



Brain Health Scotland – Touchpoints with Technology

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University of Edinburgh
Director Brain Health Scotland



The University of Edinburgh



Scottish Government
Riaghaltas na h-Alba
gov.scot

Overview of presentation

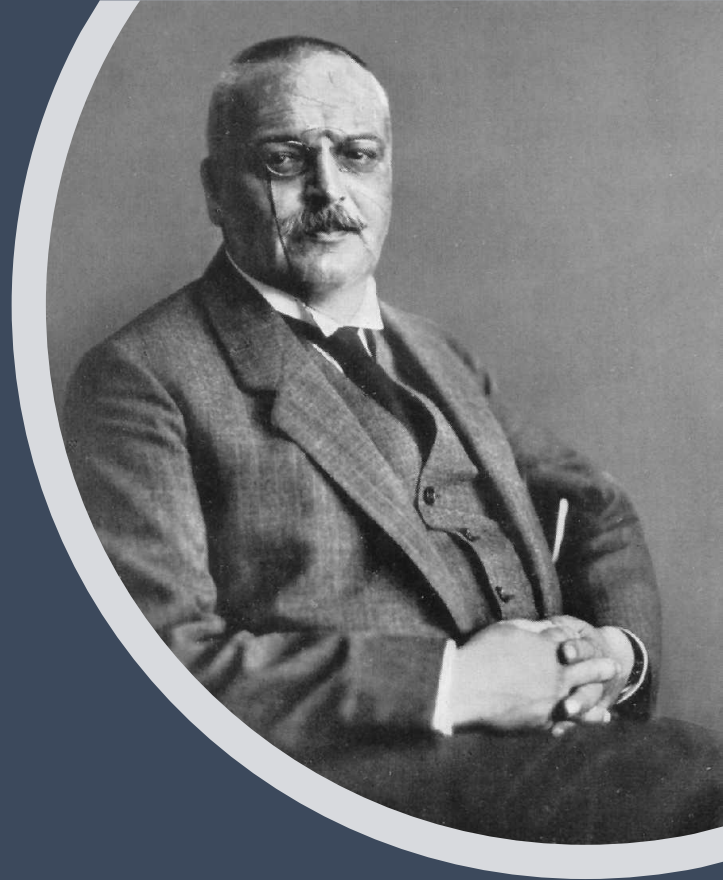
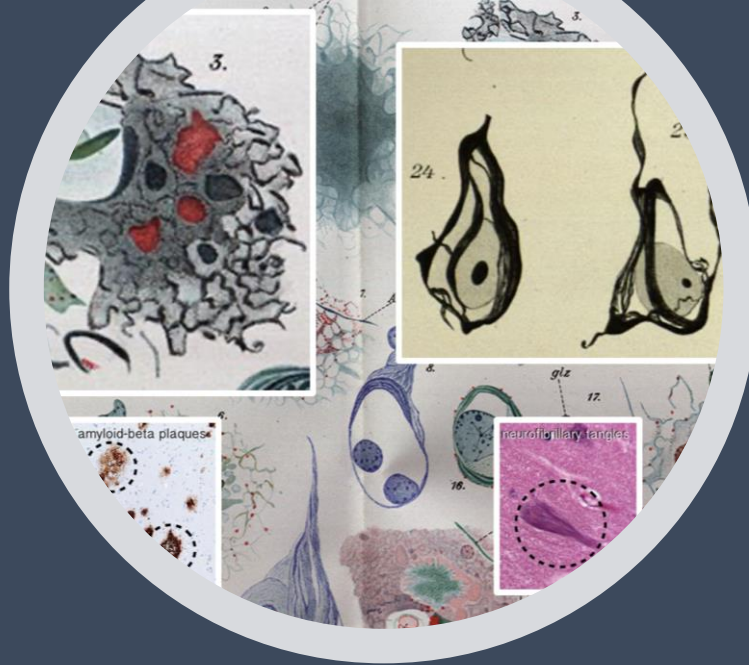
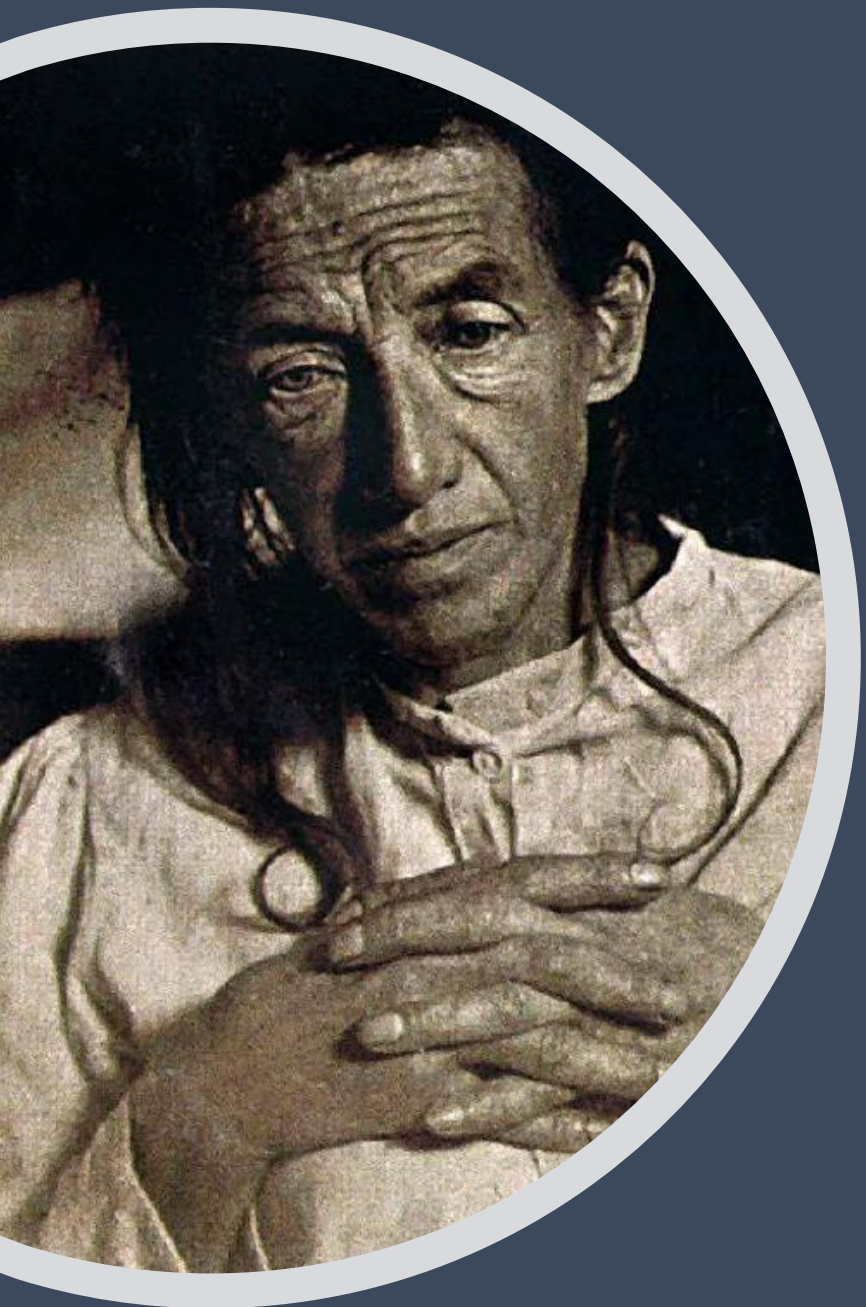


Disease before dementia

- The research direction
- PREVENT Dementia Measurement of a 'relevant' early pathology

Translation from Research into Practice (and back)

