The Women’s Healthy Ageing Project

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Consultant Neurologist
Disclosures

• may accrue revenue from patent; diagnostic assay for seizure prediction,

• has been a paid clinical consultant and speaker for the Australian Commonwealth, Pfizer, Sanofi, other relationships subject to confidentiality clauses

• has been a chief investigator on research projects receiving funds from Bayer, Merck, Piramal and GE Healthcare.

• on the Board of Executive Directors for the Western Health Service, Victoria
Evolution

• Early Detection
• Need to study people >65 to ascertain disease
• Prodrome of AD is several decades
• Midlife vascular risk factors strongest impact on late life disease (MCI, AD) diagnosis.
• Strongest therapeutic window in midlife?
• Need 20 years longit., prospect. with RF, confound. and cognitive trajectory measures
WHAP Measures n=438 - 252

- **COGNITION**: 4 times over 15 yrs
  - NeuroCognitive Testing
    - X  X  X  X  X  X  X  X  X  X

- **CLINICAL, PSYCH**: 12 times over 22 yrs
  - Clinical, Psychological
    - X  X  X  X  X  X  X  X  X  X

- **LIFESTYLE, PHYSICAL**: 11 times over 22yrs
  - Lifestyle and Examination
    - X  X  X  X  X  X  X  X  X  X

- **BIOMARKER, STORED SPEC**: 11 x over 22yrs
  - Biomarker Analysis and Biobank Storage -70 Nit
    - X  X  X  X  X  X  X  X  X  X

- **NUTRITION and DENSIT.**: 3 times over 22 years
  - Fat, bone Density Scans
    - X  X  X  X
  - Nutritional Assessment
    - X  X  X

- **BRAIN IMAGING MRI, FMRI, 18F Florbetaban**
  - Cerebral MRI and FMRI
    - X
  - Cerebral Amyloid Scans
    - X  X
15 Years
Cognitive change 67% ret^n

22 Years
Lifespan change 58% ret^n

Cross Sectional Study
Year
1990
1991
2001

Cohort Age Cohort Age Cohort Age
(range) (mean)
45-55 55-65 65-75 75-80

Government Study Size
Factors
Target group for mid-life risk factors and prevention. Active, healthy workforce
Pension and workforce issues
Risk of Alzheimer's disease doubles every 5 years after 65
High usage of medical services

Government Study Size
Factors
n = 2000 n = 438 n = 438 - 320 n = 252 -

The Women's Healthy Ageing Project

The University of Melbourne
How do WHAP survivors compare?

- A two-cohort study. AIBL BL; WHAP FU
- Not statistically significant mean age, vascular risk factors (PROCAM), education (both higher than ave pop.)
- Statistically significant difference in the proportion of APOE 4 positive participants AIBL > WHAP

Data lock 2014: Research Questions

• Lifespan risk on late life
  – Cognitive Trajectories (submitted)
  – Amyloid (O3-10-01 vascular)

• Cognitive Trajectories and amyloid accrual over 65
  – Can we see subtle decline prior to amyloid accrual (O2-10-04)

• Cognitive Trajectories and functional decline (SF 36; wellbeing; self report)
Cognition and Ageing
– Women

• CSF Ab42 reduction correlating with memory in female healthy elderly but not in males
• Amyloid load on Pib scans relating to cognition in women but not men

Pike et al, 2011, Neuropsychologia

125 with 18F Florbeteban amyloid imaging

July 16, WEDNESDAY:
POSTER Presentation (P4-082)
1145 – 1415hrs
4:00pm - 5:30pm
Who refused PET scan

- no significant differences for distance lived from assessment centre, age or education.
- Recalled fewer words on CVLT word recall
- 10 vs 11.4, p=0.008, adjusted for age and education
Interaction of Midlife PROCAM tertile x APOE ε4 status significantly associated with late-life FBB SUVR (p=0.04).

- ie. the association of high vascular risk tertile with Aβ was greatest in ε4+
- age and years of education.

