Imaging biomarkers for dementia research and clinical practice

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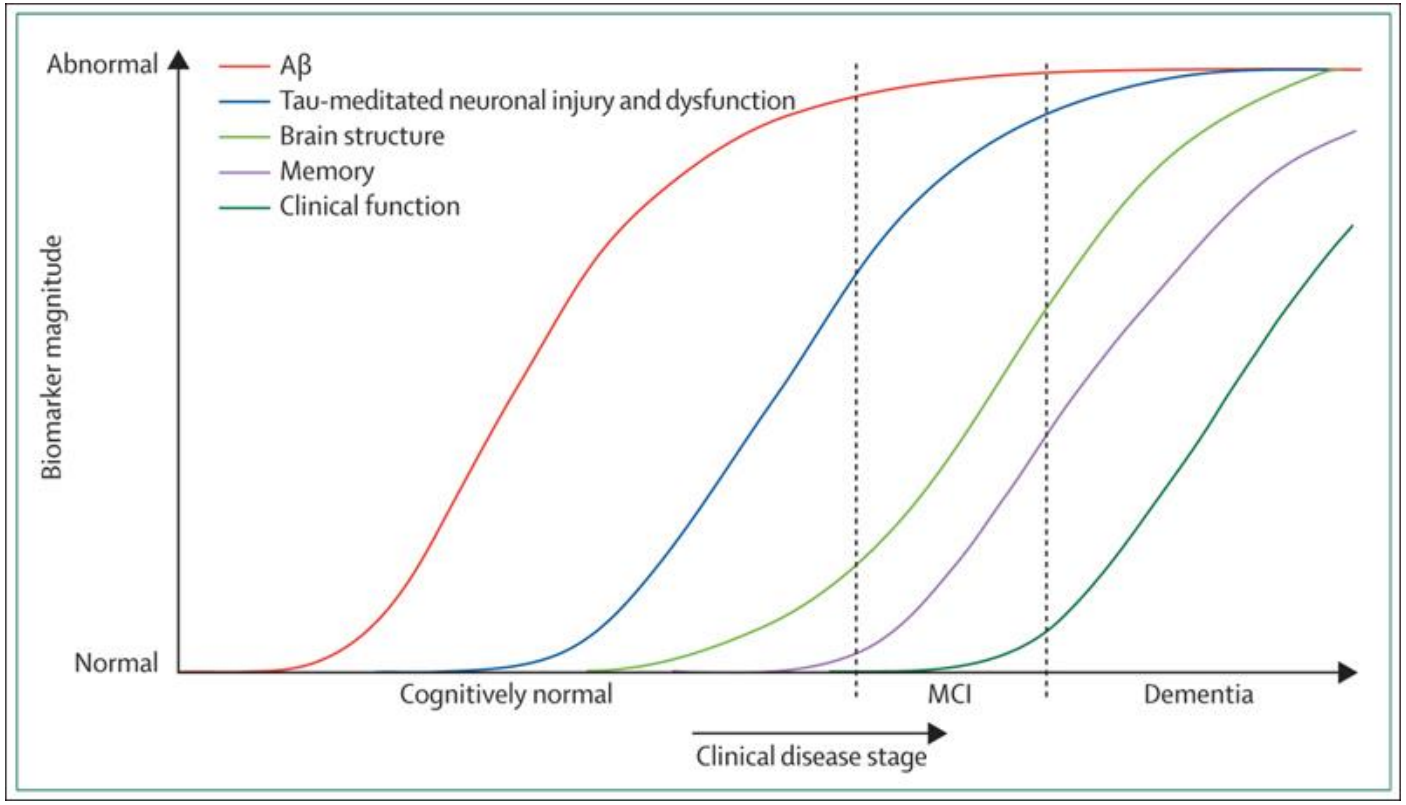
Pre-clinical markers

- G8 Dementia Summit pledge: “Cure or disease modifying therapy by 2025”
- Dementia is an umbrella term for a group of diseases with distinct pathological substrates
- Neuropathology already well advanced by diagnosis
- Neuroprotection likely to be pathology specific
- Urgent need for biomarkers sensitive to earliest changes

