Neuroradiology in sub-Saharan Africa
– what can, should, must be done

In Neurodegenerative Diseases, Dementias and Movement Disorders

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Declaration

• No conflicts of Interest
Before completing this Teaching Course, participants should have a background on:

1. **Clinical aspects** of main neurodegenerative diseases, dementia and movement disorders
2. **Neuroanatomical** basics
3. **Neuroimaging basics** (structural imaging (CT scan, MRI (sections/sequences/indications), functional imaging, molecular imaging))
Objectives

• After completing this Teaching Course, participants will be able:

1. To determine the **adapted imaging protocol** for main neurodegenerative diseases, dementias and movement disorders

2. To describe **abnormal imaging findings** in main neurodegenerative diseases, dementias and movement disorders
Introduction

• Role of Neuroimaging in **dementia and movement disorders** nowadays:
  - Extends beyond its traditional role of **excluding neurosurgical lesions or other acquired/ treatable causes (exclusionary role)**
  - **Supports/confirms diagnosis** of specific neurodegenerative disorders (NDD) (**inclusionary role**)
  - Contributes to the **early diagnosis** of NDD (in MCI ➔ early biomarkers)
  - Assesses disease **progression**

• Need for **standardized, adapted protocol**
  - For each type of NDD (dementias, parkinsonian syndromes, movement disorders)
    - Exclusion of acquired conditions

"Look and you will find it - what is unsought will go undetected."
Sophocles
What can, should, must be done?

- **Combination** of imaging techniques: often needed for complete evaluation of the patient → help establish the most likely diagnosis

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Ranganathan et al, Changing landscapes in the neuroimaging of dementia, Ann Indian Acad Neurol, 2018
CT Protocol

when contraindications prevent MRI (claustrophobia, pacemaker, very old age)
when the only reason for imaging is to rule out surgically treatable causes

CT with negative scan angle for optimal visualization of the hippocampus in the transverse plane

Spiral CT of the brain with coronal reconstructions

Calcifications
MRI: What for?

- Determine degree and pattern of general cortical atrophy (GCA)
- Assess focal atrophy
- Assess microbleeds
- Determine degree of vascular damage and occurrence of strategic infarct
- Differentiate between various etiologies
- Exclude structural lesions
# MRI Protocol in Dementia/NDD

<table>
<thead>
<tr>
<th>MRI section/Sequence</th>
<th>Indication</th>
<th>Peculiar features</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Coronal-oblique T1</strong></td>
<td>Medial temporal lobe and <strong>hippocampal atrophy</strong></td>
<td>• In a plane orthogonal to long axis of hippocampus (perpendicular to hippocampus); parallel to brainstem • 3D MPRAGAE isotropic voxels (reformatting a sagittal 3D T1 sequence through the entire brain) • Thin-section images</td>
</tr>
<tr>
<td><strong>Sagittal reconstructions</strong></td>
<td><strong>Midline</strong> structures and <strong>parietal atrophy</strong></td>
<td>-</td>
</tr>
<tr>
<td><strong>Transversal FLAIR</strong></td>
<td>Global cortical atrophy (GCA) Vascular white matter hyperintensities <strong>Infarctions</strong></td>
<td>3 mm slices, 1mm isotropic voxels</td>
</tr>
<tr>
<td><strong>Transverse T2W</strong></td>
<td><strong>Infarctions</strong> (in particular lacunar infarctions in the thalamus and basal ganglia)</td>
<td>3 mm slices, 1mm isotropic voxels</td>
</tr>
<tr>
<td><strong>Transverse T2</strong>*</td>
<td><strong>Microbleeds</strong> in amyloid angiopathy Calcification Iron deposition</td>
<td>Gradient-echo, 3 mm slices, TE &gt; 30ms, small flip angle</td>
</tr>
<tr>
<td><strong>DWI</strong></td>
<td><strong>Young</strong> patients Rapidly progressive NDD (DD – vasculitis, CJD)</td>
<td>Supplemental sequence</td>
</tr>
</tbody>
</table>

*Protocol that is used in the Alzheimer Centre in Amsterdam*
<table>
<thead>
<tr>
<th>Indications</th>
<th>DWI</th>
<th>Contrast imaging</th>
</tr>
</thead>
<tbody>
<tr>
<td>CJD</td>
<td>Restricted diffusion (basal ganglia or cortex)</td>
<td>No enhancement with contrast</td>
</tr>
<tr>
<td>Infection</td>
<td>Restricted diffusion (e.g., HSV)</td>
<td>Enhancement of inflamed areas</td>
</tr>
<tr>
<td>Vasculitis</td>
<td>Areas of infarction</td>
<td>Vascular and leptomeningeal enhancement</td>
</tr>
<tr>
<td>Recent ischemia</td>
<td>Restricted diffusion</td>
<td>Cave luxury perfusion with enhancement in subacute</td>
</tr>
</tbody>
</table>
Visual Rating Scales in Dementia

- Global cortical atrophy (GCA)
  - Pasquier scale (0-3)
- Medial temporal lobe atrophy (MTA)
  - Scheltens scale (0-4)
- Posterior cortical atrophy
  - Koedam scale (0-3)
- Fronto–temporal atrophy
  - Kipps scale (0-4)

- White matter hyperintensities (WMH)
  - global Fazekas (0-3)
  - regional ARWMC (0-24)
  - Visual rating of WMHs according to Scheltens (0-84)