- The Brain Health Scotland 'Ecosystem'
- Touch points for Technology

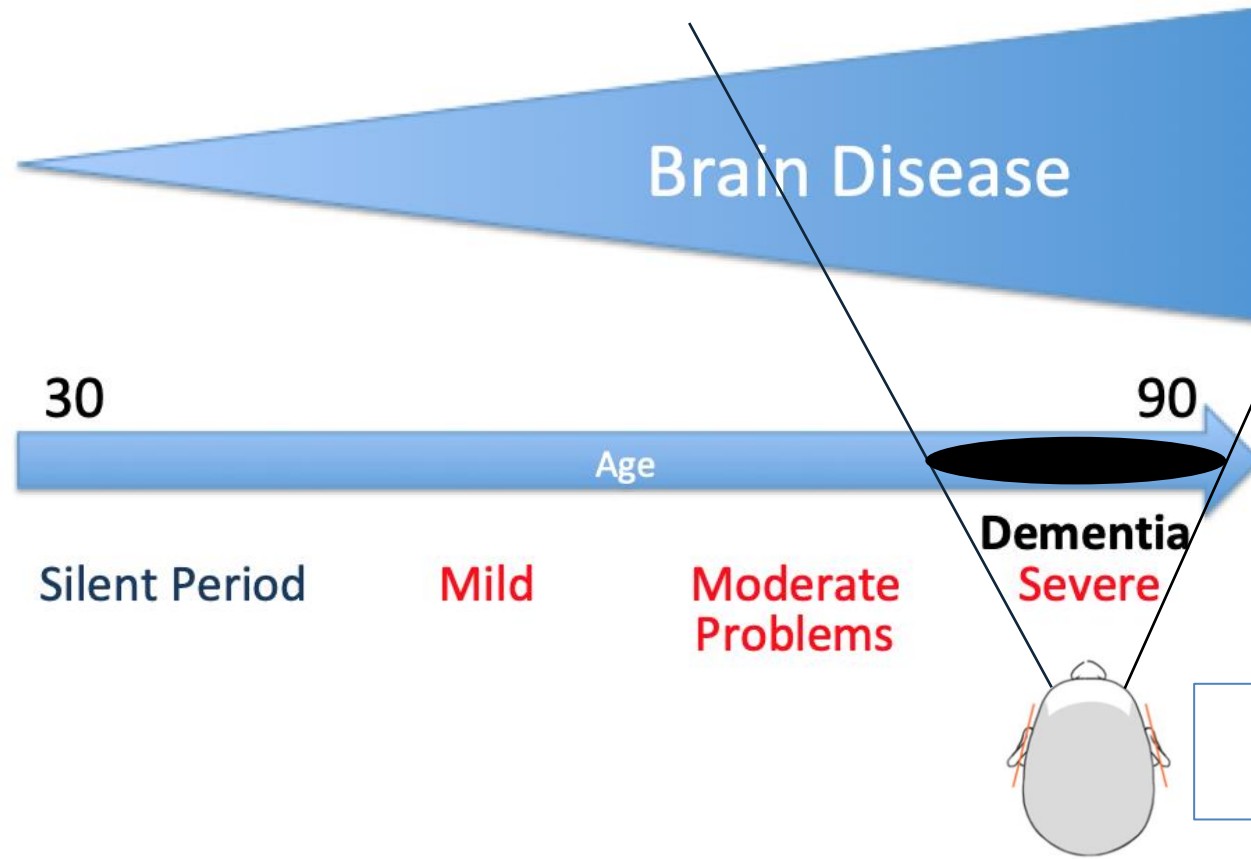


Alzheimer disease

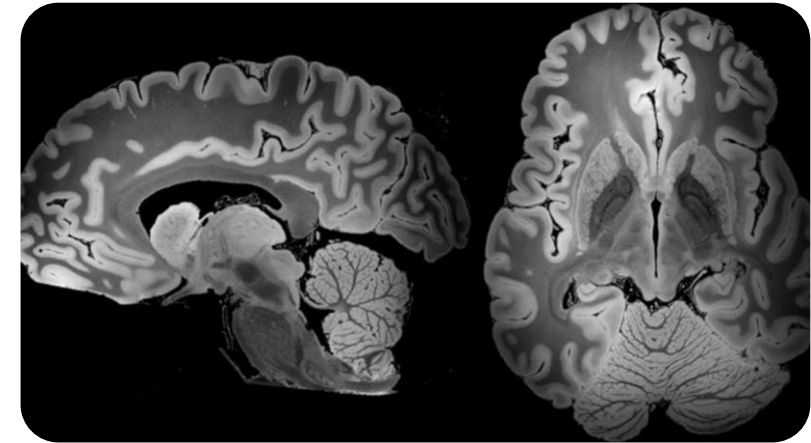
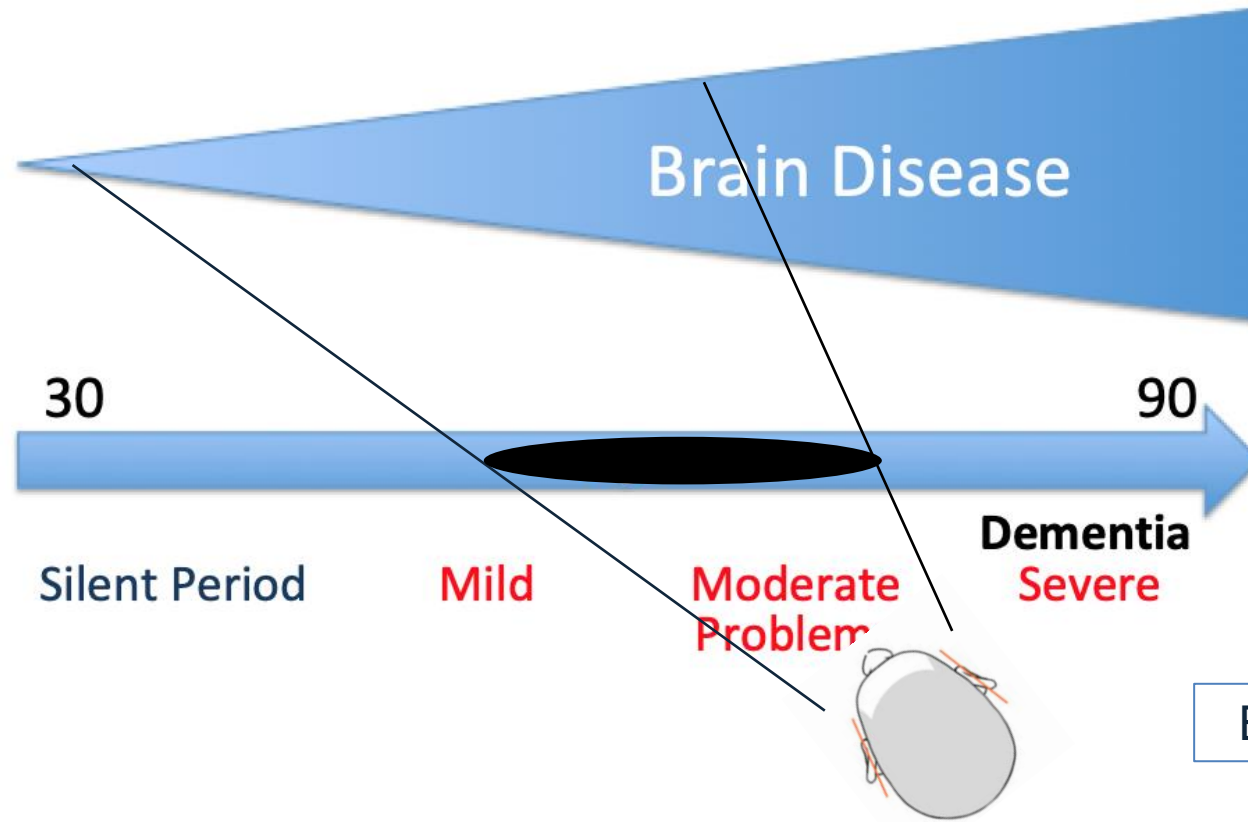
Dementia

- The term dementia is (quite rightly) under threat!
 - **SCIENCE v SYNDROME**
 - The 1990s saw the scientific breakthrough giving us the ability to measure neurodegenerative disease through brain imaging and spinal fluid
 - Alzheimer's disease itself could be 'measured'
-

Alzheimer's disease is a brain disease with cognitive symptoms NOT a cognitive disorder

