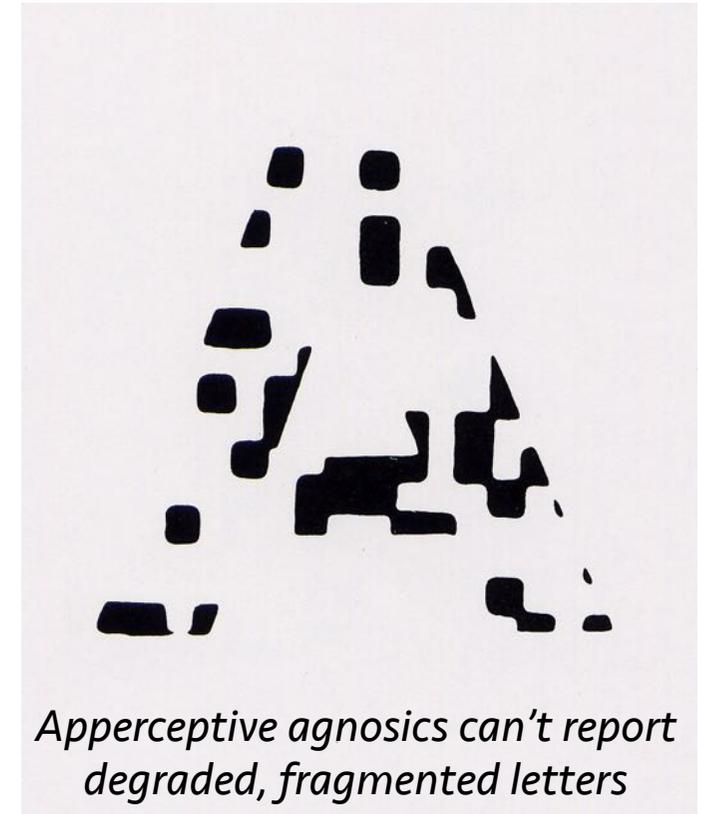
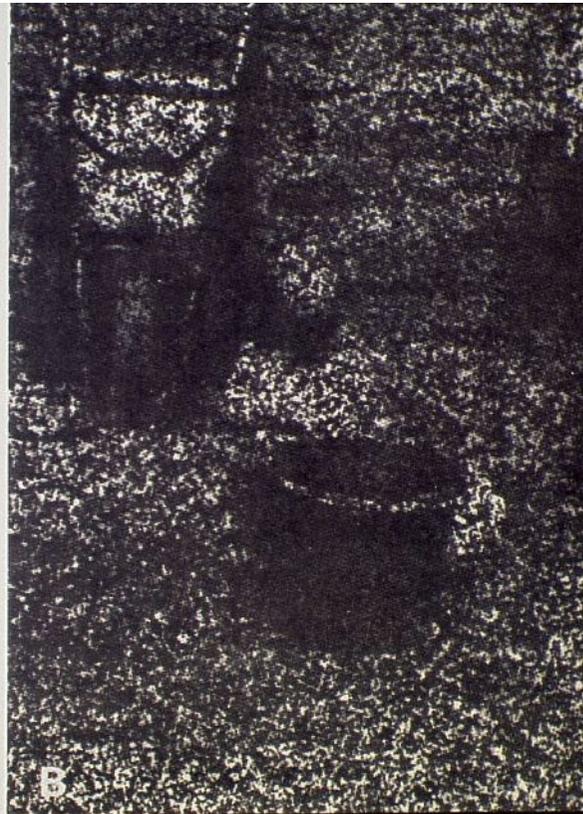
Difficulty in recognizing visual objects



Note that a patient with anomia may also respond in a similar way, but they can describe what the object is used for, whereas a patient with agnosia cannot.