- Microbleeds
  - BOMBS
  - MARS

- Enlarged perivascular spaces (EPVS)

Kaushik et al, J Neurosci Rural Pract. 2021
Global Cortical Atrophy (GCA) scale
(Pasquier scale: 0–3)

- Best assessed on FLAIR and 3D T1 images (Cortical atrophy is best scored on FLAIR images)

<table>
<thead>
<tr>
<th>Score 0</th>
<th>Score 1</th>
<th>Score 2</th>
<th>Score 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>No cortical atrophy (Normal)</td>
<td>Mild atrophy (opening of sulci - Open sulci)</td>
<td>Moderate atrophy (volume loss of gyri - Gyral atrophy)</td>
<td>Severe (end-stage) atrophy (knife blade’ atrophy)</td>
</tr>
</tbody>
</table>

J Korean Neuropsychiatr Assoc. 2018
Harper L et al. J Neurol Neurosurg Psychiatry 2015
# Medial temporal lobe atrophy (MTA) scale (Scheltens scale: 0–4)

<table>
<thead>
<tr>
<th>Score</th>
<th>Width of choroid fissure</th>
<th>Width of temporal horn</th>
<th>Height of hippocampal formation</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>N</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>1</td>
<td>↑</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>2</td>
<td>↑↑</td>
<td>↑</td>
<td>↓</td>
</tr>
<tr>
<td>3</td>
<td>↑↑↑</td>
<td>↑↑</td>
<td>↓↓</td>
</tr>
<tr>
<td>4</td>
<td>↑↑↑</td>
<td>↑↑↑</td>
<td>↓↓↓</td>
</tr>
</tbody>
</table>

- Score 0: no atrophy
- Score 1: only widening of choroid fissure
- Score 2: also widening of temporal horn of lateral ventricle
- Score 3: moderate loss of hippocampal volume (decrease in height)
- Score 4: severe volume loss of hippocampus

< 75 years: score 2 or more is abnormal.
> 75 years: score 3 or more is abnormal
MTA/Scheltens scale

- rated on coronal T1
- slice through corpus of hippocampus (level of anterior pons)
### Posterior cortical atrophy

**(Koedam scale: 0–3)**

- **Scale rated on:**
  - Sagittal and coronal T1
  - Axial FLAIR
- **Evaluates:**
  - Sulci:
    - Posterior cingulate
    - Parieto-occipital
    - Parietal Cortex (including the precuneus)

**Koedam score**

<table>
<thead>
<tr>
<th>Koedam score</th>
<th>Parietal cortical atrophy</th>
<th>Sulci</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Grade 0</strong></td>
<td>No cortical atrophy</td>
<td>Closed sulci of parietal lobes and cuneus</td>
</tr>
<tr>
<td><strong>Grade 1</strong></td>
<td>Mild parietal cortical atrophy</td>
<td>Opening of sulci (mild widening of posterior cingulate and parieto-occipital sulci)</td>
</tr>
<tr>
<td><strong>Grade 2</strong></td>
<td>Moderate/substantial parietal atrophy</td>
<td>Volume loss of gyri (substantial widening of the sulci)</td>
</tr>
<tr>
<td><strong>Grade 3</strong></td>
<td>Severe atrophy – end-stage « knife-blade » atrophy</td>
<td>Extreme widening of the posterior cingulate and parieto-occipital sulci</td>
</tr>
</tbody>
</table>

*Highest score obtained for an area*

*Koedam et al., Eur Radiol, 2011*
# Fronto–temporal atrophy

(Kipps scale : 0–4)

<table>
<thead>
<tr>
<th>Stage</th>
<th>FrONTAL LOBE</th>
<th>ANTERIOR TEMPORAL LOBE</th>
<th>POSTERIOR TEMPORAL LOBE</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Normal appearances</td>
<td>Normal appearances</td>
<td>Normal appearances</td>
</tr>
<tr>
<td>1</td>
<td>Mild atrophy of orbital or supero-medial frontal cortex – contour of the basal ganglia in the lateral ventricle is convex, as in controls, but with some prominence of the lateral ventricle</td>
<td>Slight prominence of anterior temporal sulci</td>
<td>Slight increased prominence of the lateral ventricle to form a rim around the anterior hippocampus – temporal sulci show mild prominence</td>
</tr>
<tr>
<td>2</td>
<td>Definite sulcal widening in any cortical subregion or flattened profile to basal ganglia</td>
<td>Temporal sulci definitely widened</td>
<td>Lateral ventricle unarguably dilated with subtle reduction in hippocampal size – the medial temporal gyri may be atrophic, and there may be prominence of the temporal sulci</td>
</tr>
<tr>
<td>3</td>
<td>Severe cortical atrophy with clear reduction in white matter and reduced white-grey matter differentiation – stage 3 basal ganglia have concave profile</td>
<td>Gyri severely atrophic and ribbonlike – white and grey matter cannot be distinguished (normal temporal lobe at this level is less substantial than the frontal lobe, and so the ribbon-like gyri of the stage 3 temporal lobe are similar to stage 4 frontal gyri)</td>
<td>The hippocampus is small and sits at the medial tip of a greatly expanded temporal horn – sulci are definitely widened</td>
</tr>
<tr>
<td>4</td>
<td>Cortex reduced to a ribbon and the basal ganglia virtually indiscernible</td>
<td>Temporal pole has a simple linear profile or is not seen at all</td>
<td>Hippocampus is extremely small – temporal cortex and white matter show almost complete atrophy</td>
</tr>
</tbody>
</table>