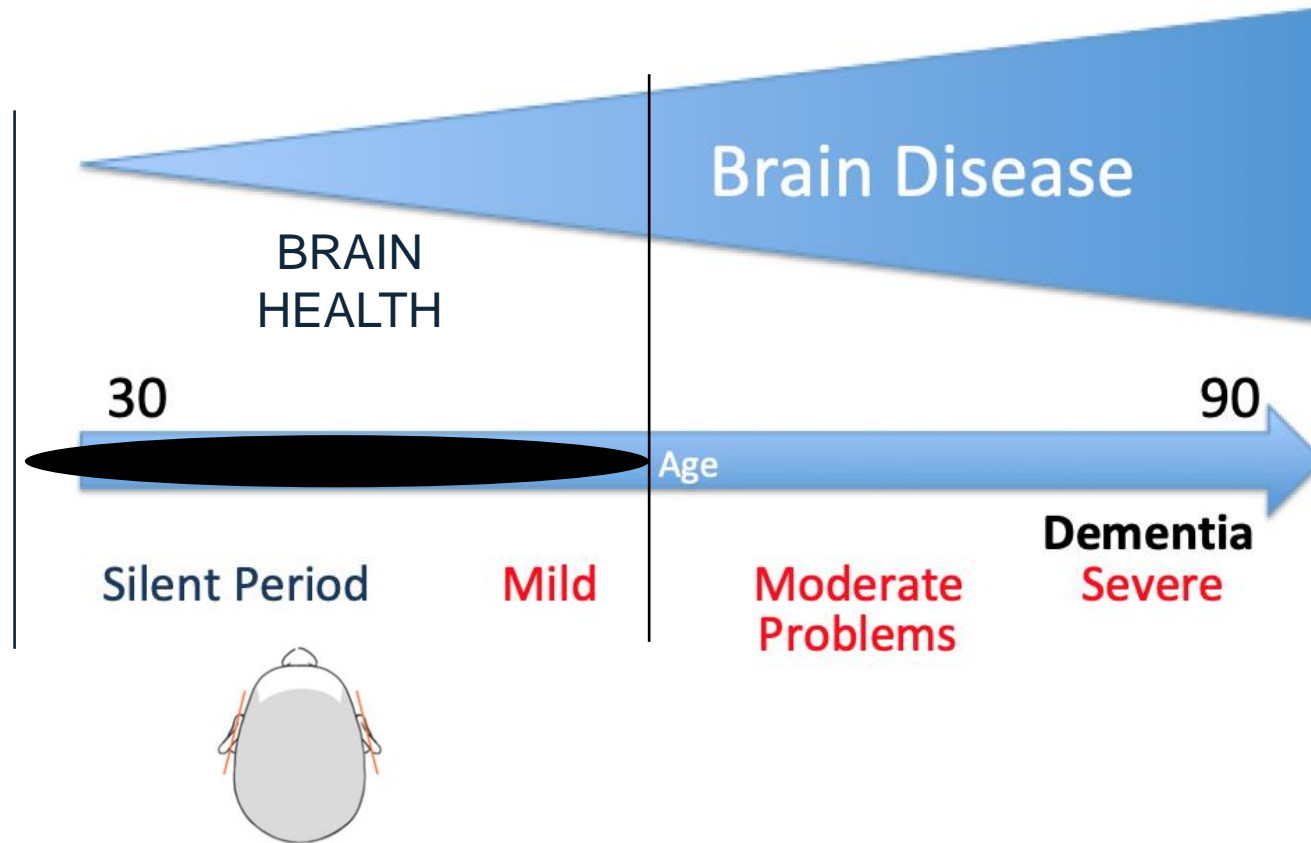


Detecting the Brain Changes Early

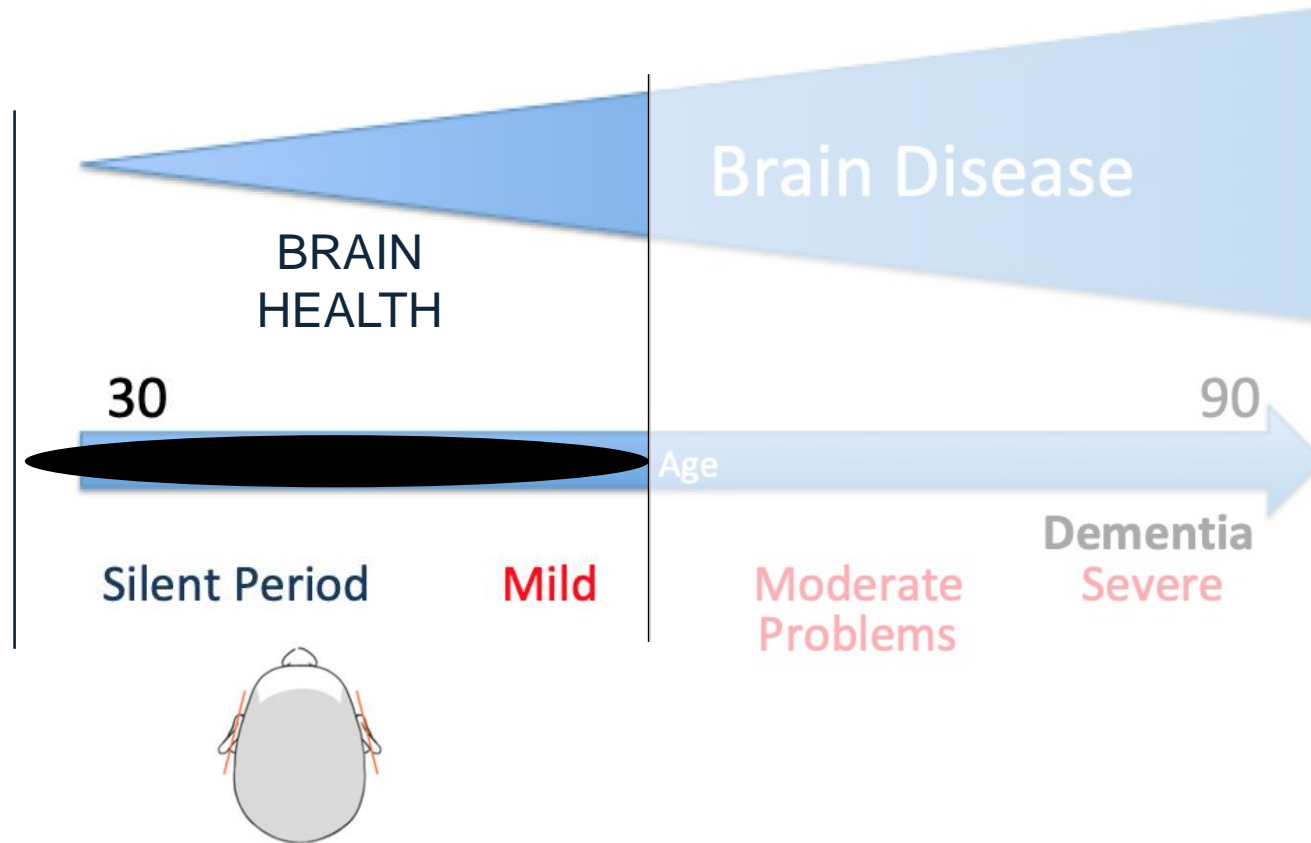


BIOMARKERS

Maintaining Brain Health = Dementia Prevention



Maintaining Brain Health = Dementia Prevention



The PREVENT Dementia Project

Population: n=700 aged 40-59 at baseline with up to 5 years of Follow Up in 5 Centers in UK and Ireland

Funded: Alzheimer's Society (UK) and Alzheimer's Association (US)

Objective: To identify risk/disease interactions in an at-risk population in mid-life

Risk Factor Assessment in PREVENT Dementia Programme

Domain	Risk	Measurement
Principal Risk Model	ApoE Genotype	
	Family History	
Genetic	ApoE and GWAS	
Environmental	Diet	Scottish Food Frequency Questionnaire
	Life-events	Life Stressor Checklist
	Sleep	Pittsburgh Sleep Evaluation
	Exercise	Study Proforma
Clinical	Head Injury	Brain Injury Screening Questionnaire
	Inflammation	Biomarkers
	Cardiovascular/Metabolic Syndrome	Biomarkers/ECG/History and Examination
	Depression	GED-D
	Respiratory	Spirometry/History and Examination
	Stress	Salivary Cortisol/Resilience Questionnaire
	Endocrine	Haematology/Biochemistry and History & Examination

Expression of Disease in PREVENT Dementia Programme

Domain	Modality	Measurement
Neuroimaging	MRI	fMRI with task, Magnetic Resonance Spectroscopy, Diffusion Tensor Imaging, vMRI, WML volume
	PET	PET-Tau and Amyloid Imaging (sub-studies)
Retinal Imaging		Fundus photography, OCT
Wet Lab Biomarkers	CSF	Crick
	Blood	Insulin
	Urine	
	Saliva	Cortisol
Cognition	Global	
	Binding Paradigms	
	Visuospatial	

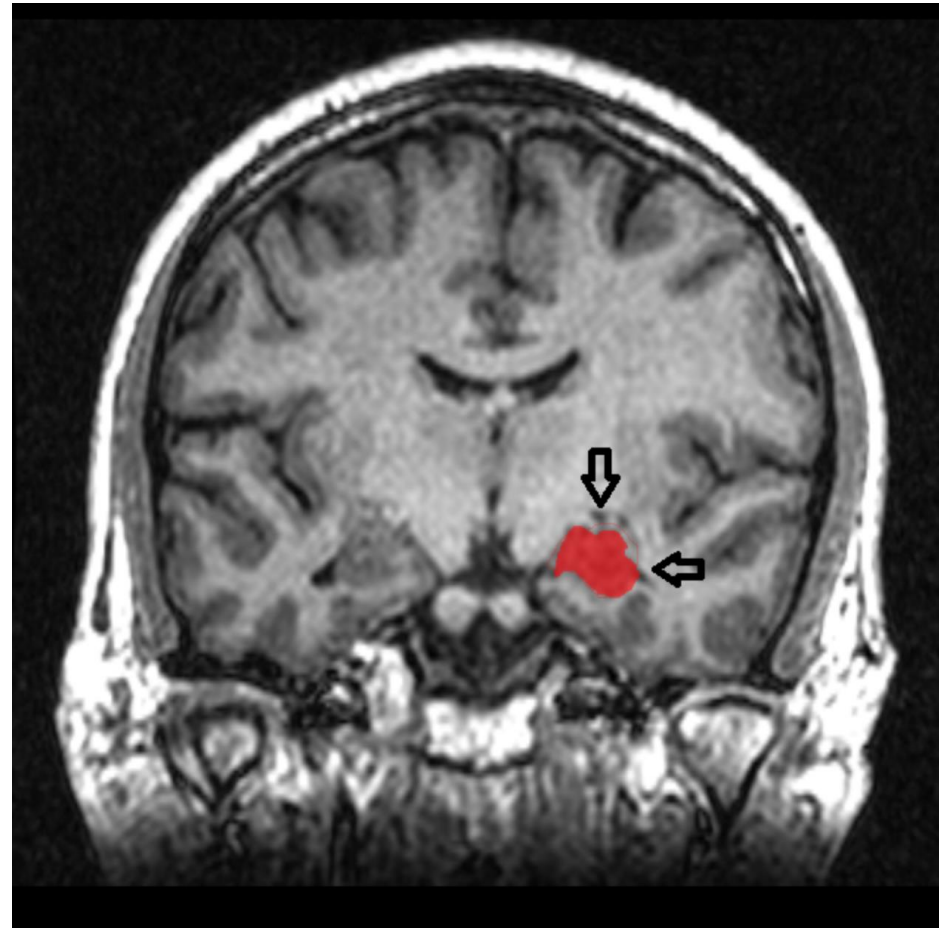
Sub-studies

- AIP (Amyloid Imaging in PREVENT) Capacity n=300
- 7T MRI Study (Cambridge) n=50 (Scanned) and n=300 (VR)
- Retinal Imaging (Edinburgh Only) n=85 (95% agree) target 100+ (18 have year 2 Imaging)
- PET Tau (n=50)
- Language analysis
 - Dialogue (Edinburgh MRC Fellowship)
 - Syntax (Cardiff) n=115
- Lab work (Edinburgh)
 - Global Screening Array (Edinburgh)
 - Salivary Cortisol (Edinburgh)
- Oral Health [Edinburgh]
- PREVENT RFC and PREVENT FC
 - Edinburgh Site (n=200)
- Intimate Partner Violence
 - Drake Foundation



Alzheimer's disease 'starts' in the Hippocampus

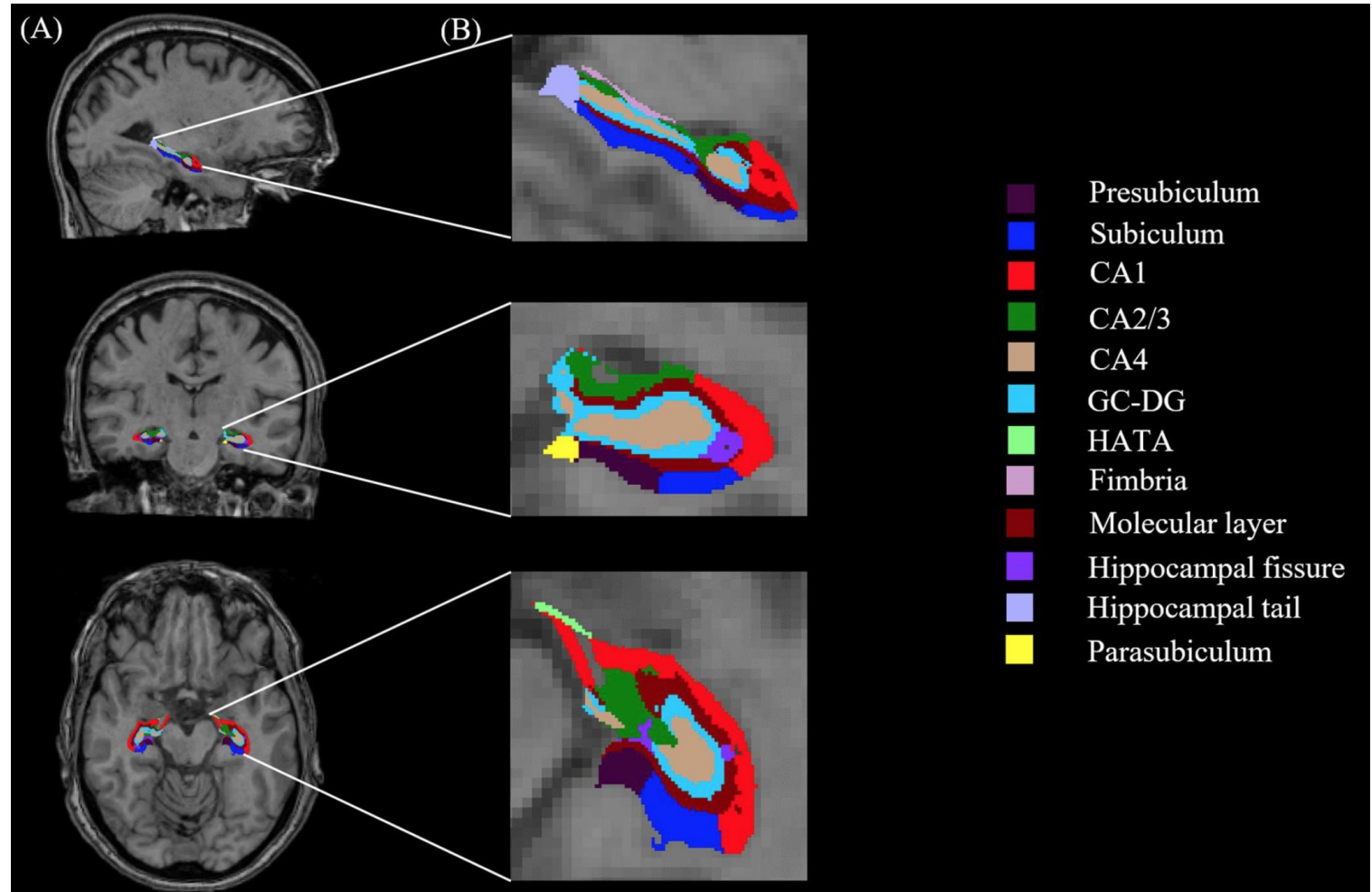
Testing the hippocampus....