Elizabeth Warrington's view on apperception

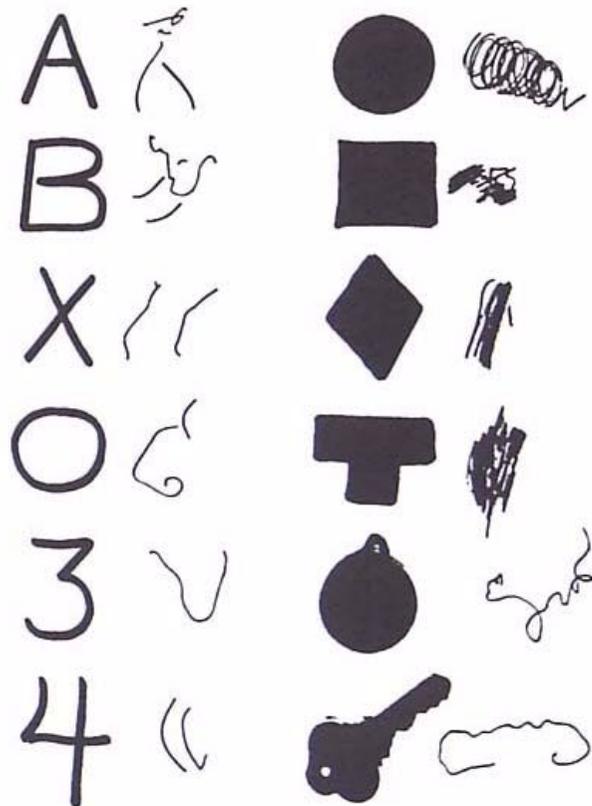
What it must be like to see the world with apperceptive agnosia – early visual processing disrupted



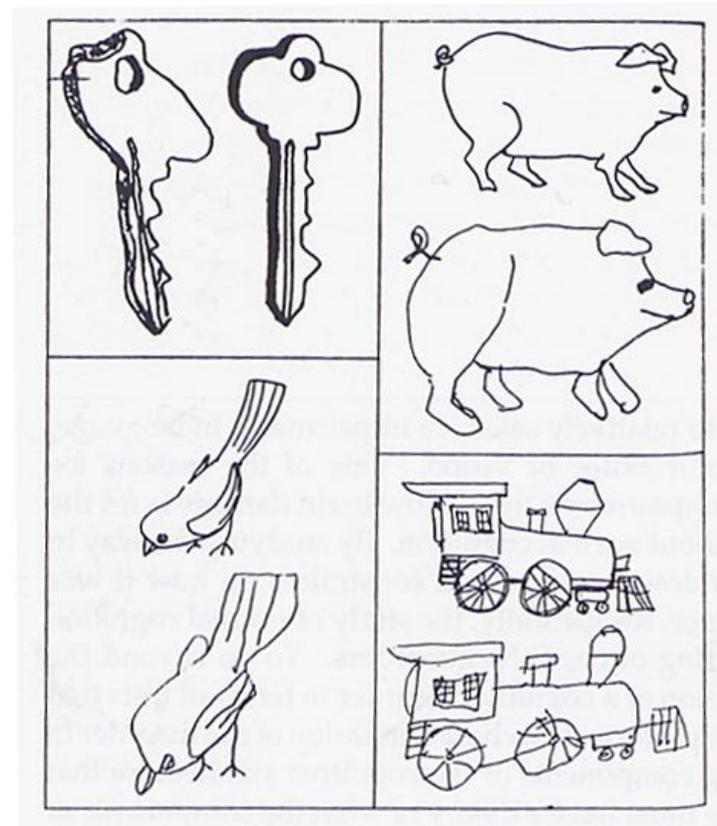
Apperceptive agnosics can't report degraded, fragmented letters

Copying in agnosics: neither type recognize what they see

Copying poor in apperceptive agnosia but can be good in associative agnosia



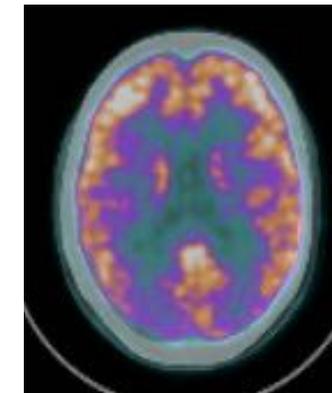
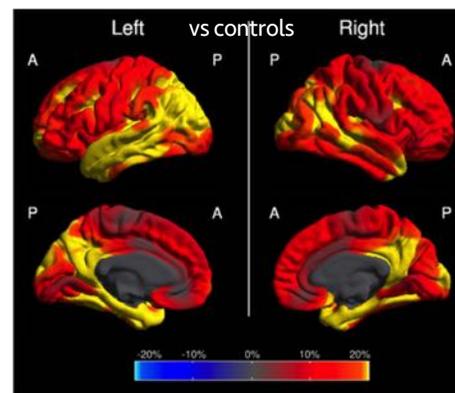
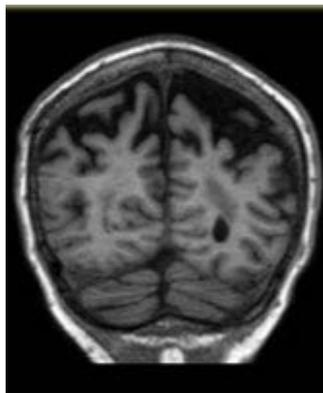
Apperceptive agnosia