Scale rated on T1-weighted coronal

*Kipps et al., Dement Geriatr Cogn Disord 2007*
### White Matter Hyperintensities: Global Fazekas scale (0–3)

*best scored on transverse FLAIR or T2-weighted images*

<table>
<thead>
<tr>
<th>Fazekas score</th>
<th>White Matter Hyperintensities (WMH)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fazekas 0</strong></td>
<td>None or a single punctate WMH lesion</td>
</tr>
<tr>
<td><strong>Fazekas 1</strong></td>
<td>Multiple punctate lesions</td>
</tr>
<tr>
<td><strong>Fazekas 2</strong></td>
<td>Beginning confluency of lesions (bridging)</td>
</tr>
<tr>
<td><strong>Fazekas 3</strong></td>
<td>Large confluent lesions</td>
</tr>
</tbody>
</table>
Fazekas: CT vs MRI

Box 1 | Visual rating of WMHs according to Fazekas

Fazekas 0
No WMHs

Fazekas 1
Focal or punctate lesions:
- Single lesions ≤9 mm
- Grouped lesions <20 mm

Fazekas 2
Beginning confluent lesions:
- Single lesions 10–20 mm
- Grouped lesions >20 mm in any diameter
- No more than connecting bridges between individual lesions

Fazekas 3
Confluent lesion:
- Single lesions or confluent areas of hyperintensity ≥20 mm in any diameter

Abbreviation: WMHs, white matter hyperintensities.
Age-Related White Matter Changes (ARWMC) scale

Applicable to both CT and MRI that has almost equal sensitivity (except for certain regions (MRI>CT: parieto-occipital and infratentorial areas; FLAIR frontal and parieto-occipital)

Wahlund et al, Stroke, 2001
**Age-Related White Matter Changes (ARWMC) scale**

<table>
<thead>
<tr>
<th>ARWMC Score</th>
<th>White matter lesions</th>
<th>Basal ganglia lesions</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No lesions</td>
<td>No lesions</td>
</tr>
<tr>
<td>1</td>
<td>Focal lesions</td>
<td>1 focal lesion (&gt;5 mm)</td>
</tr>
<tr>
<td>2</td>
<td>Beginning confluence of lesions</td>
<td>&gt;1 focal lesion</td>
</tr>
<tr>
<td>3</td>
<td>Diffuse involvement of entire region, with or without involvement of U fibers</td>
<td>Confluent lesions</td>
</tr>
</tbody>
</table>

*Wahlund et al., Stroke, 2001*
Visual rating of WMHs according to Scheltens (0–84)


Microbleeds

best scored on T2*-weighted (SWI) images

The Microbleed Anatomical Rating Scale (MARS)
Reliability of a tool to map brain microbleeds

Improving Interrater Agreement About Brain Microbleeds
Development of the Brain Observer MicroBleed Scale (BOMBS)
Charlotte Cordonnier, PhD; Gillian M. Potter, FRCR; Caroline A. Jackson, MSc; Fergus Doubal, MRCP; Sarah Keir, MD; Cathie L.M. Sudlow, DPhil; Joanna M. Wardlaw, FMedSci; Rustam Al-Shahi Salman, PhD

MARS
Gregoire et al., Neurology, 2009

BOMBS
Cordonnier et al., Stroke, 2009
### Microbleeds Rating Scale

#### Brain Observer Micro Bleed Scale (BOMBS)

<table>
<thead>
<tr>
<th>Date of MRI <strong><strong>/</strong></strong>/____</th>
<th>Date of Birth <strong><strong>/</strong></strong>/____</th>
<th>Study ID</th>
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</table>

#### Microbleeds

- **Infratentorial**: Small, round, well-defined, hypointense on GRE T2*; ≥0.5-1 mm; not well seen on T2
- **Cerebrum**: Small, round, well-defined, hypointense on GRE T2*; ≥0.5-1 mm; not well seen on T2
- **White matter**: Small, round, well-defined, hypointense on GRE T2*; ≥0.5-1 mm; not well seen on T2

### Rating Scale

<table>
<thead>
<tr>
<th></th>
<th>Right</th>
<th>Left</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Infratentorial</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brainstem (B)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cerebellum (C)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Deep (VWM)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thalamus (Th)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Internal Capsule (IC)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>External Capsule (EC)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Corpus Callosum (CC)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Deep and periventricular (PVM)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Fornix (F)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Putamen (P)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Temporal (T)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Occipital (O)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Insula (I)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Others</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Rating Criteria

1. **Sure absence of BMBs**: Flow voids in small cortical vessels (check T2FLAIR), Hypointensity at site of deep perforators from precentral MCA, Symmetrical hypointensity in globus pallidus (check CT: calcium), Rate as 'uncertain' if only partial volume effects (adjacent to previous temporal bone or orbit).
2. **Sure presence of BMBs**: Flow voids in small cortical vessels (check T2FLAIR), Hypointensity at site of deep perforators from precentral MCA, Symmetrical hypointensity in globus pallidus (check CT: calcium), Rate as 'uncertain' if only partial volume effects (adjacent to previous temporal bone or orbit).