Imaging is an essential tool in the early diagnosis and experimental medicine armory

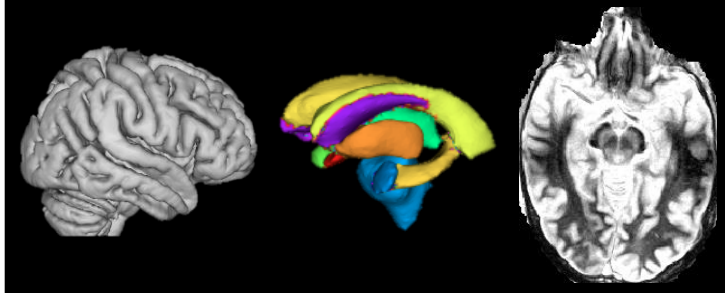


Jack et al, 2010

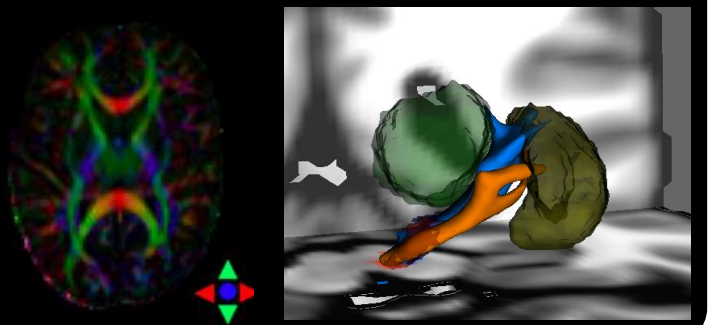
State-of-the-art MRI

FMRIB

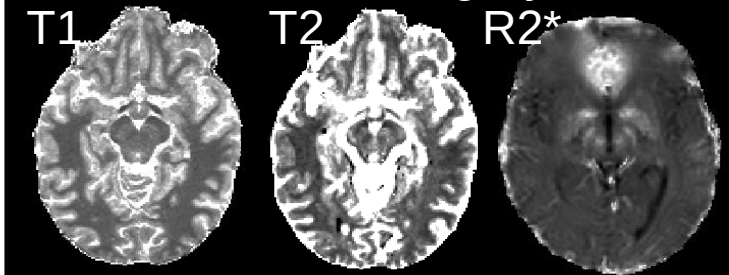
Brain structure



White matter connectivity

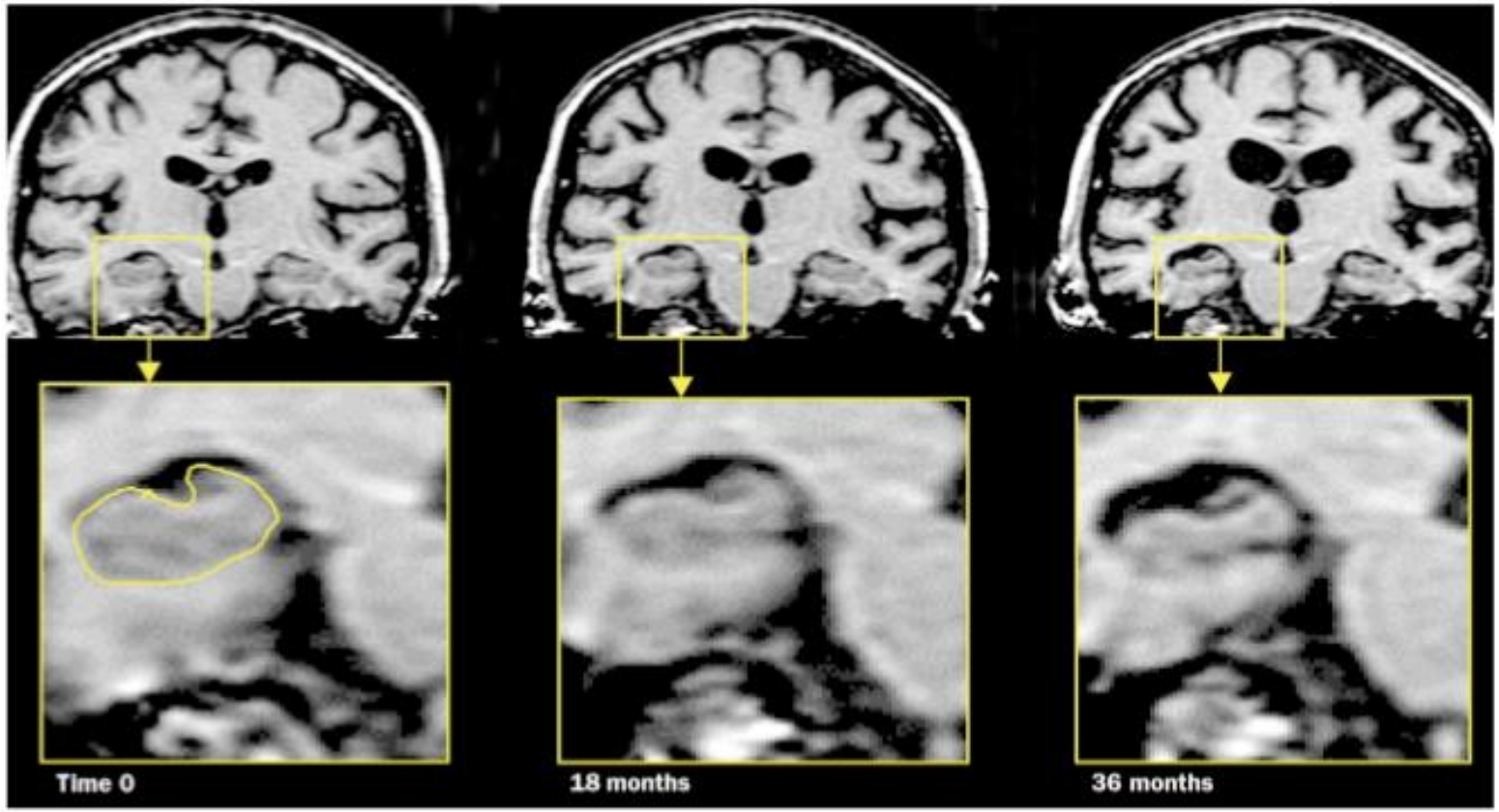


Tissue integrity



Functional MRI

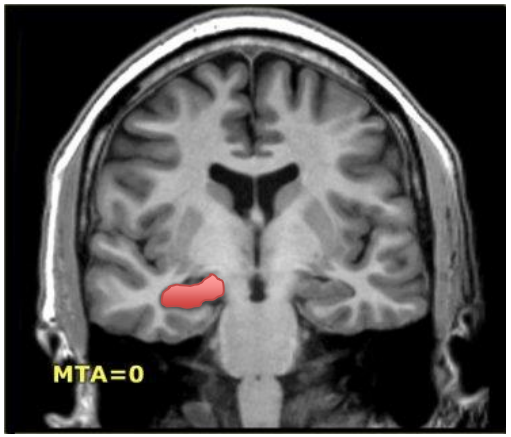
Imaging markers

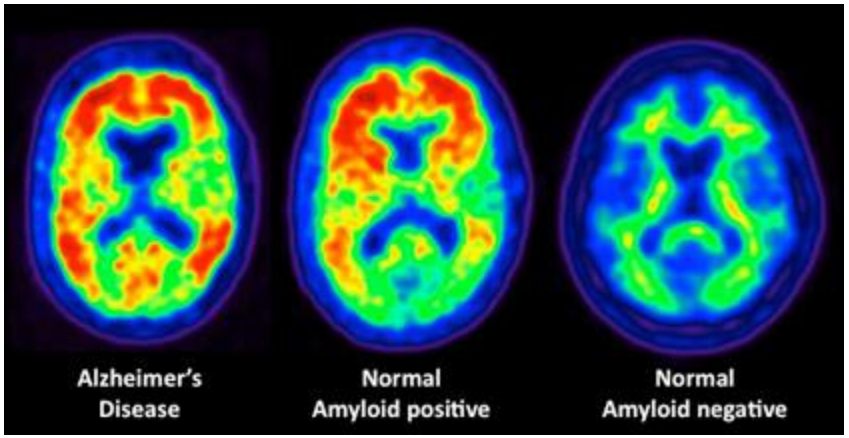