Alzheimer's disease 'starts' in the Hippocampus

Testing the hippocampus....

Hippocampal Subfields....

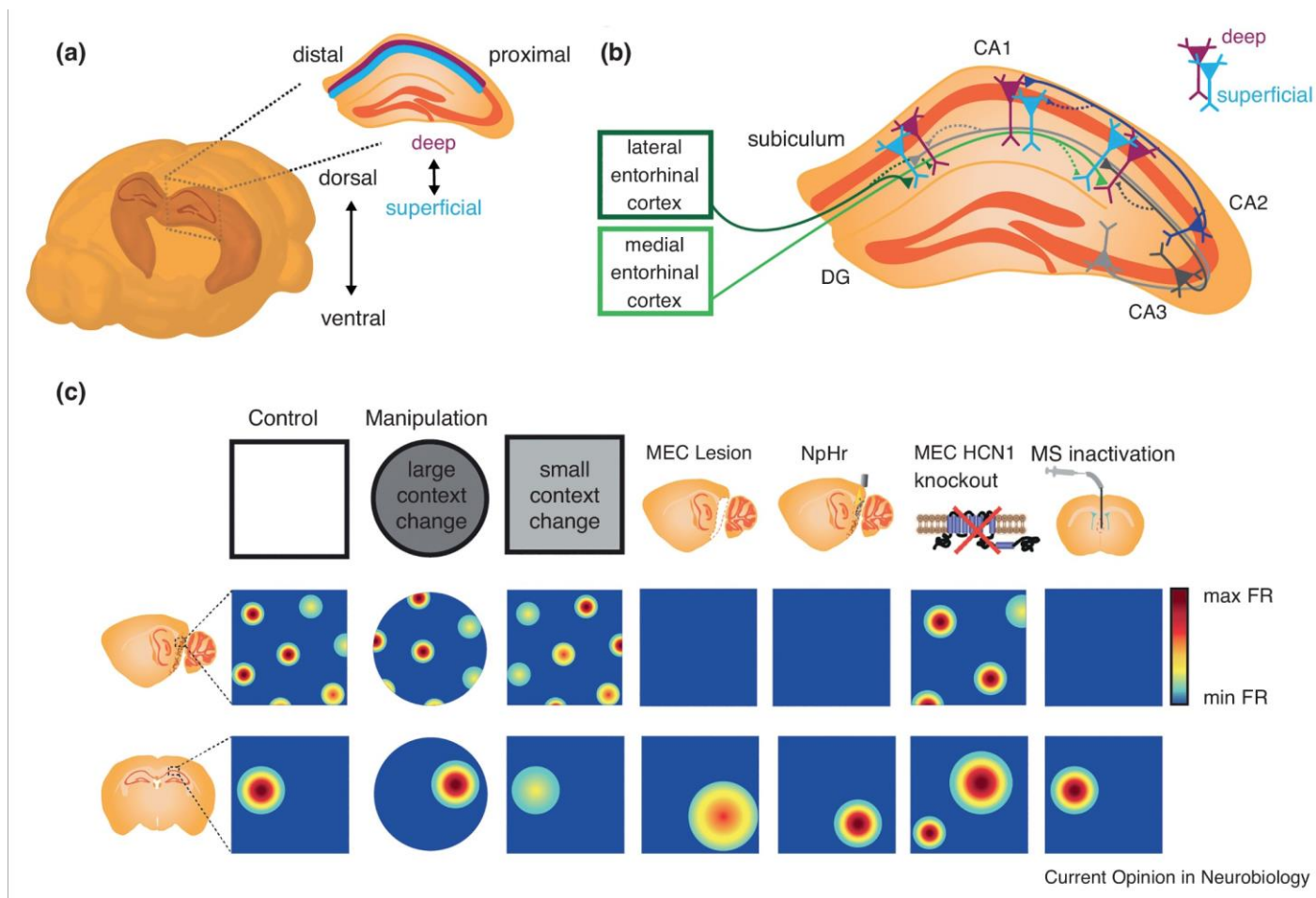


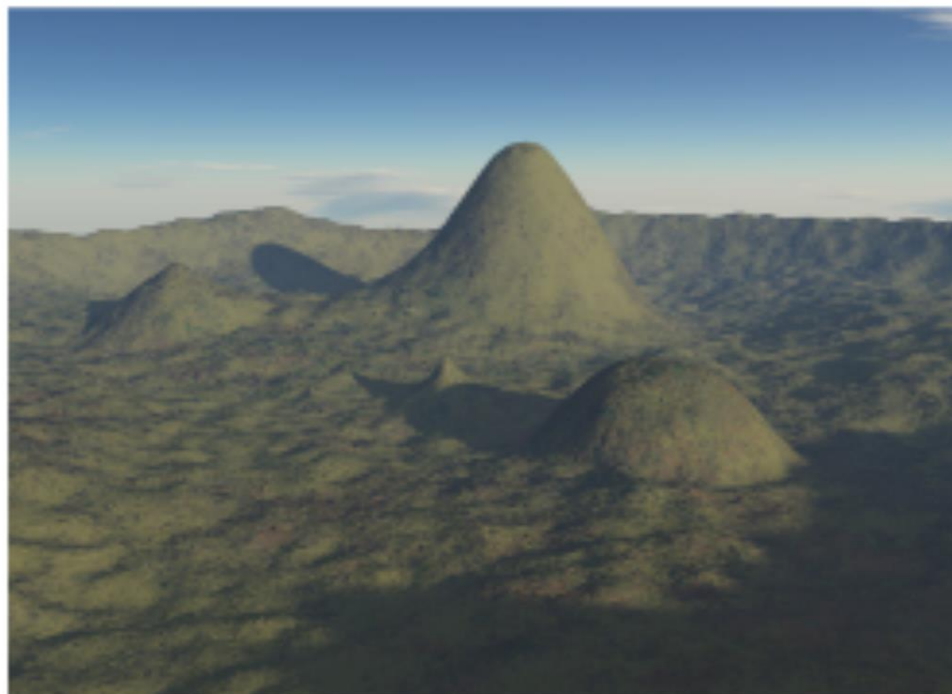
Alzheimer's disease 'starts' in the Hippocampus

Testing the hippocampus....

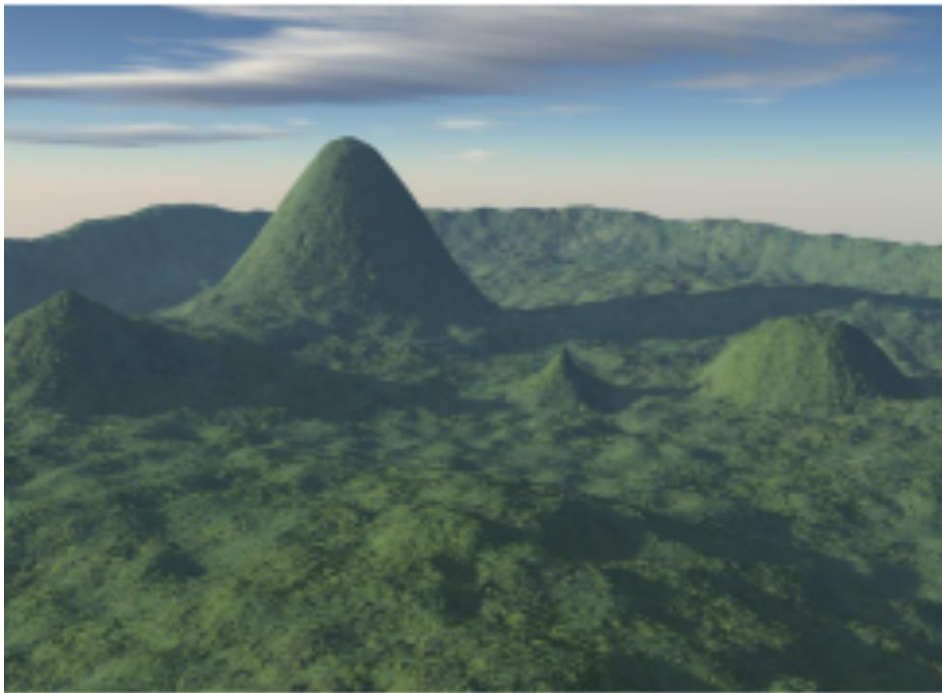
Hippocampal Subfields....

Hippocampal Place Cells....