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*Gregoire et al., Neurology, 2009*

*Cordonnieret al., Stroke, 2009*
Microbleeds: BOMBS scale

‘Certain’ BMBs

‘Uncertain’ BMBs

Examples of common ‘BMB mimics’

1. Basal ganglia calcification
2. Cortical vessels
3. Partial volume artefact

From petrous temporal bone
From orbit

Cordonnier et al., Stroke, 2009
Enlarged perivascular spaces (EPVS) scale

best scored on T1/T2/FLAIR images, regions: centrum semiovale (CSO), basal ganglia (BG), hippocampus, in most affected hemisphere

- 0 - no EPVS
- 1 - <10 EPVS
- 2 - 10–20 EPVS
- 3 - 21–40 EPVS
- 4 - > 40 EPVS

**EPVS: Differential Diagnosis**

**Motion Artifacts**

**WMH**

**Infarcts**

**Subtle Enlargement**

Maclullich et al., J Neurol Neurosurg Psychiatry. 2004
Dubost et al. NeuroImage 2018
Advanced MR techniques

- **Perfusion Weighted imaging (PWI)**

Type of information obtained comparable to nuclear medicine

- **BOLD fMRI**

  fMRI typically refers to images obtained by using the blood oxygen level dependent (BOLD) contrast

  Differences in magnetic susceptibility between oxygenated and deoxygenated blood serves as an intrinsic contrast medium

- **MR spectroscopy**

  In patients with NDD: usual finding = change in the ratio between metabolites or a general decrease in metabolites

- **Diffusion Tensor Imaging (DTI)**

  DTI in dementia have consistently shown altered diffusion (tract) properties in accordance with the pattern of neurodegenerative pathology
The EPAD core and advanced sequences
What should be done

A radiological report should describe:

- Medial temporal lobe atrophy (MTA) (Scheltens score with explanation)
- General or local widening of sulci (Global Cortical Atrophy stage with explanation)
- Width of ventricles
- White matter hyperintensities (WMH) (score according to Fazekas scale with explanation)
- Size and position of infarcts
- Other changes (tumour, normal pressure hydrocephalus, subdural hematoma etc.)
- Comparison with previous examinations (progression of atrophy or white matter changes etc.)
- CONCLUSION: assessment of findings in relationship to clinical suspicion and other examinations such as CSF, PET or SPECT.
Normal ageing or pathological conditions?

- «Successful» ageing:
  - minimal morphological (physiological) loss
  - Brain imaging abnormalities without overt clinical deficits or symptoms

- Global cortical atrophy:
  - Brain weight peaked by the mid-to-late teens.
  - 0.2% / year: 30-50 years
  - 0.3 to 0.5% / year: 50-70 years
  - Shrinkage of cortical grey matter predominates over white matter loss
  - The parietal and frontal lobes are equally affected.

- Medial temporal atrophy:
  - MTA score 2 is normal in nondemented pt over 75 year age.
  - 0.2% per year: 30-50 yr
  - 0.8% per year: 50-70yr
  - 1.5 to 2% per year: above 80 yr

- Microbleeds:
  - Usually found in the basal ganglia or thalamus and posterior fossa in hypertensive patients.

- Enlarged Virchow Robin space:
  - Most enlarged VRS < 2 mm in diameter
  - Usually found in the striatum, ant perforated substance and ant comissure
  - Diffuse widening of VRS in basal ganglia is suggestive of focal atrophy

- White matter hyper intensities:
  - Periventricular hyperintensities suggestive of increase extracellular fluid and subependymal gliosis.
  - Represent usual aging phenomenon.
  - Panecticform and early confluent deep WMH often have little clinical consequences.

- Iron accumulation:
  - Usually involves globus pallidus, striatum, substantia niagra and dentate nucleus
  - Hypointensity on T2 images
  - Started appearing around third decade

- Reduced resting-state fMRI activity (anterior frontal, precuneus, and posterior cingulate cortices) in ageing.

- Grey matter perfusion decreases by 0.45% per year in healthy adult subjects, predominantly in the frontal cortex.

- Hypometabolism in frontal and post cingulate cortex on FDG-PET.

- Abnormal uptake in amyloid-PET is seen in 30% normal elderly subjects.
Brain Imaging in dementia and movement disorders

- Gray matter
  - Cortex
- White matter
  - Basal ganglia
- Other sectors
  - Vacular
  - CSF
♂, 75 years old,  
Progressive memory deficits of hippocampal profile, slow worsening (since 70 y.o.)

Oblique coronal CT  Oblique coronal T1  Axial FLAIR  Axial FLAIR  Sagittal T1

GCA (Pasquier) score: 3  
MTA (Scheltens) score: 4  
Posterior cortical atrophy (Koedam) score: 3

Alzheimer’s disease (AD)  (Late onset, typical amnestic form, advanced stage)
Imaging patterns of AD

- **Typical amnestic form**: Hippocampal and precuneus atrophy
- **Late AD (>65 years) + APOE ε4**: Predominant hippocampal atrophy
- **Early AD (<65 years)**: More posterior cortical atrophy

Staffaroni et al, Neuroimaging in dementia, Semin Neurol. 2017
Atypical Forms of AD

Behavioral (Frontal) variant

Logopenic progressive primary aphasia (PPA) variant

Corticobasal syndrome (CBS) variant

Posterior Cortical Atrophy (PCA) variant

dorsolateral, ventrolateral, and ventromedial prefrontal and insular cortical atrophy

left-lateralized temporal cortical atrophy

left-lateralized peri-Rolandic and parietal cortical atrophy

bilateral occipitoparietal atrophy

Camsari et al., J Neurol Clin. 2016
Dickerson et al., CNS Spectr. 2017
From Mild cognitive Impairment (MCI) to AD?

