Investigation of genes involved in Alzheimer's disease in a case-control population in the Illawarra region

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Alzheimer Disease = world looming epidemic

- 2006 = More than 26 million of Alzheimer disease (AD) cases in world
- 2040 = Estimation of 106 millions AD people
- Currently 200,000 people with dementia in Australia

Real socio and economic challenges for the society
Loss of productivity = **5.6 billion** in 2002
including 3.2 billion direct health costs

Real burden for society

AD sufferers

Family carers

University of Wollongong
What is AD?

- Neurodegenerative disease
- β amyloid plaques + Neurofibrillary Tangles (NFT) in brain
- Leads to cognitive disturbances
- Impairments in behavior and decline in daily living activities

No cure available

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Causes of AD

- Still unknown albeit extensive researches

- 2 major risk factors:
  - age: + 65 years old
    50% if over 85 years old
  - family history (genetic)

- Other risk factors: head injuries, cardiovascular disease, stroke
AD genetics

- 2 forms of AD =
  * early onset (between 30 to 60 years old)
    - rare form of AD ≥ 5% AD cases
  * late onset (after 60 years old)
    - called common form of AD

- two different set of genes involved
Late onset AD genes

- ≥ 500 genes proposed as “genetic risk factors”
- Only one “risk factor gene” validated: Apolipoprotein E (APOE) gene
  - APOE protein involved in cholesterol transport
  - 3 APOE alleles: -APOE2: very rare
    - -APOE3: most common, neutral AD
    - -APOE4: 40% of AD sufferers

Mechanism for implication of APOE in AD still unknown
Currently still no gene available for diagnostic purpose
AD diagnosis so far...

- no single test – except when autopsy
- Imaging (MRI, PET scan) $$$
- Cerebro-spinal fluid (CSF) analysis
- Medical history, neurological evaluation (memory and mental tests etc...)

late stage diagnostic
Identify genes involved in late onset AD form using gene expression array technology in cases vs. controls population.

Gene analysis from patients at 3 different stages of AD:
- early dementia (mild) n=12
- moderate dementia n=12
- advanced dementia (severe) n=12

Correlate genetic study with complete aging profile (lifestyle, mental and cognitive tests etc..)
Gene expression array

- Extraction of material genetic extraction from saliva of 4 groups of participants:
  - early-mild dementia
  - moderate dementia
  - severe dementia
  - Controls (matched for age and ethnicity)

- Array: analysis of the whole genome for each patient
Expected results

- Characterize new gene expression profile (upregulated or downregulated or identical) between different tested groups
- Selection of potential candidate genes (pathways of genes)
- Identify new actors in the mechanisms underlying AD by comparing the gene expression in different stages of the disorder
Conclusion

Identify new mutations in genes specific of each stage of AD

RELIABLE DIAGNOSTIC

Get better understanding of this devastating disease

Help therapy and AD sufferers
Acknowledgments

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Thanks for your attention!

"My memory's terrible these days."