July 15, TUESDAY:
ORAL Presentation (03-10-01)
1600 – 1730hrs
Results – CVLT-long delay

Adjusted mean (95% confidence interval) for CVLT-delay z-score by FBB Tertile

- Adjusted for age, education and E4 status

* p<0.1, ** p<0.05, ***p<0.001

July 14, MONDAY:
ORAL Presentation (O2-10-04)
4:00pm - 5:30pm
Reported SCI and amyloid accrual

SMC not associated with amyloid accrual

July 13, SUNDAY:
ORAL Presentation (P1-181)
4:00pm - 5:30pm

The diagram shows a comparison of counts between the "Not confused" and "Confused" groups across different tertiles of FBB SUVR. The p-value is indicated as < 0.01.
Work Plan

• Earlier detection for those at risk for cognitive decline
  • From 45
  • Hormones and hormone therapy

• Lifespan approach to risk of cognitive decline
  • Cumulative risk
  • Critical windows, Timing
  • Impact on QOL and Functional measures

• Lifespan biobank
  • ? Biomarker at 45 which can determine risk of cognitive decline
  • ? Biomarker at 45 which can determine risk of amyloid accrual

• Imaging biomarkers
  • Change in MRI 2002 to 2012, amyloid accrual 2012
Participants and their families

**WHAP**
A/Prof Cassandra Szoeke
Prof Lorraine Dennerstein
Prof Philippe Lehert

Research Team
Rafael Smith
Jacqui Giumarra
Morgan Radler

**PUBLIC HEALTH**
Bioinformatics
Prof John Hopper
Prof Danny Liew
Dr Mark Tacey
Dr Chuhui Chan

**ENDOCRINOLOGICAL**
Prof Henry Burger
Prof Elizabeth Farrell
Dr Charlene Chua
David Thawley
Dr Jo Ryan

**MUSCULOSKELETAL AND BONE HEALTH**
Prof John Wark
Prof Flavia Cicuttini
Alexander Blizzard

**NEURO PSYCHIATRIC**
Prof David Ames
Katherine Campbell
Dr Jo Robertson
Katherine Burns

**CARDIOVASCULAR HEALTH**
Prof Helena Teede
Arti Appannah
Karen Chen
Dr Paul Yates

**NEUROIMAGING**
PET
Prof Christopher Rowe
A/Prof Victor Villemagne
Lana Pejoska
Narelle Langdon
Robyn Veljanovski
Dr Fiona Lamb
Denise El-Sheikh
Dr Kevin Ong

**MRI**
Prof Patricia Desmond
Dr Chris Steward
Mary Barnes

**Biomarkers**
Prof Colin Masters
Dr Alan Rembach
Brett Trounsen

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July 12, SATURDAY:
POSTER Presentation (IC-P-020)
“Evidence of amyloid on Florbetaben-PET is associated with reduced episodic memory 10 years prior: results from the Women's Healthy Ageing Project“

POSTER Presentation (IC-P-021)
“Midlife Vascular Risk, Apolipoprotein E-4 and Amyloid status 20 years later: Results from the Women's Healthy Ageing Project

POSTER Presentation (IC-P-023)
“Subjective memory complaints ten years prior have no relationship with brain amyloid - data from the Women's Healthy Ageing Project”

July 13, SUNDAY:
POSTER Presentation (P1-181)
“Subjective memory complaints ten years prior have no relationship with brain amyloid - data from the Women's Healthy Ageing Project”

POSTER Presentation (P1-335)
“A simple test of episodic memory predicts conversion to disease (MCI/AD) A DECADE later – data from the Women’s Healthy Ageing Project (WHAP)”

July 14, MONDAY:
POSTER Presentation (P2-381)
“Grandparenting is associated with cognitive functioning in older women: results from the Women’s Healthy Ageing Project”

ORAL Presentation
1600 – 1730hrs
Location: HALL A1 (BCCC)
“Midlife Vascular Risk, Apolipoprotein E-e4 and Amyloid status 20 years later: Results from the Women's Healthy Ageing Project.”

POSTER Presentation (P3-090)
“Apolipoprotein E4 gene predicts changes in episodic memory from midlife to late-life: data from the Women’s Healthy Ageing Project (WHAP)”

July 15, TUESDAY:
POSTER Presentation (P3-090)
“Apolipoprotein E4 gene predicts changes in episodic memory from midlife to late-life: data from the Women’s Healthy Ageing Project (WHAP)”

July 16, WEDNESDAY:
POSTER Presentation (P4-082)
“Participants who refuse PET scan had significantly lower episodic memory than those who consented to scan – data from the Women’s Healthy Ageing Project”

POSTER Presentation (P4-056)
“Participants with a positive amyloid scan in the Women’s Healthy Ageing Project had significantly worse episodic memory than those with a negative scan”