Dementia

Introduction
We need to talk about memory
“Short term memory”

• Like “dizziness” – not a technical term

• Working memory
  – “The filing clerk”
  – Manifests as difficulties with attention and concentration
  – (Information never gets into the filing cabinets)

• Hippocampal memory
  – “The filing cabinets”
  – Longer term
  – Difficulty learning new information
  – Rapid forgetfulness (over minutes)
  – Repetitive questioning (after minutes)
• 1 in 20 people over 60 have a diagnosis
• 1 in 5 people over 80
• UK dementia: 800,000 people (Alzheimer's society, 2012)
• Around 2/3 people with Dementia are cared for at home
• Dementia mainly affects people over the age of 65 and the likelihood increases with age
• However, it can affect younger people: THERE ARE OVER 17,000 PEOPLE IN THE UK UNDER THE AGE OF 65 WHO HAVE DEMENTIA (Alzheimer's society, 2012)
Dementia

• Umbrella term
• Does not presume aetiology
• Subtypes important(-ish)
  – Why?
Anatomical subtypes

• Cortical
  – Cortical stroke
  – Alzheimer’s
  – D.L.B.
  – F.T.D.

• Subcortical
  – Subcortical stroke
  – Subcortical Vascular Disease
  – M.S. (caveats)
  – Huntington’s
  – AIDS Dementia Complex
Anatomical subtypes (deficits)

- **Cortical**
  - Memory
  - Language
  - Vision (PCA)

- **Subcortical**
  - Slow but accurate processing
  - Less language
  - Arguably more subjective impairment
By timecourse

- Acute
- Subacute
- Chronic

Intellectual Function

- Normal pressure hydrocephalus
- Creutzfeldt-Jakob
- Encephalitis
- Alzheimer's disease
Alzheimer disease

• Insidious decline
• No other cause
• Often insightless
Alzheimer disease 2011 consensus criteria

• 2 notable differences from the AD criteria published in 1984
  – incorporation of biomarkers of the underlying disease state
  – formalization of different stages of disease in the diagnostic criteria.
• much additional work is needed to validate the application of biomarkers for diagnostic purposes.
• a semantic and conceptual distinction is made between AD pathophysiological processes and clinically observable syndromes that result, whereas this distinction was blurred in the 1984 criteria.
The continuum of Alzheimer’s disease

- Cognitive function
- Aging
- Preclinical
- MCI
- Dementia

Hypothetical model of AD pathophysiological cascade

- Age Genetics
- Cerebrovascular risk factors Other age-related brain diseases

- Amyloid-β Accumulation
- Synaptic Dysfunction Glial Activation Tangle Formation Neuronal Death

- Cognitive Decline

- Brain and cognitive reserve ? Environmental factors
Stage 1
Asymptomatic amyloidosis
- High PET amyloid tracer retention
- Low CSF Aβ₁-₄₂

Stage 2
Amyloidosis + Neurodegeneration
- Neuronal dysfunction on FDG-PET/fMRI
- High CSF tau/p-tau
- Cortical thinning/Hippocampal atrophy on sMRI

Stage 3
Amyloidosis + Neurodegeneration + Subtle Cognitive Decline
- Evidence of subtle change from baseline level of cognition
- Poor performance on more challenging cognitive tests
- Does not yet meet criteria for MCI

MCI ➔ AD dementia
The FTD spectrum shares proteinopathies and anatomic loci

- Behavioral Variant FTD
- PPA-S (semantic variant)
- PPA-G (Nonfluent/agrammatic variant)
- PPA-L (logopenic variant)

FTLD-TDP43
- Frontal/ventral Temporal lobe
- FTLD-Tau (3R), FTLD-TDP43
- Prefrontal lobe, Temporal lobe

FTLD-FUS
- Cortex, Motor neurons

TDP43, SOD1, FUS
- Upper, lower MNs

ALS

FTLD-Tau
- More than FTLD-TDP43 or AD pathology

AD pathology
- More than FTLD-Tau or TDP43
- Left post/supr temporal lobe & Medial parietal

Progressive Supranuclear Palsy
- FTLD-Tau (4R)
- Basal ganglia, Brainstem

Corticobasal Syndrome
- FTLD-Tau (4R)
- Frontal, temporal lobe, Basal ganglia

ALS

Motor Neuron Disease/ALS
A Spectrum of Genetic Causes: Estimated 50% of all FTD have a hereditary component *

* C9ORF72, GRN, MAPT are the most common gene mutations
Dementia with Lewy Bodies

- Very very similar disease process to Parkinson’s disease
- In DLB, the cognitive deficit has simply come first
- In PD, age is the best predictor of PD dementia
- Lewy body disease presenting first with motor or cognitive symptoms?
Dementia with Lewy Bodies

• Core features
  – Fluctuating cognition with pronounced variations in attention and alertness.
  – Recurrent complex visual hallucinations, typically well formed and detailed.
  – Spontaneous features of parkinsonism.
Dementia with Lewy Bodies

Suggestive

- REM sleep behavior disorder (RBD), which can appear years before the onset of dementia and parkinsonism.
- Severe sensitivity to neuroleptics occurs in up to 50% of LBD patients who take them.
- Low dopamine transporter uptake in the brain's basal ganglia as seen on SPECT and PET imaging scans.
Dementia with Lewy Bodies

Supportive features

• Repeated falls and syncope (fainting).
• Transient, unexplained loss of consciousness.
• Autonomic dysfunction.
• Hallucinations of other senses, like touch or hearing.
• Visuospatial abnormalities.
• Other psychiatric disturbances.
DLB Cognitive profile

• Early:
  – Nonspecific difficulties in attention and concentration
    • Working memory
      – Serial subtraction
      – Learning curve / address repetition

• Later:
  – More impairment evident in the domains of visuospatial function
    • Clock drawing
    • Cube copy
    • RBANS / Rey Osterreith