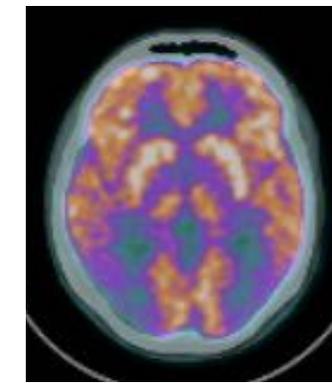
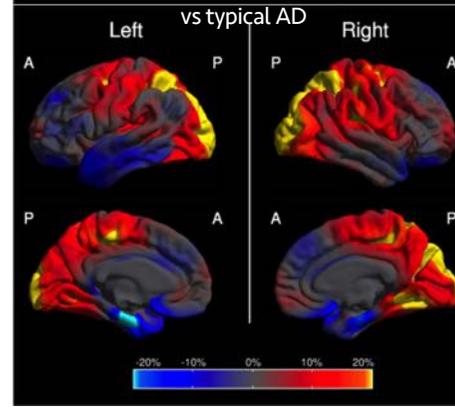
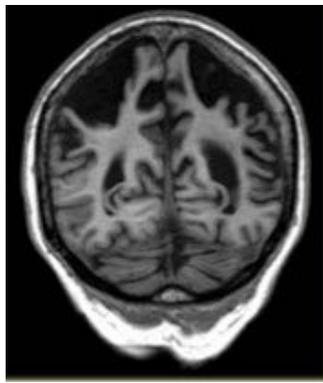
Associative agnosia – great copying but “perception stripped of its meaning”

Neuroimaging

Predominant posterior atrophy / hypometabolism on FDG-PET



Patient JN

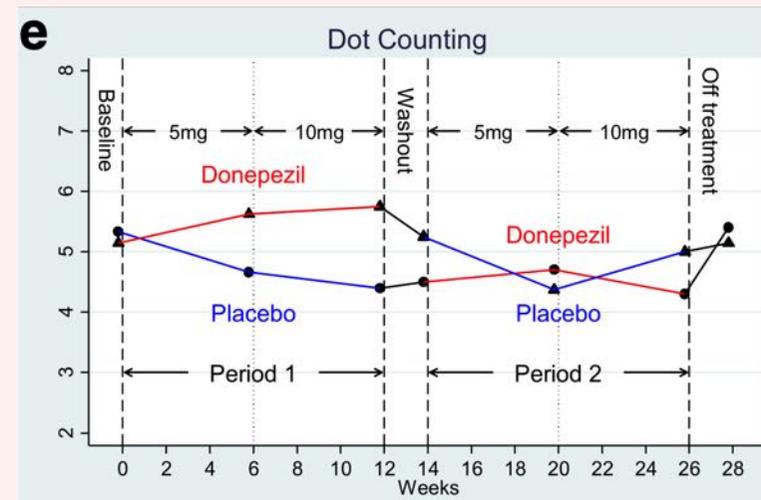
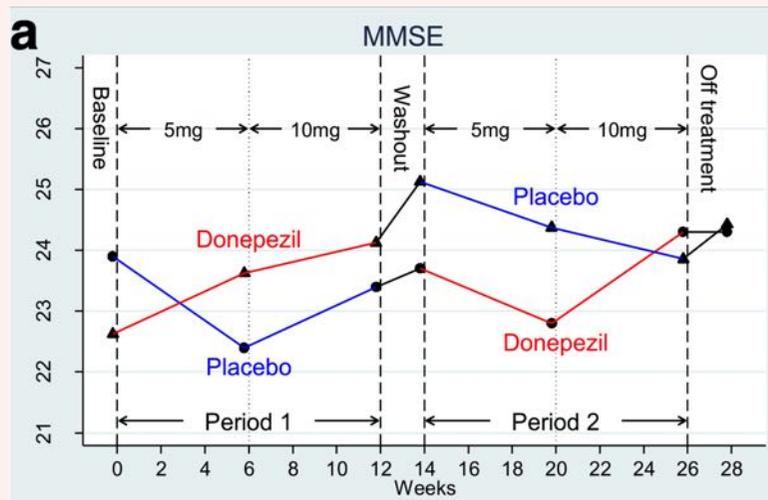


Lehmann et al (2012) *Neurobiol Aging*

Treatment of PCA

No good trial evidence for effective therapy of any drug used specifically for PCA

- DONIPAD study | 18 Patients
- Double-blind, placebo controlled RCT with cross-over design (2 x 12 week periods ON and OFF)
- No significant effect on MMSE or specific tests such as dot counting, number location etc.



