Brain White Matter Lesions are part of the burden of ageing with measurable effects on cognition

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Summary of presentation

• Age-related cognitive decline
• The Scottish Mental Surveys 1932 & 1947
• Brain imaging – MRI atrophy
• Brain imaging – White matter lesions
• “brain burden” and cognitive ageing
• Cognitive reserve: theory and applications
Terminology

cognition

age

threshold

load

cognitive reserve

cognitive aging

?
Which mental tests?

cognitive abilities do not age independently

cognition

Age 25

Age 75

fluid

crystalised

examples:

language

culture

examples:

memory

problem solving

AGE
Do cognitive abilities age differently?

Data from Pushkar-Gold et al, 1995
Structural model of the effects of age on different cognitive abilities

Data from Deary et al, 2004
The Scottish mental Surveys of 1932 and 1947

tested 95% eligible children

born in 1921 or 1936

1932:- 89,498 tested
1947:- 70,532 tested

results archived by
Scottish Council for Research
In Education
Pupils of Skene Street Primary School, Aberdeen 1932
Study design: MRI scans
Analysis 1936: Investigating extremes

Individuals doing less well than expected: Decliners

Individuals doing better than expected: Sustainers
Age related pathological changes

- Brain atrophy measured using the T1W MR images by calculating the brain fraction (BF)

- The ratio of parenchymal brain (PB) to total intra-cranial volume (TICV) used to measure brain atrophy

Rudic RA et al. *Neurology* 1999. 53;1698-1704
Brain imaging and mental decline in old age

<table>
<thead>
<tr>
<th>Shrinkage</th>
<th>brain cavity expands with brain growth, but remains fixed when brain shrinks</th>
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</thead>
<tbody>
<tr>
<td>Lesions</td>
<td>brain lesions accumulate with age, then impair brain function</td>
</tr>
<tr>
<td>Function</td>
<td>failing brains work harder to maintain function (early)</td>
</tr>
<tr>
<td></td>
<td>failing brains function less well (late)</td>
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</tbody>
</table>
Brain volumes

- Segmented into grey (GM) white (WM) and CSF
- TICV = GM + WM + CSF
- PB = GM + WM
- BF = PB / TICV

SPM99. FIL, ION, University of London
Lesions: white matter hyper-intensities

- Assess visually by 3 observers using the Fazekas scale
  0 normal
  1 punctate
  2 coalescing
  3 confluent
Possible pathogenesis

- WML - ischaemia, small vessel disease
- PVL - altered CSF dynamics

White matter lesions…not so easy

• Frequent finding on T2W MRI in older subjects
• Many names (hyperintensities, lesions, UBOs etc.)
• Varying reports of relationship with cognitive function\(^1,2\)
• Concept of “vascular cognitive impairment”\(^3\)
• White matter (WML) v periventricular (PVL) lesions
• Variety of MRI rating scales

WML associations in elderly cohort

- Impaired fluid intelligence\(^1\)
- Impaired balance and gait\(^2\)
- Account for 13% of cognitive variance in old age\(^3\)
- Independent of childhood intelligence\(^3\)
- Associated with hypertension, impaired respiratory function and elevated glycated haemoglobin\(^4\)

Measurement of brain “burden”

• 356 with MRI (ABC21-107; ABC36 - 248)

• T1W 3D volumetric acquisition of whole brain – measures brain volumes

• T2W axial images – measures white matter changes

Coffey et al Neurology 1999; 53:189-96
Leaper el al Radiology 2001; 221:51-5
Murray et al. Radiology 2005; 237(1); 251-7
White matter abnormalities and lifetime cognitive change

White matter lesions

hypertension

reasoning

memory

mental speed

verbal fluency

cognitive ability age 77

IQ age 11

Deary et al, Psychol Aging 2003, 18:140
A brief history of “reserve”

- First proposed by David Kay in 1964
- Many synonyms
- Explains lack of direct relationship between brain pathology and clinical manifestation
- Various proxies of reserve - intelligence, brain size, education, occupational complexity
- May explain individual differences in rates of progression to AD

Models of reserve

• **Passive** - capacity to withstand a greater burden of detrimental pathology before cognitive deficits appear

• **Active** - ability to overcome detrimental pathology using alternative cognitive paradigms and/or recruiting compensatory neuronal pathways

Hypothesis

• a proxy of ‘reserve’ should account for significant variance in old age intelligence, after adjusting for factors known to influence old age cognitive ability
Testing the reserve hypothesis

- Pre-morbid ability
- Burden
- Old age ability
- Reserve
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