The Diabetes-Alzheimer’s disease Connection and Targeting Beta Amyloid Production

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Understanding Alzheimer’s disease and how risk factors promote disease progression.

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Alzheimer’s Disease progression occurs over decades

- Early diagnostic biomarkers
- Lifestyle modification
- **How risk factors promote disease progression.**
- Greater understanding of disease mechanisms and drug targets

Disease Modifying Strategies

- Tau Accumulation
- Neuroinflammation
- Beta amyloid accumulation
- Neuron Dysfunction
- Neuron Death
- Brain Atrophy
- Memory Impairment
- Reduced Clinical Function

Current treatments

“Temporary cognitive stabilisers”
Most common form of Diabetes and a chronic progressive disease commonly characterized by insulin resistance and high blood glucose levels.

Currently 415 million people have Diabetes-world wide (1 in 11 of world adults). Predicted to increase to 642 million by 2040.

Currently 1.7 million Australians with Diabetes at an annual cost of $6 billion.

6th Leading cause of death in Australia

Type 2 diabetes doubles the risk of developing dementia.
Brain Atrophy (shrinkage) in patients with type 2 diabetes

Geert Jan Biessels and Yael D. Reijmer, Diabetes 2014;63:2244–2252
Brain Changes Underlying Cognitive Dysfunction in Diabetes: What Can We Learn From MRI?
Insulin resistance is associated with early changes in cognition and AD pathology

Insulin Resistance associated with:

• Reduced Verbal Memory (Memory of events, recall of word lists)
• Reduced Executive Function (Organizational skills, Decision making).
• Reduced Global Cognition
• Increases in “abnormal” pTau

When does insulin resistance impact on cognitive functioning and the progression to AD?

Miss Amy Woodfield
A/Prof Simon Laws
Dr Tenielle Porter

The Type 2 Diabetes-AD connection

- Chronic diseases with slow progression
- Type 2 Diabetes increases risk of cognitive decline and Dementia
  - Brain atrophy (shrinkage)
  - Amyloid deposition
- Type 2 Diabetes promotes AD pathology (amyloid beta and Tau)
  - Inflammation
  - Impaired Metabolism
  - Insulin resistance
  - Lifestyle Risk Factors
Understanding how Type 2 Diabetes and AD are connected

**AD**

Pathology (Aβ/Tau)
- Loss of neuron connections
- Neuron Death
- Cognitive Dysfunction

- Reduced Insulin to the Brain
- Reduced ability of the brain to respond to insulin.

**Type-2 Diabetes**

- Body Insulin Resistance
- Reduced Insulin levels

**Beta amyloid /Tau**

- Reduced Insulin to the Brain
- Reduced ability of the brain to respond to insulin.

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**Speakers**

- Mrs Joanne Rowles
- Prof. Paul Fraser (University of Toronto)
- Prof. Ralph Martins (ECU/Macquarie University)
- Professor Philip Newsholme (Curtin)
- Dr Kevin Keane (Curtin)

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**Body Insulin Resistance**

- Reduced Insulin levels

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**Professionals**

- Miss Amy Woodfield
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Current treatments
“Temporary cognitive stabilisers”

Miss Melissa Eccles
Targeting Beta
Beta Amyloid Production

Message passed between healthy brain cells

Beta Amyloid prevents message passing across brain cells in Alzheimer’s

Long beta-amyloid builds up

Short beta-amyloid is protective

Enzyme cuts in different positions
Targeting Beta Amyloid Production

‘Handles’ determine long vs short

Long vs Short

Project goal:
Identify optimal drug targets to reduce long beta-amyloid