Scheltens et al, Lancet Neurology, 2002

Imaging markers

- Established markers:
  - Hippocampal volumetry
  - Amyloid PET
- Novel markers
  - Functional imaging
  - DTI
  - ASL
  - Tau PET





Statistical challenges for neuroimaging in dementia

1. Scaling up to large scale epidemiological studies
2. Image-space vs derived variables – combining variables
3. Multi-modality – extracting the maximum discriminative power
4. Translation – logistical barriers to the translational pathway
5. Cost-benefit – how can we make the health economics case for advanced imaging?

1) Scaling up

- Whitehall II Imaging sub-study (PI: Klaus Ebmeier)

(N=800)

- biobank uk
  Improving the health of future generations

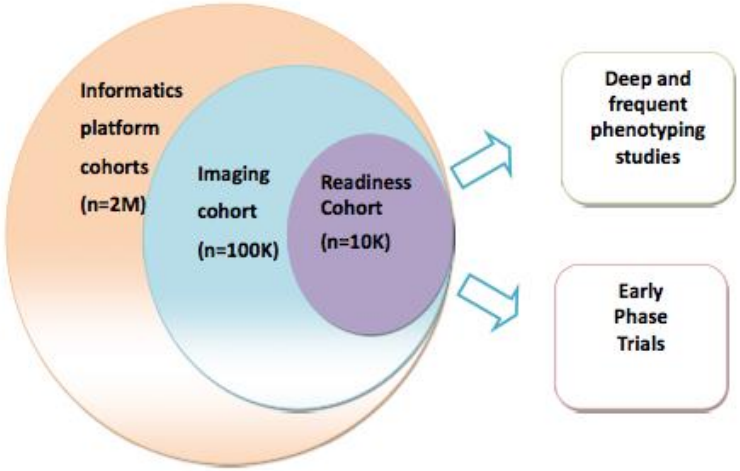
(Neuroimaging lead: Steve Smith)

(N=10,000)

- MRC UK Dementia Platform

  (PI: John Gallacher, Cardiff)

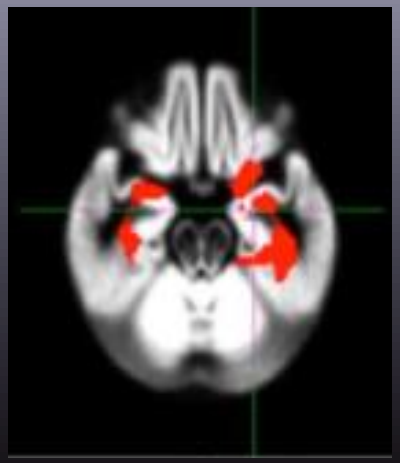
(N=2M)