- **hippocampal** atrophy + concomitant widening of the collateral **sulcus** - both signs of progressive MTA
- Slight **parietal** atrophy: independent predictive value for conversion from MCI to AD

**MTA in AD vs other dementias**

<table>
<thead>
<tr>
<th></th>
<th>Present</th>
<th>Absent</th>
</tr>
</thead>
<tbody>
<tr>
<td>AD</td>
<td>100%</td>
<td>-</td>
</tr>
<tr>
<td>VaD</td>
<td>87%</td>
<td>13%</td>
</tr>
<tr>
<td>DLB</td>
<td>62%</td>
<td>38%</td>
</tr>
<tr>
<td>Controls</td>
<td>4%</td>
<td>96%</td>
</tr>
</tbody>
</table>

*Staffaroni et al., Neuroimaging in dementia, Semin Neurol. 2017*
♂, 65 years old, similar cases in family
Since age 61, personality changes, apathy, then behavioral disorders (hyperorality, disinhibition, aggressiveness), no overt memory deficits

Fronto-temporal lobar degeneration (FTLD): behavioral variant (BvFTD)
Asymmetric fronto–insular atrophy extended to anterior temporal

Pick’s disease (3R)

More Posterior atrophy
Preserved frontoinsular area

CBD (4R)

Specific MRI patterns

PSP (4R)

FTLD–Tau

Bang et al., Lancet. 2015
FTLD–Tau

Progressive supranuclear palsy (PSP) (4R)

- Marked dilation of third ventricle
  - Dorsal mesencephalic atrophy
  - Thinning of superior cerebellar peduncles
  - Atrophy of thalamus, basal ganglia and frontal cortex

- Mickey mouse sign
- Hummingbird/penguin sign

Reduced midbrain area compared with the pons

Thinned superior cerebellar peduncles on coronal section (B; arrows) compared with the middle cerebral peduncles (C; arrows)

Staffaroni et al., Neuroimaging in dementia, Semin Neurol. 2017
FTLD–Tau
Progressive supranuclear palsy (PSP (4R))

The “hypointense substantia nigra” sign. A novel MRI marker of progressive supranuclear palsy

-Hypointense area at the medial substantia nigra in T1

Constantinides et al., J Neurol Sci, 2021
Primary Progressive Aphasia (PPA)

Semantic variant (svPPA)
Substratum: TDP-43C
Anterior and inferior temporal atrophy
Asymmetric—Left Hemisphere

Agrammatic/non fluent variant (naPPA)
Substratum: Tau (4R)
Atrophy: Inferior frontal, insular, premotor cortex
Asymmetric—Left Hemisphere

Logopenic variant (lvPPA)
Substratum: AD
Marked temporoparietal atrophy
Asymmetric—Left Hemisphere

Staffaroni et al, Neuroimaging in dementia, Semin Neurol. 2017
♀, 85 years old, Personal history of RBD 
Since the age of 80, complex visual hallucinations, delirium, fluctuations, then parkinsonism, frequent upward falls, camptocormia

GCA (Pasquier) score: 1
MTA (Scheltens) score: 0
Posterior cortical atrophy (Koedam) score: 1

Dementia with Lewy Bodies (DLB)
Synucleinopathies: PD, DLB, MSA

Dementia with Lewy bodies
- Generalized atrophy
- Less medial temporal atrophy than AD
- Possible parieto-occipital WM lesions

If medial temporal lobe preserved ➔ supports DLB diagnosis
If medial temporal lobe atrophied ➔ Not diagnostically helpful

Parkinson’s disease (PD)
- Vs healthy controls,
- Medial temporal and frontal atrophy
- Severe dementia (PDD) with temporal atrophy
- Frontal, temporal and occipital WM lesions

Multiple system atrophy (MSA)
- Vs PD and PSP:
  - greater striatum, brainstem, and cerebellar atrophy
- Specific features:
  - Hot-cross bun sign (cruciform sign)
  - Putaminal rim sign

Staffaroni et al., Neuroimaging in dementia, Semin Neurol. 2017
Rodriguez et al., Alzheimer’s & Dementia, 2012
Petrou et al., Imaging Med. 2012
Synucleinopathies

Multiple system atrophy (MSA): MSA-c and MSA-p

Hot-cross Bun sign (HCB) or “cruciform T2” sign (MSA-c>>MSA-p)

Putaminal rim sign
MSA-p>>MSA-c

Putaminal hypointensity with a hyperintense “putaminal rim” sign on an axial T2-weighted MRI

