Clinical MRI and ASL patterns in AD

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Aging and dementia: grey and white matter involvement

MRI, FDG-PET, and ASL

- FDG-PET relates to local metabolism of the synaptic terminals at the neuron-astrocyte functional unit
- ASL regional CBF is coupled with metabolism
ASL regional CBF and DMN

- The default mode network is a group of structures/regions coupled together (hypermetabolic) during resting activity and introspection.
- DMN relates to ASL regional CBF.
- Facilitating role in plaque deposition and damage?

Aims/Structure

- Aging and Dementia
- Role of imaging in dementia
- Imaging in AD
- Morphology and function
  - MRI
  - PET, ASL
- ASL patterns in AD
- Atypical forms of AD:
  - Presenile AD
  - Posterior cortical atrophy
- Biomarkers

Aging, imaging and dementia
• Successful aging
• Need to understand aging process
  – structure
  – function
• Modifiers
• Differences from pathology

R.A. Sperling et al. / Alzheimer’s & Dementia (2011) 1–13

The continuum of Alzheimer’s disease

Aging
MCI
Prodromal AD
AD
Cognitive decline
Memory
NRI Biomarkers

R.A. Sperling et al. / Alzheimer’s & Dementia (2011) 1–13
Postmortem studies of aging

- Reduced weight and volume, ventriculomegaly and sulcal prominence
- Loss of neurons in the neocortex, hippocampus, and cerebellum
- Loss of myelin in subcortical white matter
- Rarification of vessels
- Reduction of synaptic density, and loss of dendritic spines
- Global and focal
- Chronological stages

Aging Brain: Imaging findings

- Global volume loss
  - Enlarged sulci and ventricles
  - Decrease in WM
- Basal Ganglia and WM hyperintensities
  - Periventricular
  - Subcortical
  - Corona radiata
- Microbleeds
- T2 Hypointensities (Iron deposition and Striatonigral system)

Cortical thickness in aging

Correlation map; FreeSurfer: r = -0.320; p = 0.04

FDG-PET in aging

- There is no change in PCG/precuneus metabolism with aging.
- Normal aging is characterized by brain glucose metabolism decline predominantly in the prefrontal cortex.
- Metabolism decline in the elderly predominates in the left inferior frontal junction (LIFJ).
- LIFJ hypometabolism is associated with macrostructural and microstructural WM disturbances in long association fronto-temporo-occipital fibers.


ASL patterns in aging

- ASL perfusion patterns demonstrate age-related changes in perfusion signal.
- Pediatric patients in the 5-15 year old range demonstrate high perfusion values.
- Adults demonstrate a gradual age-related decline in brain perfusion.
- The use of bipolar crusher gradients can have an effect on perfusion patterns in elderly subjects.
- In aged subjects, the anterior and posterior watershed territories are frequently hypoperfused because of prolonged transit times in these regions.


Role of imaging in dementia
Changing role

• From exclusion of:
  – Treatable diseases
  – Reportable diseases:
    – Prion disease

• To specific antemortem diagnosis

Neuroimaging in dementia

• Current guidelines recommend imaging
• Imaging is not 100% specific
• Diagnosis of a specific cause of dementia can only be confirmed by brain biopsy or postmortem
• Imaging may be more specific than clinical/psychometry
• This is particularly the case for quantitative and functional imaging
  – Combined approach

Neuroradiology in dementia

Clinical practice / Research

• CT/design MR protocol (3D T1-w, T2-w, DWI)
• Treatable causes
• Reportable causes
• Structured reporting approach:
  – Volume loss?
  – Pattern?
  – Specific brain regions
  – Infarcts, WMH, microbleeds?
  – Scales for MTL and WM

• MR is not able to predict AD on an individual basis
• Biomarkers may be identified
Imaging in AD

- In 2007, Dubois proposed a revision of the NINDS-ADRA criteria, to include supportive neuroimaging/CSF
- Neuroimaging biomarkers for AD are:
  - Hippocampal atrophy
  - FDG-PET hypometabolism
- Revised criteria for AD 2011 place imaging at center stage in clinical practice and drug development

Ageing and Aged Care Unit, Australian Institute of Health and Welfare, 2010 (Evon Bowler)