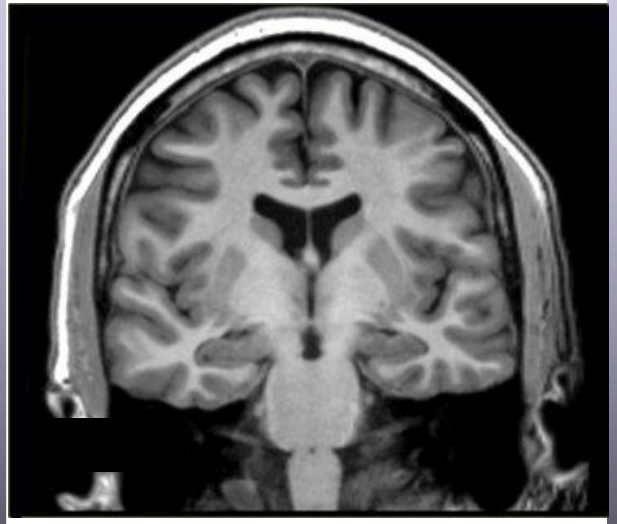


2) Imaging statistics

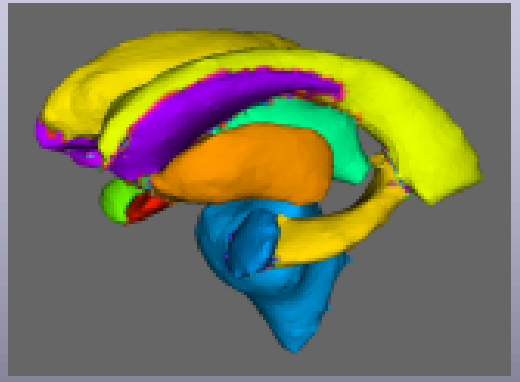
Automated analysis

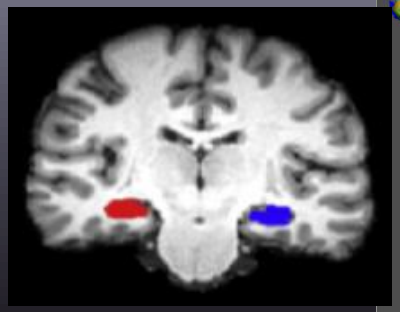
Voxel based morphometry (VBM)