Chelban et al., Journal of Neurology (2019)
Staffaroni et al, Neuroimaging in dementia, Semin Neurol. 2017
<table>
<thead>
<tr>
<th>Disease Entity</th>
<th>MR Imaging</th>
<th>FDG PET</th>
<th>Amyloid PET</th>
<th>123I Ioflupane SPECT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parkinson disease</td>
<td>Often normal, occasional diffuse atrophy</td>
<td>Usually normal, preserved putaminal activity, occasional decreased uptake in the parieto-occipital cortex</td>
<td>Normal</td>
<td>Decreased striatal activity (usually asymmetric)</td>
</tr>
<tr>
<td>MSA</td>
<td>Putaminal atrophy and marginally increased T2 signal, “hot cross bun sign”</td>
<td>Decreased putaminal or cerebellar uptake, subtype dependent</td>
<td>Normal</td>
<td>Symmetric or asymmetric decreased striatal activity</td>
</tr>
<tr>
<td>PSP</td>
<td>“Hummingbird sign,” “Mickey Mouse sign”</td>
<td>Decreased uptake in the posterior frontal lobes, midbrain, and basal ganglia</td>
<td>Normal</td>
<td>Symmetric or asymmetric decreased striatal activity</td>
</tr>
<tr>
<td>DLB</td>
<td>Diffuse atrophy</td>
<td>Generalized decreased uptake (more prominent in the occipital lobes)</td>
<td>Positive in most cases</td>
<td>Symmetric or asymmetric decreased striatal activity</td>
</tr>
<tr>
<td>CBD</td>
<td>Asymmetric parietal and/or frontal cortical atrophy</td>
<td>Asymmetric decreased uptake in the parietal and/or frontal lobes</td>
<td>Normal</td>
<td>Decreased striatal activity (usually asymmetric)</td>
</tr>
</tbody>
</table>

Note.—APS = atypical parkinsonian syndromes, CBD = corticobasal degeneration, DLB = dementia with Lewy bodies, MSA = multiple system atrophy, PSP = progressive supranuclear palsy.
♂, 62 years old, rapidly progressive cognitive decline, myoclonus, dystonia, chorea (within few months)

Creutzfeldt Jakob disease (CJD)
Greutzfeldt Jakob disease (CJD): Sporadic and variant CJD

vCJD

Striatal hyperintensity

sCJD

Double hockey stick sign

Pulvinar sign

Cortical ribonning hyperintensity

Staffaroni et al., Neuroimaging in dementia, Semin Neurol. 2017
Greutzfeldt Jakob disease (CJD): Sporadic and variant CJD

### UCSF 2017 Proposal of MRI Criteria for CJD Diagnosis

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>UCSF 2017 Modified CJD MRI criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRI definitely CJD</td>
<td>DWI &gt; FLAIR cortical ribboning hyperintensity in:</td>
</tr>
<tr>
<td></td>
<td>1. Classic pathomorphology: cingulate, superior frontal, and &gt;1 neocortical gyri (often precentral, angular, superior parietal, superior temporal, middle frontal, or lateral temporal gyri)</td>
</tr>
<tr>
<td></td>
<td>a. Supportive for subcortical involvement</td>
</tr>
<tr>
<td></td>
<td>i. Striatum with decreasing anterior-posterior gradient</td>
</tr>
<tr>
<td></td>
<td>ii. Corresponding ADC hypointensity</td>
</tr>
<tr>
<td></td>
<td>b. Supportive for cortical involvement:</td>
</tr>
<tr>
<td></td>
<td>i. Asymmetric involvement of midline neocortex or cingulate</td>
</tr>
<tr>
<td></td>
<td>ii. Spraying of precentral gyri</td>
</tr>
<tr>
<td></td>
<td>iii. Corresponding ADC cortical ribboning hypointensity</td>
</tr>
<tr>
<td></td>
<td>2. Cortex only (&gt;3 gyr) - supportive for cortex (above)</td>
</tr>
<tr>
<td>MRI probably CJD</td>
<td>1. Unilateral striatum or cortex (≤3 gyr); see supportive for subcortical and cortex (above)</td>
</tr>
<tr>
<td></td>
<td>2. Bilateral striatum (see supportive for subcortical) or postero medial thalamus; see supportive for subcortical (above)</td>
</tr>
<tr>
<td></td>
<td>3. DWI &gt; FLAIR hyperintensities only in limbic areas, with corresponding ADC hypointensity</td>
</tr>
<tr>
<td>MRI probably not CJD</td>
<td>1. Only FLAIR/DWI abnormalities only in limbic areas, where hypointensity can be normal (e.g., insula, anterior cingulate, and hippocampi), and ADC map does not show corresponding restricted diffusion (hypointensity)</td>
</tr>
<tr>
<td></td>
<td>2. DWI hyperintensities due to artifact (signal distortion); see other MRI issues (below)</td>
</tr>
<tr>
<td>MRI definitely not CJD</td>
<td>1. Normal</td>
</tr>
<tr>
<td></td>
<td>2. Abnormalities not consistent with CJD</td>
</tr>
<tr>
<td>Other MRI issues</td>
<td>In prolonged courses of sCJD (&gt;1 year), brain MRI might show significant atrophy with loss of DWI hyperintensity, particularly in areas previously with restricted diffusion.</td>
</tr>
<tr>
<td></td>
<td>To help distinguish abnormality from artifact, obtain b2000 diffusion sequences in multiple directions (e.g., axial and coronal).</td>
</tr>
</tbody>
</table>