<table>
<thead>
<tr>
<th>Dementia type</th>
<th>Number</th>
<th>Per cent</th>
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<tr>
<td>Alzheimer's disease</td>
<td>79,300</td>
<td>76%</td>
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<tr>
<td>Vascular dementia</td>
<td>10,500</td>
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<tr>
<td>Other dementias</td>
<td>8,650</td>
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<td>Dementia in other diseases</td>
<td>4,200</td>
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<tr>
<td>Mixed dementia (any combination)</td>
<td>1,800</td>
<td>1.7%</td>
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<tr>
<td>Total</td>
<td>104,400</td>
<td>100%</td>
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</table>

Uses higher level ACAP dementia codes
Based on ICD-10-M and comparable with SDAC codes
Pathology in AD/MCI

Neurofibrillary tangles
Amyloid plaques

Distribution of tangles and plaques in AD

Selective vulnerability in AD

Entorhinal cortex
Hippocampus
Amygdala

Temporal pole
Posterior parahippocampus
Cingulate
Dorsolateral frontal cortex
Insula

Lateral temporal lobe
Dorsolateral frontal lobe
Parietal lobe

Enthorinal thickness AD vs Controls


P<0.05

Typical imaging findings in AD


Healthy; CI 70 yo

57 yo AD patient

Typical ASL maps in AD

Metabolic important areas on FDG-PET

- PCG/precuneus, posterior parietal, lateral frontal cortex hypometabolism
- MTL hypometabolism is less consistent
- FDG-PET 85% sensitivity and specificity for AD diagnosis


Typical involvement on PET in AD

- Temporal poles
- MTLs (hypo or hyperperfusion?)
- PCG/Precuneus (‘bright spot’)
- Temporo-parietal cortex (holes)
- Frontal cortex

Perfusion important areas on CBF-ASL
Direct comparison of FDG-PET and ASL

- Regional abnormalities in AD are similar
- Comparable sensitivity and specificity for AD diagnosis on visual inspection of maps
- Both global uptake or whole brain blood flow show good diagnostic accuracy
- ASL CBF<32 had high S/S


Limitations of ASL maps

- Frontal hypometabolism in ASL is less profound (contradictory results)
- ASL maps more likely to be influenced by vascular disease (stenosis)
- Posterior cortical hypoperfusion and watershed?
- Inferior temporal difficult
- Conflicting results in the hippocampi (hyperperfusion due to compensatory mechanisms?)


Mild Cognitive Impairment
Prodromal AD
AD

MR Biomarkers:
- Global and focal atrophy
- Progressive brain atrophy
- Cortical thickness measurements
- MRS, DWI/DTI, fMRI

Cognitive decline: Memory domain
Volumetrics on structural MRI

Y. Xu et al. Neurology 2000; 54:1760-1767

Hippocampal volumes in MCI
Semiautomated segmentation method (ITK-SNAP)


R.A. Sperling et al. / Alzheimer's & Dementia- (2011) 1–13
Clinical Case: 78 yo woman, with a 3 years’ history of language problems, and more recent memory impairment.

Clinical diagnosis: MCI / early AD

- On 3D-MPRAGE, mild bilateral, asymmetrical TP (L>R) volume loss, and intact PCG/precuneus
- ASL shows bilateral, asymmetric (L>R) temporo-parietal hypoperfusion
- PET shows a similar pattern of involvement as ASL. Intact PCG/precuneus

Beta-Amyloid Imaging: PET & PIB

Specific/atypical AD patterns
- Presenile AD
- PCA
- Frontal AD
Presenile AD

Posterior cortical atrophy: case 1

Case 1: 61 yo woman, started with 55 y having impairment in visuospatial tasks, in grasping and manipulating objects. Posteriorly, impairment in all cognitive domains.

Initial NPs: Altered episodic and semantic memory, nomination, and constructive and visuospatial praxias. MMSE 20/30.
Clinical case

- 4 years of visual recognition impairment, then behavioural problems (divorce)
- More behavioural problems, finally frontal (language) and memory impairment
- Initially thought to be frontal MCI
- After 2 years of deterioration, PIB-PET +, diagnosis of PCA

Frontal AD
**Neuroradiology in dementias**

- Increasing role of imaging in dementia
- Integrative approach: MRI, FDG-PET, ASL
- Specific needs for:
  - Incorporation of postprocessing tools
  - Handling large amounts of data (variables)
  - Automated classification tools

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