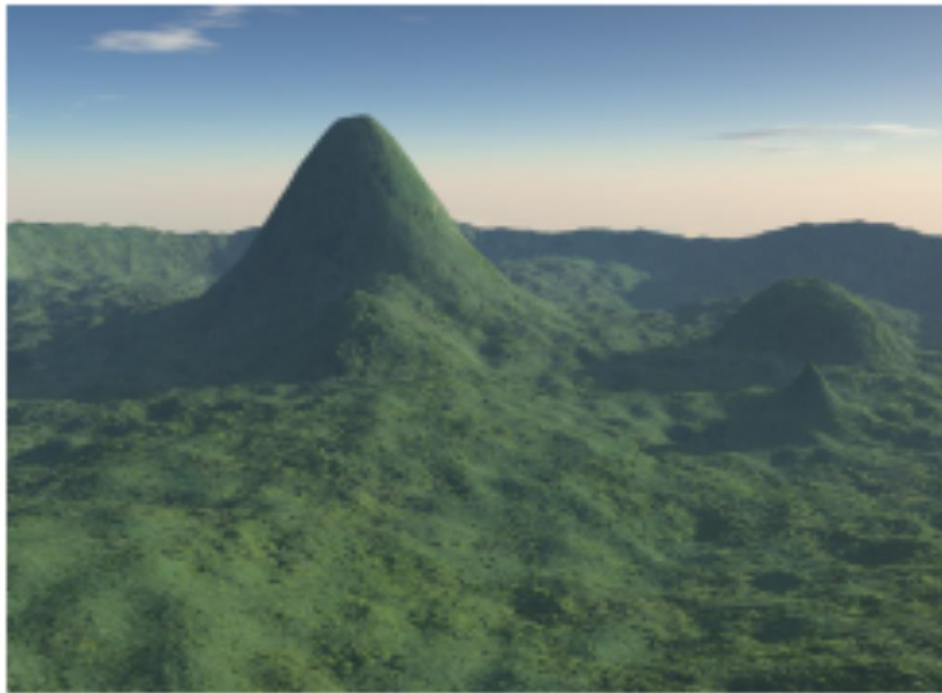




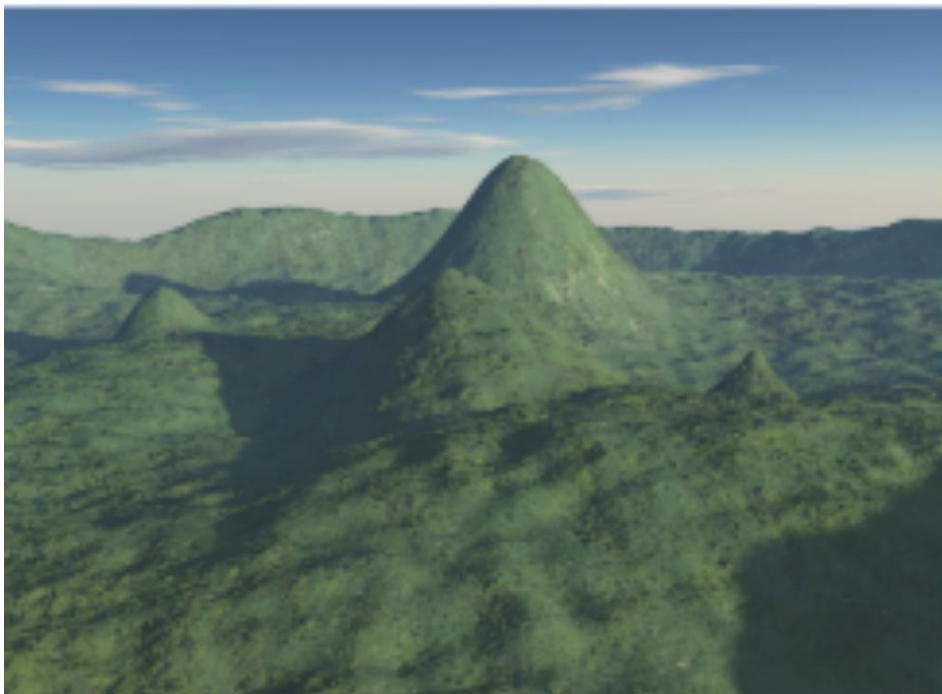
A



B



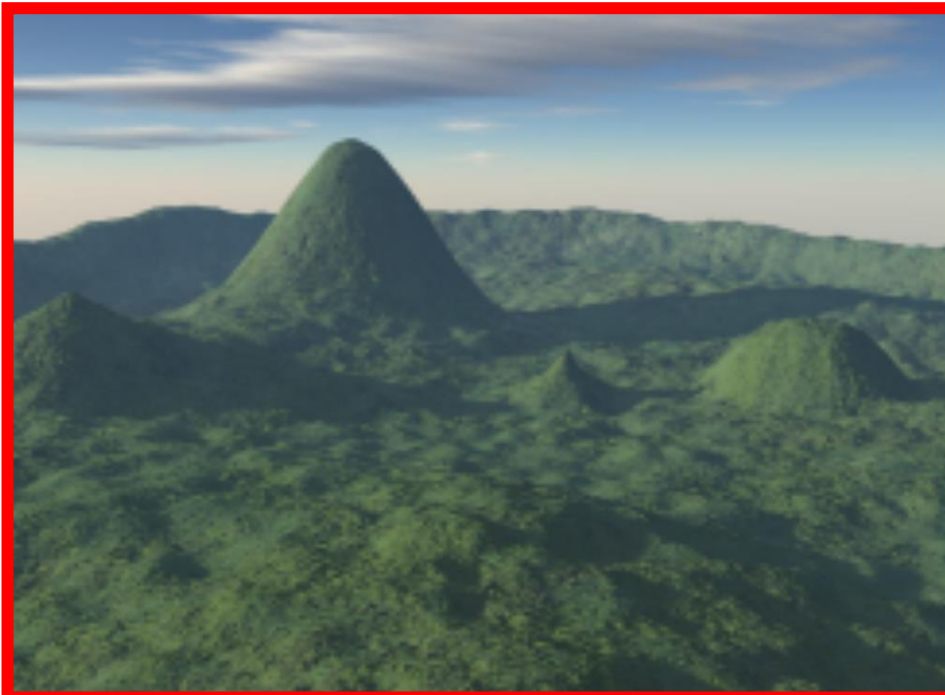
C



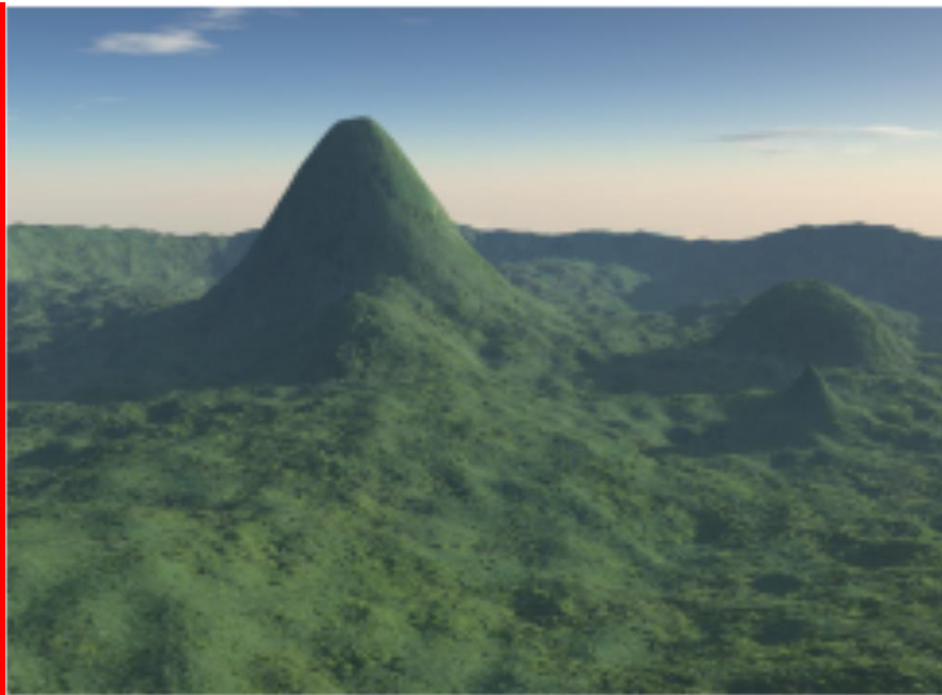
D



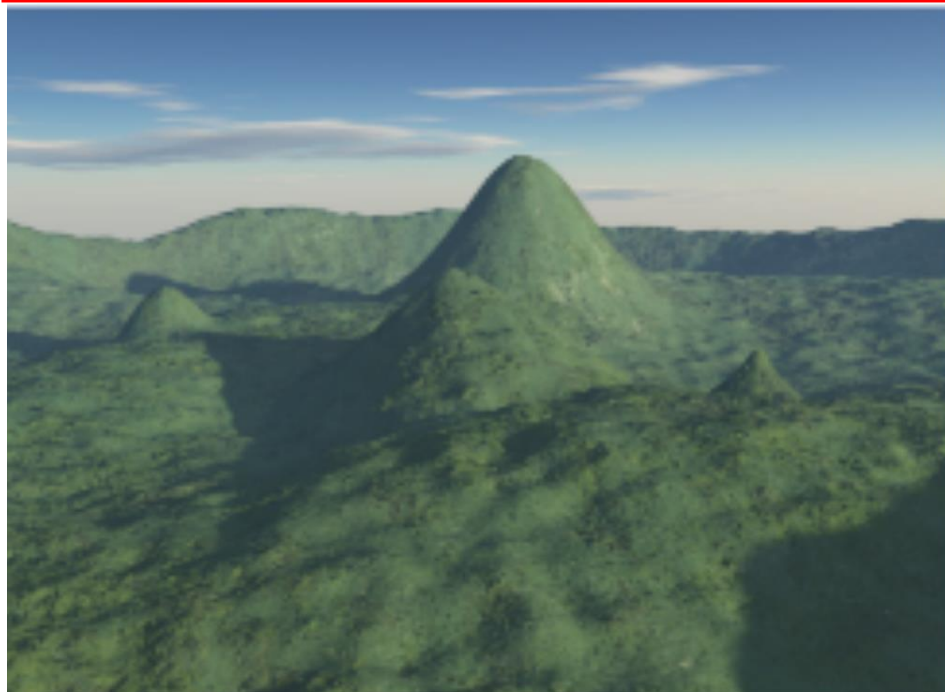
A



B



C



D





Alzheimer's disease starts in the Hippocampus

Ritchie K. *et al.*, 2018

'A significant negative association was found between the DRS and 4MT (Spearman Correlation – 0.26, $p=0.0006$)'

CAIDE SCORE*

- Weight
- Age
- Sex
- Education
- ApoE
- Systolic Blood Pressure
- BMI
- Total Cholesterol
- Physical Activity



4 Kivipelto M, Ngandu T, Laatikainen T, *et al.* Risk score for the prediction of dementia risk in 20 years among middle aged people: a longitudinal, population-based study. *Lancet Neurol* 2006;5:735–41.