### Table 2. Findings in different types of CJD

<table>
<thead>
<tr>
<th>CJD Type</th>
<th>Features</th>
<th>sCJD</th>
<th>vCJD</th>
<th>fCJD</th>
<th>GSS</th>
<th>FFI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean age at onset</td>
<td>60–70 yrs</td>
<td>28 yrs</td>
<td>60 yrs</td>
<td>60 yrs</td>
<td>50 yrs</td>
</tr>
<tr>
<td></td>
<td>Duration of illness</td>
<td>6 mos</td>
<td>14 mos</td>
<td>6 mos</td>
<td>14 mos</td>
<td>6 mos</td>
</tr>
<tr>
<td></td>
<td>Predominant clinical features</td>
<td>Rapid cognitive decline, myoclonus and akinetic mutism</td>
<td>Early psychiatric symptoms, then mental decline</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MRI findings</td>
<td>60%–70% have hyperintensity in basal ganglia or cortex</td>
<td>Pulvinar sign in 90%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EEG findings</td>
<td>PSWQs in 60%–70%</td>
<td>PSWQs negative</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14–3 status</td>
<td>Positive in 90%</td>
<td>Positive in 50%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Genetics</td>
<td>MMT most common (70%)</td>
<td>MMT in 100%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Figure:**
- A. Pulvinar sign: Hyperintensity in pulvinar
- B. Double Hockey stick sign: Hyperintensity in pulvinar + dorsomedial thalamus

\[\text{Staffaroni et al., Neuroimaging in dementia, Semin Neurol, 2017, Engleberg et al., 2015}\]
♀, 50 years old, non consanguineous marriage
Chorea (45 y.o.) then psychiatric disorders and cognitive deficits (48 y.o.)

Huntington disease (chorea)
Huntington disease: MRI findings
Huntington disease like (HDL-2): same findings

HDL-2: most common Huntington's disease (HD) phenocopy in populations with an African ancestry
♂, 54 years old, Progressive cognitive decline, cerebellar ataxia, dystonia since the age of 48

Family history: Mixed movement disorders (dystonia+chorea) in his son /Dystonia in his daughter

Basal ganglia calcification is also known as Fahr’s disease or Fahr’s syndrome
Incidental

Cockayne disease

Aicardi–Goutières syndrome

Hyperparathyroidism

Saade et al., Intracranial calcifications on CT: an updated review, Radiology Case. 2019
Fahr’s syndrome

On MRI: best appreciated on GRE/T2* or SWI, may be paradoxically hyperintense on T1

Hyperintensity on T1WI  Hypointensity on SWI

CT>>MRI: Problem of differential diagnosis

**T1 Hyperintensities**

*(in basal ganglia+++)*

- Calcifications
- Wilson disease
- Carbon monoxide (delayed)
- Neurofibromatosis type 1
- Manganese Intoxication

- (Hemi)chorea-(hemi)ballismus
- (Hemi)chorea-(hemi)ballismus
- Non ketotic hyperglycemic chorea
- Hepatic encephalopathy
- Confusion + Flapping tremor (Asterexis)
- Methemoglobinemia
cyanosis, microcephaly, encephalopathy, axial hypotonia, dystonia with hyperkinetic movements

- Hypoxia–ischemia, newborns

*Bejtekowska-Figatowska* et al., *Basal ganglia lesions in children and adults, European Journal of Radiology, 2013*
T2\* or SWI Hypointensities

Calcifications

Hemosiderin (hemorrhage)

Physiological

Iron

Pathological

Ageing

NBIA

Calcifications

Hemosiderin (hemorrhage)

Physiological Pathological

Ageing

NBIA

T2-hypointensity

Old age
Parkinson’s disease (globus pallidus)
Calcifications
Hemosiderin (old hemorrhage) or deoxyhemoglobin

T2-hyper- AND hypointensity

Pantethenate kinase-associated neurodegeneration – “eye-of-the-tiger”
Parkinson variant of multiple system atrophy

Hegde et al., Radiographics, 2011
♂, 30 years old, consanguineous marriage
Since the age of 24, difficulties with walking, speech, and writing, followed by dystonia and emotional and behavioral symptoms

PKAN: Pantothenate Kinase Associated Neurodegeneration
Neurodegeneration With Brain Iron Accumulation

Lee et al., Brain MRI Pattern Recognition in Neurodegeneration With Brain Iron Accumulation, Frontiers in Neurology, 2020
♀, 25 years old, consanguineous marriage, similar cases, Movement disorders (hyperkinetic (chorea + dystonia) + hypokinetic (since 22 y.o.) then cognitive deficits (23 y.o.)
Altererd liver /copper tests

Wilson’s disease
Wilson’s disease: MRI findings

- MRI abnormal in all patients.
- Putamen most involved (85.3%).
- Sensitivity of T2 and FLAIR was highest 97.1% each.
- MRI load correlated with age, tremor, psychiatric disorder, choreoathetosis, and severity.

Classical Brain MRI findings

Atypical Brain MRI findings

Sign of the "giant Panda face"

Poujois et al., Wilson's disease. A 2017 update. astroentérologie Clinique et Biologique, 2018
♂, 71 years old, presented with decreased consciousness (fluctuating Glasgow Coma Scale score of 5–7). He had a background of atrial fibrillation and was anticoagulated with dabigatran, a novel oral anticoagulant. Computed tomography (CT) scan showed a mildly reduced attenuation in the region of the left thalamus. He later kept cognitive deficits with progressive decline (memory, language).