Red flag 1: Visual hallucinations

- ▶ **Are rare in PCA**
Ask if patient ever sees things that aren't there?
Or is ever concerned by what they see?
- ▶ **Are common in DLB (Dementia with Lewy bodies)**
Often poorly formed, shadowy figures / animals
- ▶ **Consider carefully if history is rapidly progressive**
See Red flag 3



Red flag 2: Signs of a movement disorder

- ▶ **Parkinsonism**

Consider DLB (Dementia with Lewy bodies)

- ▶ **Dystonia / alien limb**

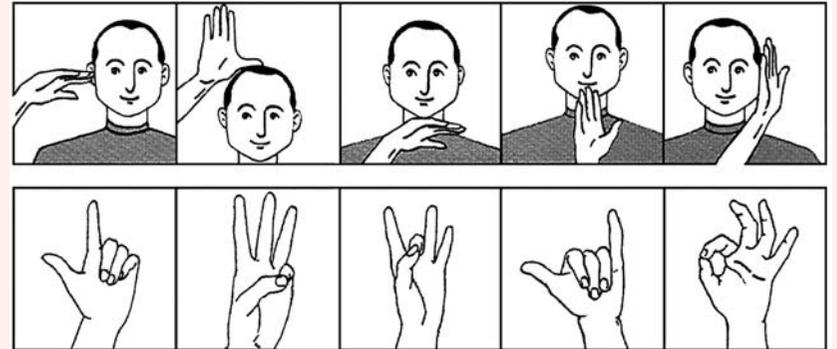
Consider CBS (Corticobasal Syndrome)

- ▶ **Limb apraxia**

Consider CBS but apraxia is also very common in AD

- ▶ **Myoclonus**

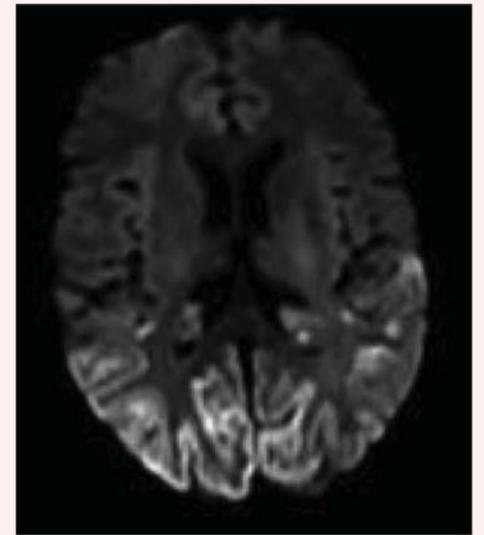
Also common in AD but consider carefully if history is very rapid!



Red flag 3: Rapid progression

- ▶ **Rapid progression with visual symptoms, then dementia**
Over weeks or <6 months
- ▶ **Visual field defects, disturbed colour perception, hallucinations**
Both dorsal and ventral visual stream signs may be present
- ▶ **Myoclonus, ataxia, pyramidal signs**

Consider Heidenhain variant CJD (Creutzfeldt-Jakob disease)



Reading

Reviews, primary sources and textbook chapters

- Crutch *et al* (2012) Posterior cortical atrophy *Lancet Neurology* 11:170-78
- Crutch *et al* (2017) Consensus classification of posterior cortical atrophy *Alzheimer's & Dementia* 13: 870-84
- Maia da Silva *et al* (2017) Visual dysfunction in posterior cortical atrophy *Frontiers in Neurology* 8: 389
- Lehmann *et al* (2011) Cortical thickness and VBM in PCA and typical AD *Neurobiology of Aging* 32: 1466-76
- Baiardi *et al* (2016) Revisiting Heidenhain variant CJD *J Alzheimer's Disease* 50: 465-76
- Ridha *et al* (2018) DONIPAD study *Alzheimer's Res & Therapy* 10: 44
- Frith *et al* (2019) Longitudinal neuroanatomical and cognitive progression of PCA *Brain* 142: 2082-95.

- Chapters on visual processing deficits, disorders of attention, parietal and temporal lobe syndromes, variants of AD, DLB and prion diseases in *Cognitive Neurology & Dementia* (2016) Husain & Schott, OUP.