Allocentric and Egocentric Spatial Processing in Middle-Aged Adults at High Risk of Late-Onset Alzheimer's Disease: The PREVENT Dementia Study

Article type: Research Article

Authors: Ritchie, Karen^{a, b, 1, *} | Carrière, Isabelle^{a, b, 1} | Howett, David^c | Su, Li^d | Hornberger, Michael^e | O'Brien, John T.^d | Ritchie, Craig W.^b | Chan, Dennis^c

Affiliations: [a] INSERM, University of Montpellier, Neuropsychiatry: Epidemiological and Clinical Research, Montpellier, France | [b] Centre for Dementia Prevention, University of Edinburgh, UK | [c] Department of Clinical Neurosciences, University of Cambridge, UK | [d] Department of Psychiatry, University of Cambridge, Cambridge, UK | [e] Norwich Medical School, University of East Anglia, Norwich, UK

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Note: [1] These authors contributed equally to this work.

Abstract: Impairments in spatial processing due to hippocampal degeneration have been observed in the years immediately preceding the diagnosis of Alzheimer's disease (AD) dementia. The demonstration of changes in spatial processing in preceding decades would provide a cognitive marker for pre-clinical AD and an outcome measure for early intervention trials. The present study examined allocentric and egocentric spatial processing in relation to future dementia risk in a middle-aged cohort. The CAIDE Dementia Risk Score (DRS) was calculated for 188 persons aged 40 to 59, of whom 94 had a parent with dementia. Participants underwent the Four Mountains Test (4MT) of allocentric spatial processing, the Virtual Reality Supermarket Trolley Task (VRSTT) of egocentric spatial processing, and 3T MRI scans. A significant negative association was found between the DRS and 4MT (Spearman correlation – 0.26, $p=0.0006$), but not with the VRSTT. The 4MT was also found to be a better predictor of risk than tests of episodic memory, verbal fluency, or executive functioning. The results suggest that allocentric rather than egocentric processing may be a potential indicator of risk for late-onset AD, consistent with the hypothesis that the earliest cognitive changes in AD are driven by tau-related degeneration in the medial temporal lobe rather than amyloid-only deposition in the medial parietal lobe.

Keywords: Alzheimer's disease, cognition, diagnosis, magnetic resonance imaging, neuropsychology, preclinical, prognosis, spatial memory

DOI: 10.3233/JAD-180432

Journal: *Journal of Alzheimer's Disease*, vol. 65, no. 3, pp. 885-896, 2018



Neurobiology of Aging 91 (2020) 36–44



Contents lists available at ScienceDirect

Neurobiology of Aging

journal homepage: www.elsevier.com/locate/neuaging



Volumetric alterations in the hippocampal subfields of subjects at increased risk of dementia



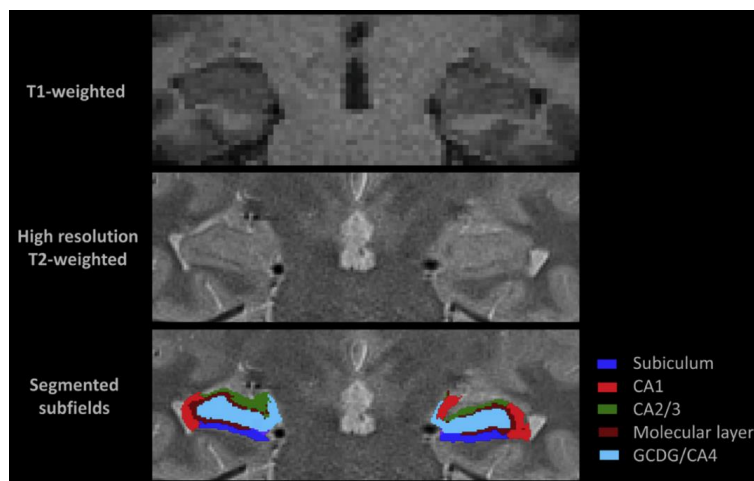
Maria-Eleni Dounavi^a, Elijah Mak^a, Katie Wells^b, Karen Ritchie^{c,d}, Craig W. Ritchie^d, Li Su^{a,1,*}, John T. O' Brien^{a,1}

^a Department of Psychiatry, School of Clinical Medicine, Addenbrooke's Hospital, University of Cambridge, UK

^b The Centre for Psychiatry, Imperial College, London, UK

^c INSERM, University of Montpellier, Neuropsychiatry: Epidemiological and Clinical Research, Montpellier, France

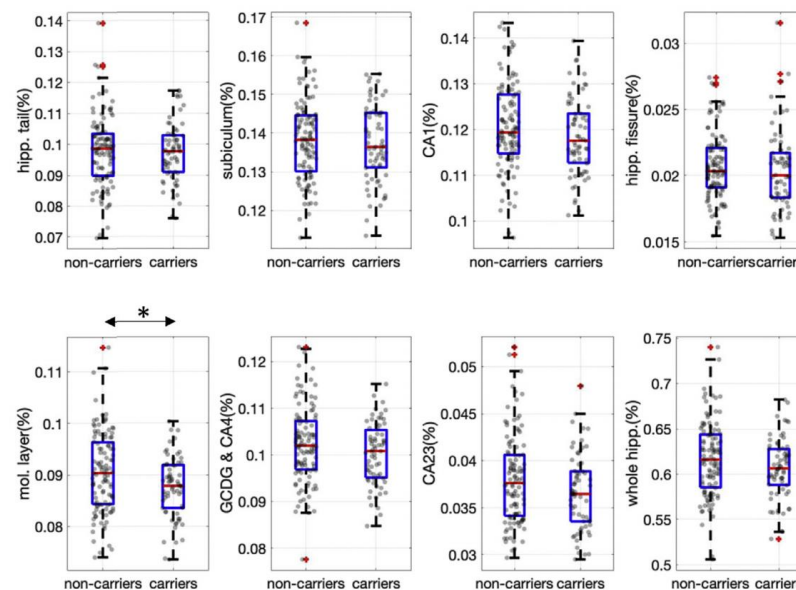
^d Centre for Dementia Prevention, University of Edinburgh Centre for Clinical Brain Sciences, Edinburgh, UK



In terms of measuring outcomes – could these imaging biomarkers be a specific measure of disease related temporally to an early manifestation of (preclinical) disease. If downstream from amyloid aggregation and NFT deposition in a focal area of relevance (i.e. where 'total' measures of A β and Tau in e.g. CSF are not substantial enough to be notable), then possible outcome for both anti-amyloid and anti-tau strategies in high-risk populations

In PREVENT Dementia Cohort at Baseline (n=180) and 2-year FU (n=156): there was a significant association (p<0.05) between ApoE ϵ 4 status and atrophy of molecular layer of hippocampus. A region believed to be an early region for NFT build up (Braak and Braak, 1997; Thal, 2000)

APOE genotype



Not measurable in high-risk preclinical population in early 50's using traditional MRI and cognitive tests



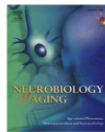
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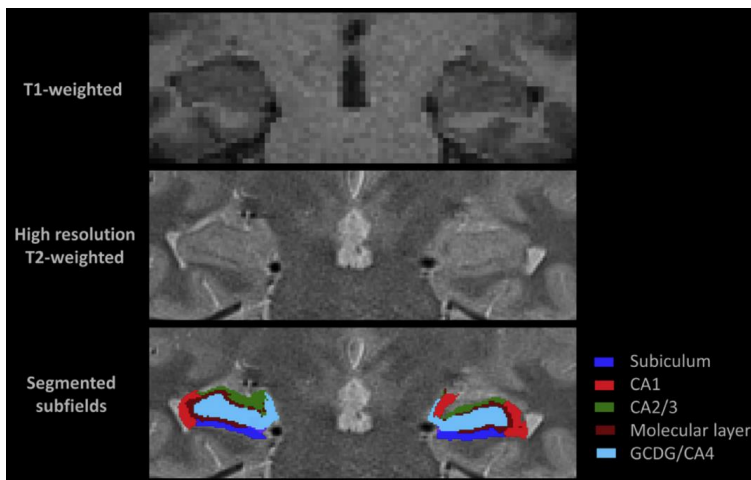
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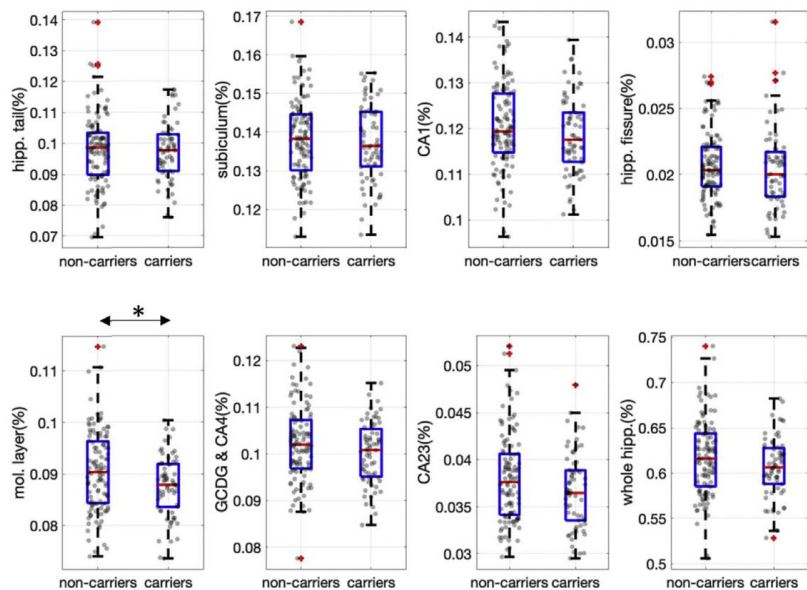
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APOE genotype



Now measurable in high-risk preclinical population in early 50's using sub-field MRI and correlated cognitive tests

Brain Health Scotland

Research into practice

Your brain is amazing.
Let's keep it that way.



