The human brain

- 100 billion neurons
- The most complex organization of matter known
- 80% water
An Italian

Camillo Golgi

- Physician & scientist
- In 1872 he discovered neurons were stained with silver
A Spaniard

Santiago Ramón y Cajal
• Utilised Golgi’s stain very effectively
• The father of neurobiology
Nobel prize-winners (1906)

Camillo Golgi  Santiago Ramon y Cajal

For their work on the structure of the nervous system
Two Germans

Frau Auguste D (51 years)

Alois Alzheimer
“A peculiar disease of the cerebral cortex”
Alzheimer’s disease vs senile dementia

- Alzheimer's disease was thought only to affect individuals less than 65 years.
- Senile dementia was regarded as a ‘natural consequence’ of old age.
- But John Corsellis and Bernard Tomlinson showed plaques and tangles in demented individuals of both age groups.
- Incidence of AD increases with age:
  - 10% of those >65 years
  - 49% of those >80 years
There will be more people aged >65 years in the decades ahead

<table>
<thead>
<tr>
<th></th>
<th>1950</th>
<th>2000</th>
<th>2050</th>
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</thead>
<tbody>
<tr>
<td>Number &gt;65 (millions)</td>
<td>131</td>
<td>419</td>
<td>4,419</td>
</tr>
<tr>
<td>% of total population</td>
<td>5</td>
<td>7</td>
<td>16</td>
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<tr>
<td>Life expectancy</td>
<td>47</td>
<td>67</td>
<td>77</td>
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What are the symptoms of AD?

- Progressive impairment of memory
- Non-cognitive changes
  - Anxiety
  - Depression
  - Wandering
  - Impulsive behaviour

It is non-cognitive changes in behaviour that usually lead to institutionalisation of patients.
The cholinergic story

- Reduced ChAT activity
  - Bowen et al 1976
  - Davies et al 1976
  - Perry et al 1976

- Loss of cholinergic cell bodies
  - Whitehouse et al 1982
  - Arendt et al 1983

- Reduced ACh synthesis
  - Sims et al 1983
Pharmacotherapy of Alzheimer’s disease: progress & prospects

• Symptomatic therapy
  – AChE inhibitors
    • Rivastigmine
    • Donepezil
    • Galantamine
  – NMDA receptor antagonist
    • Ebixa (Memantine)

• Disease-modifying therapies
  – Amyloid metabolism is the main target