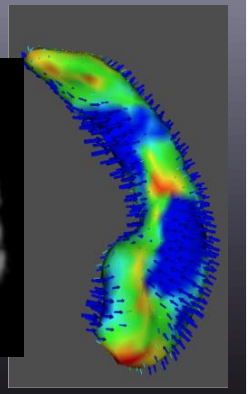




FIRST Automatic segmentation

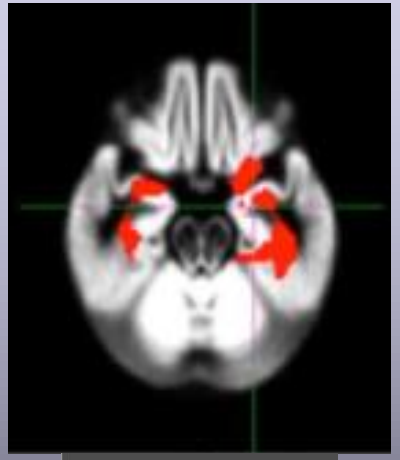


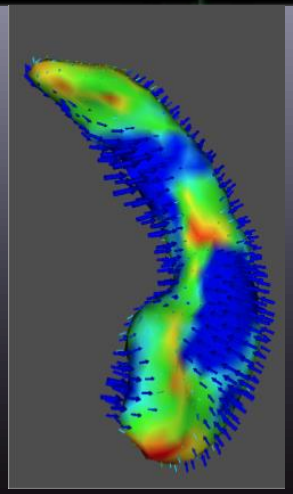




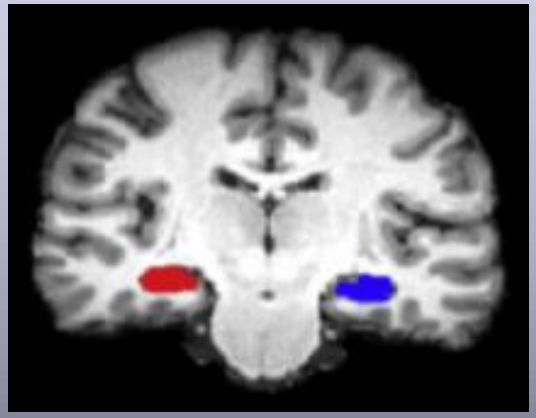
2) Imaging statistics

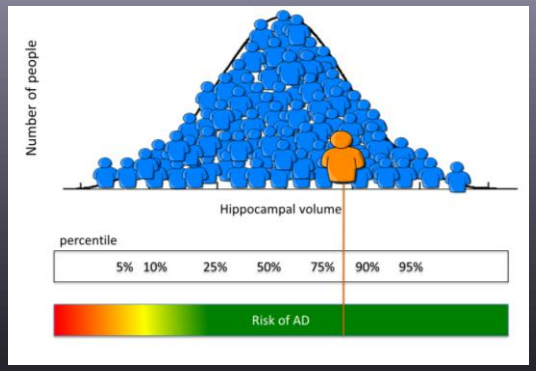
Image space



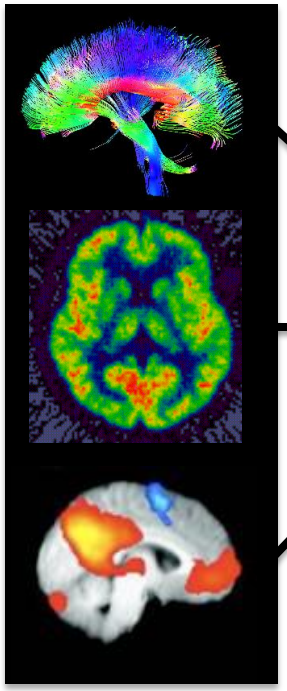


Extracted variables





3) Multivariate integration



Wellcome Trust Strategic Award

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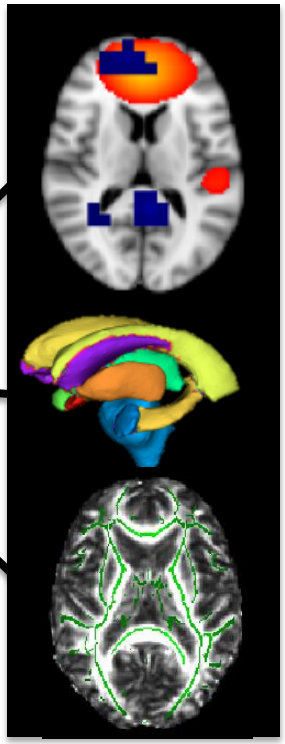
(PI: Steve Smith)

FMRIB OHBA Donders Institute



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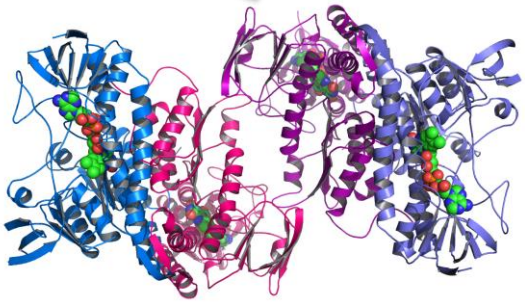
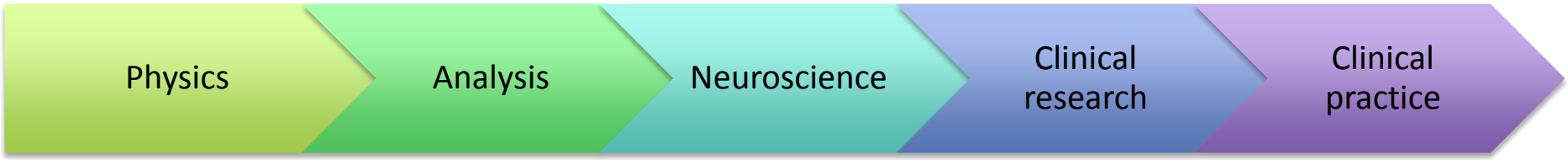


4) Barriers to translation



Clinical research

- Replication
- Clinical correlation
- Establish normal variation
- Establish stability
- Establish cut-offs
- Validation (inc cross-scanner)
- Creation reference database
- Establish QC routines (acquisition and analysis)
- Simplify/refine methodology
- Generate meaningful report
- Education
- Roll out to specialist centres
- Roll out to NHS

Clinical practice

5) Health economics

Memory clinic imaging

- CT ~ £150, but information so limited its use is in jeopardy
- MRI ~£300
- PET ~£2.5K
- Early, accurate diagnosis makes minor difference to current care pathways

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