**Anna
Borthwick**
Executive Lead
Brain Health Scotland



**Craig
Ritchie**
Director
Brain Health Scotland
*Prof of Psychiatry of Ageing
University of Edinburgh*



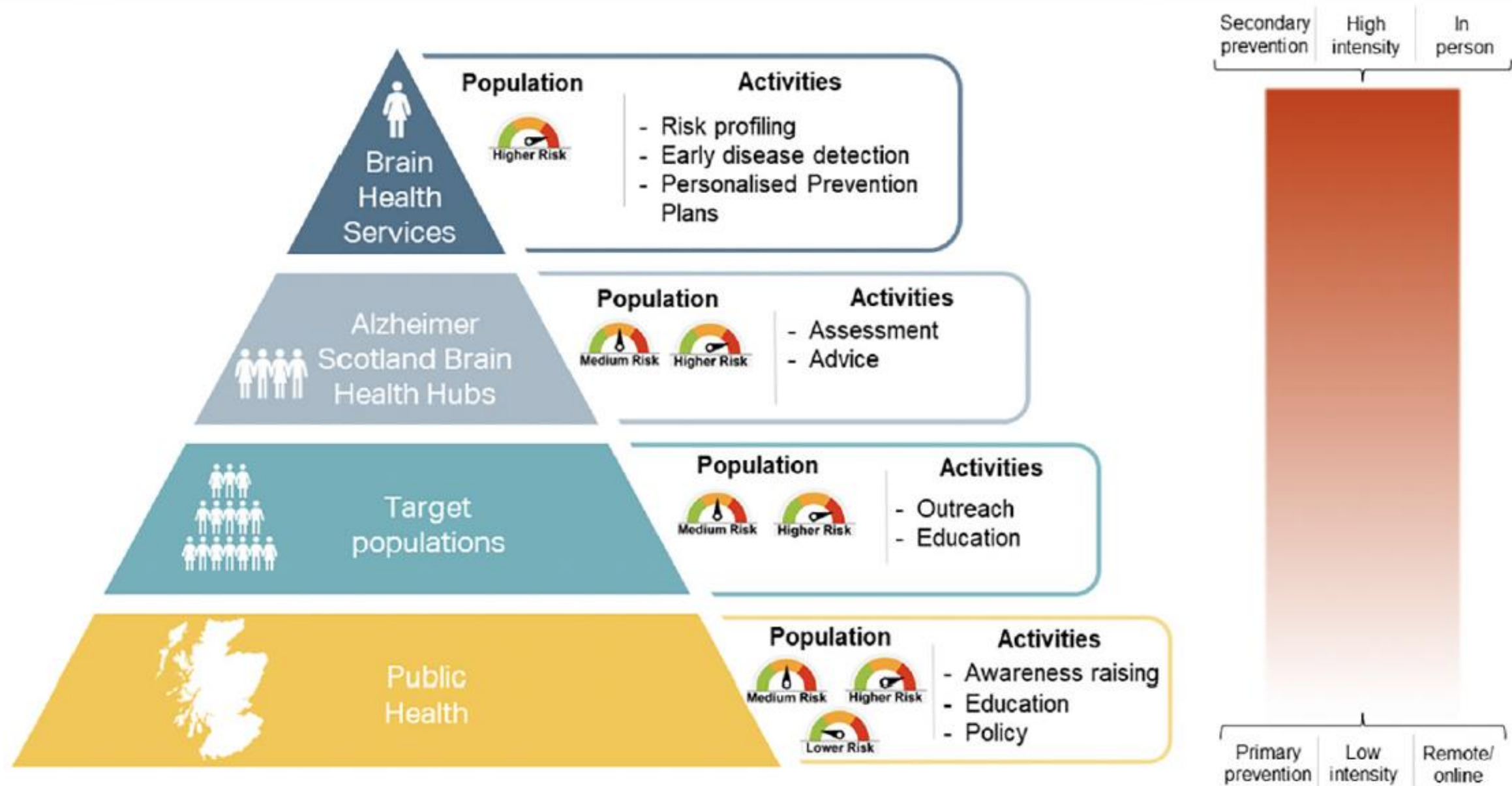
**Henry
Simmons**
Associate Director
Brain Health Scotland
CEO Alzheimer Scotland

A close-up profile of a woman's face, looking towards the right. Her hair is dark with some blue and purple highlights. Overlaid on the left side of her head is a complex, glowing wireframe structure representing a brain or neural network. The background is dark and out of focus.

**YOUR BRAIN
IS AMAZING.
LET'S KEEP IT
THAT WAY.**

.YAW TAHT

Figure 1. Pyramid of approaches to reduce incident dementia in Scotland, from public health interventions for the Scottish population (bottom tier) to clinical Brain Health Services for the individual (top tier)



The Scottish Brain Health Service Model

J Prev Alz Dis 2021;
Published online

Review

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The Scottish Brain Health Service Model: Rationale and Scientific Basis for a National Care Pathway of Brain Health Services in Scotland

C.W. Ritchie^{1,2,3}, J.M.J. Waymont^{2,4}, C. Pennington^{1,2,5}, K. Draper², A. Borthwick², N. Fullerton², M. Chantler⁶, M.E. Porteous^{1,3}, S.O. Danso¹, A. Green¹, L. McWhirter¹, G. Muniz Terrera¹, S. Simpson⁷, G. Thompson¹, D. Trépel^{8,9}, T.J. Quinn⁷, A. Kilgour^{1,2}

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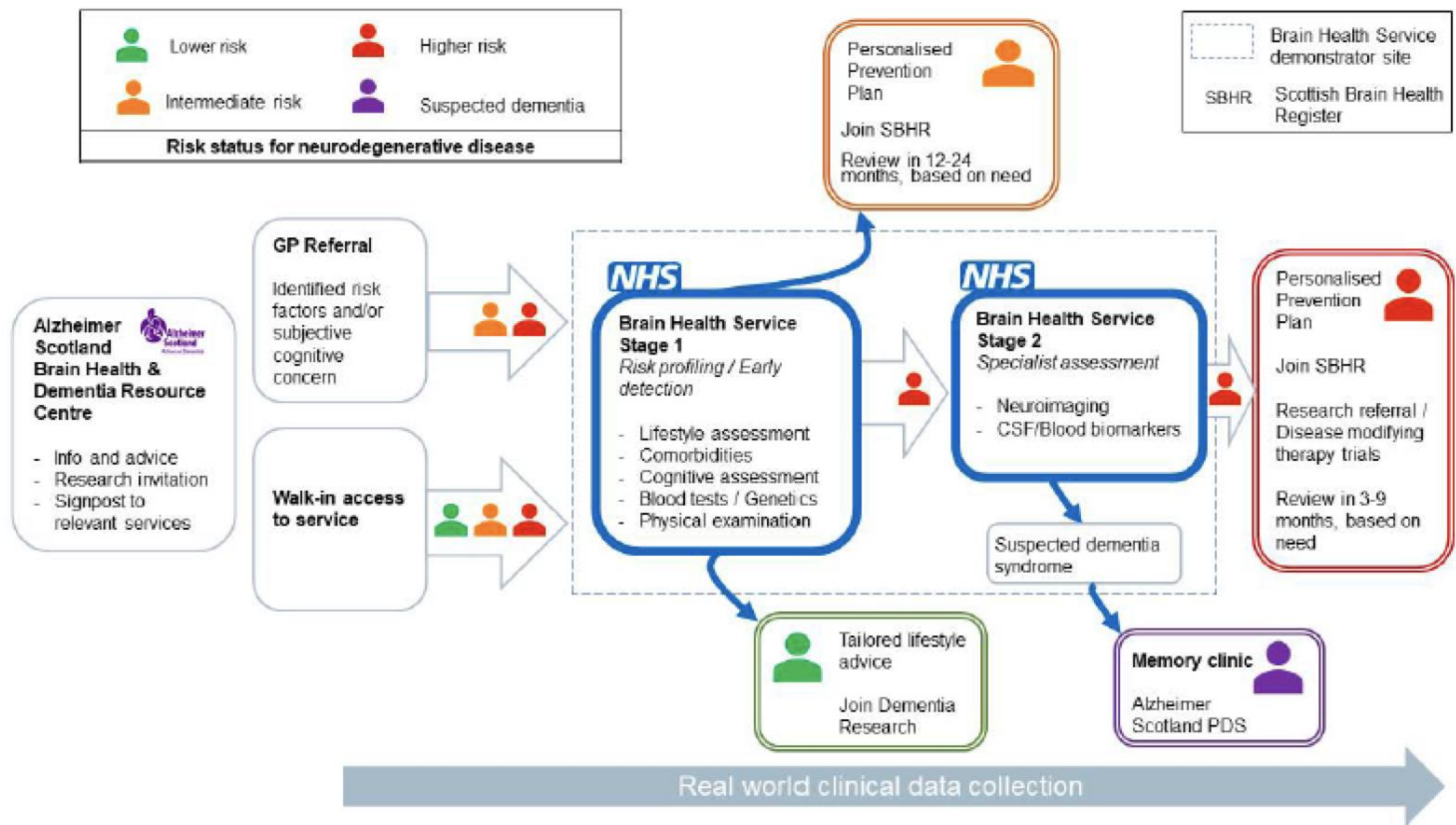
THE UNIVERSITY
of EDINBURGH



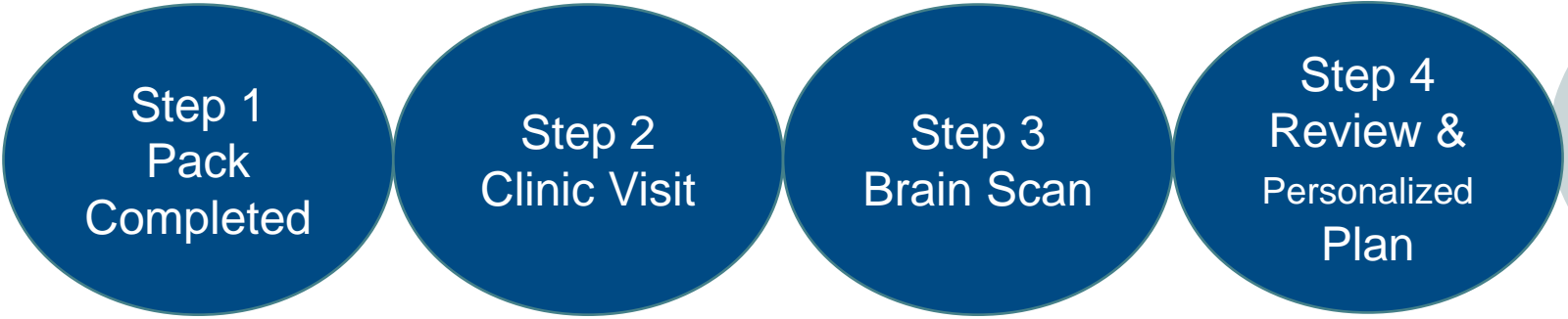
Trinity College Dublin
Coláiste na Tríonóide, Baile Átha Cliath
The University of Dublin



GLOBAL
BRAIN HEALTH
INSTITUTE



- Risk Profiling +
- Early Disease Detection =
- Personalized Prevention Plans



Risk Profiling

- Risk profiling is conducted early in the care pathway, with an aim of identifying modifiable risk factors suitable for immediate intervention.