---

**Bilateral thalamic infarction (artery of Percheron): Strategic Infarct**
Vascular dementia (VaD)

Cognitive dysfunction in VaD can be the result of:

- **Large vessel infarctions**
  - Bilateral in the anterior cerebral artery territory.
  - Parietotemporal- and temporo-occipital association areas of the dominant hemisphere (angular gyrus included).
  - Posterior cerebral artery territory infarction of the paramedian thalamic region and inferior medial temporal lobe of the dominant hemisphere.

- **Watershed infarctions** in the dominant hemisphere (superior frontal and parietal).

- **Small vessel disease**
  - Multiple lacunar infarctions in frontal white matter (>2) and basal ganglia (>2).
  - WMLs (at least more than 25% of WM).
  - Bilateral thalamic lesions.

<table>
<thead>
<tr>
<th>Strategic infarctions</th>
<th>Site</th>
</tr>
</thead>
<tbody>
<tr>
<td>Med Cerebral artery</td>
<td>Parieto-temporal or temporo-occipital association areas</td>
</tr>
<tr>
<td></td>
<td>Angular gyrus</td>
</tr>
<tr>
<td>Post Cerebral artery</td>
<td>Superior frontal or parietal</td>
</tr>
<tr>
<td>Watershed infarctions</td>
<td></td>
</tr>
<tr>
<td>Lacunar infarctions</td>
<td>Bilateral thalamic</td>
</tr>
</tbody>
</table>

*Poujois et al., Wilson’s disease: A 2017 update, astroentérologie Clinique et Biologique, 2018*
♂, 65 years old, Family history: Stroke (hemorrhagic and ischemic), dementia
Personal history of cerebral hemorrhage and Infarcts
Progressive cognitive decline since the age of 62

Cerebral Amyloid Angiopathy (CAA)
CADASIL: Typical imaging findings

- Multifocal and bilateral FLAIR/T2 hyperintensities in the periventricular and deep white matter
- External capsule lesions
- Microhemorrhage in SWI and T2*
- Focal T1 hypointensities
- Anterior temporal lobe lesions
♂, 72 years old, progressive cognitive decline, gait disorders, impairment of bladder control
On examination: major cognitive impairment, parkinsonian syndrome prevailing in lower limbs

NPH (Normal pressure hydrocephalus)
NPH (Normal pressure hydrocephalus)

**EVANS Index**
- 0.30 to 0.33
- Variable for localisation and angle of section
- Not specific

**Corpus callosum angle**
- 50–80° vs hydrocephalus ex vacuo (100–120°)

DESH, the combination of high-convexity tightness, Sylvian fissure dilation, and ventriculomegaly, increasingly recognized as a neuroimaging hallmark of iNPH.
Approach to signal change assessment in cognitive impairment

- MR artefacts: flow voids, signal from temporal bones
- T2* hypointensity?
- FLAIR/T2 hyperintensity?
- Located in cerebral WM?
- Strategic location?
- Thalamus (bilaterally)
- VCI due to large vessel disease
- VCI due to small vessel disease
- Multifocal/confluent hyperintensities affecting >1/4 of the total WM?
- WMH of presumed vascular origin
- Located in deep GM (basal ganglia including thalamus)?
- Subcortical hyperintensities of presumed vascular origin
- AND/OR
- Located in deep GM including thalamus?
- Central CSF signal and rim of hyperintensity on FLAIR
- Lacune of presumed vascular origin
- AND
- Temporal pole involvement?
- VCI due to small vessel disease
- Infection, inflammatory demyelinating disease, leukodystrophy or leukoencephalopathy
- Territory of a single deep perforating artery?
- Recent small deep brain infarct
- Subcortical infarcts and leukoencephalopathies
- Cerebral arteriosclerotic dominant arteriopathy with subcortical infarcts and leukoencephalopathies
- CJD: Creutzfeldt-Jakob disease
- GM: Grey matter
- VCI: Vascular cognitive impairment
- WM: White matter
- WMH: White matter hyperintensities

CAA: Cerebral amyloid angiopathy
CADD: Cerebral autosomal dominant arteriopathy

| Global atrophy with hippocampal atrophy | Global atrophy with relatively preserved hippocampi DLB – diffuse neocortical | Asymmetric atrophy involving whole hemisphere bvFTD (PGRN) – TDP43A | Parietal/occipital atrophy PCA – AD Braak stage VI | Temporo-parietal atrophy, L>R LPA – AD Braak stage VI |
| Severe and focal anterior medial temporal atrophy bvFTD – Tau MAPT | L>R temporal lobe atrophy Semantic FTD - TDP43C | Asymmetric (L>R) frontal and temporal atrophy bvFTD – FUS aFTLDU | Asymmetric (R>L) MTL atrophy bvFTD – Tau Pick’s | Frontal lobe atrophy bvFTD – Tau Pick’s |
| Atrophy of the frontal gyrus/insula, L>R PNFA – Tau Pick’s | “Hummingbird” appearance of sagittal midbrain PSP – Tau PSP | Confluent hyperintensities in temporal poles CADASIL | Cortical-subcortical CMBs on T2+ *CAA | Hyperintensity in cortex and basal ganglia on DWI CJD – iatrogenic CJD |
Conclusion

• Large *panel of imaging assessments* for a large spectrum of diseases

• Need for a *systematic* (Gray matter, White matter, vascular, CSF) vs *adapted* strategy (use of visual scales, use of sequences,..) for both Clinicians and Radiologists

• Expending imaging findings and imaging techniques
  ➔ Need to keep « informed » (*updates and basics*)
Thank you for your attention