- Risk factors examined include lifestyle factors, family history, **ApoE status** and comorbidities.

- Where risk is minimal and no disease is detected, tailored risk reduction advice is provided, and patients are invited to return at a future date for progression monitoring.

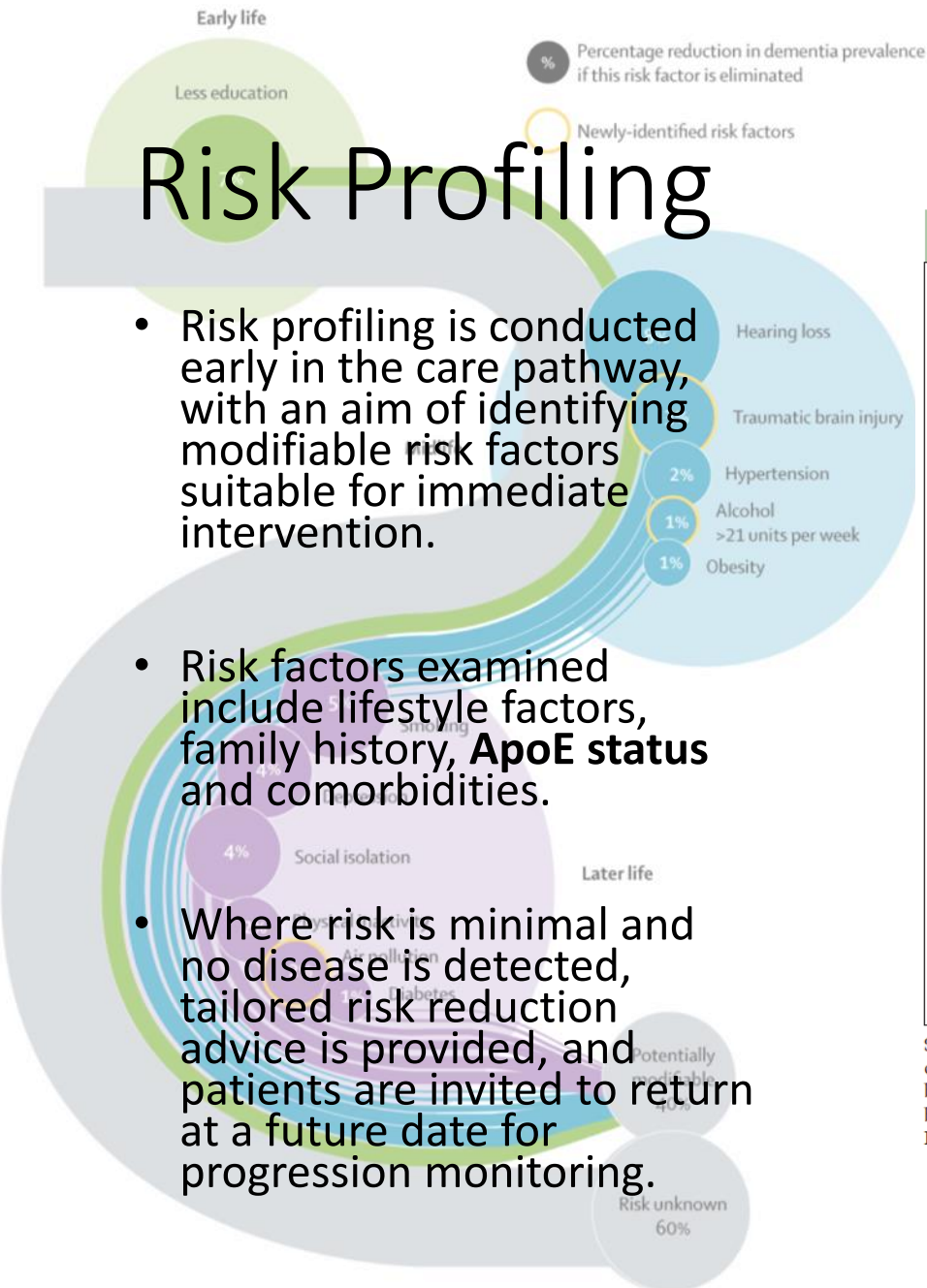
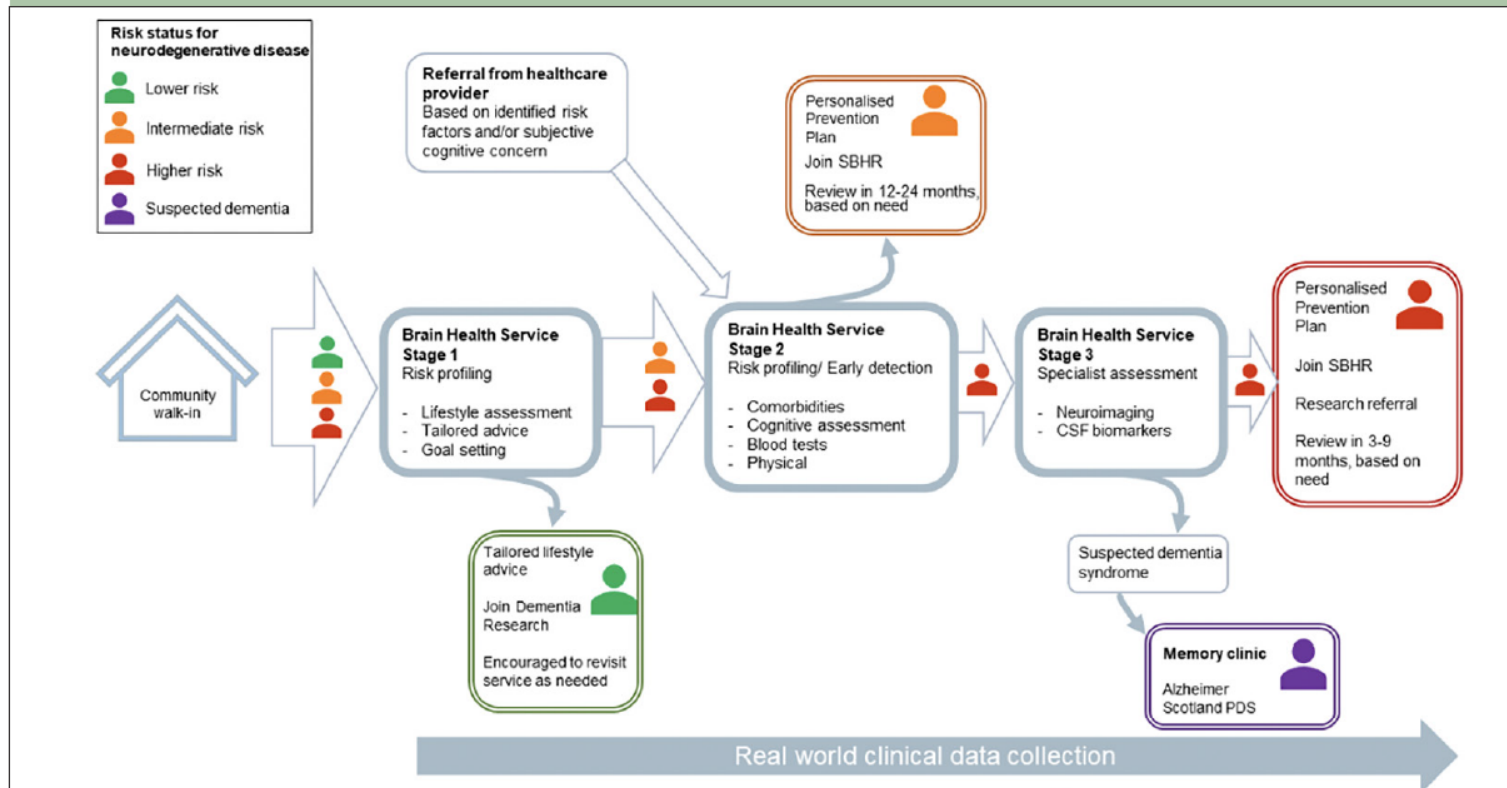


Figure 2. Care pathway for the Scottish model of Brain Health Services



Stage 1: generic, non-clinical support (advice, light-touch lifestyle assessment, information and signposting). Stage 2: initial clinical service (risk profiling, early disease detection, personalised prevention. Parallel referral to external services for management of comorbidities where appropriate). Stage 3: specialised clinical service (brain biomarker assessment, personalised prevention and intervention. Outwards referral to memory clinic for those with an established clinical dementia syndrome unlikely to benefit from continued care in Brain Health Services, parallel referral to external services for comorbidity management where appropriate). SBHR – Scottish Brain Health Register; CSF – cerebrospinal fluid; PDS – Post Diagnostic Support

Early Disease Detection and Expression Routine Clinical Care

- Risk profiling may reveal early stages of neurodegenerative disease.
- Those at higher risk will be assessed for biomarkers of neurodegenerative disease (disease detection)
 - Neuroimaging, cerebrospinal fluid, and blood biomarkers for $A\beta$ and p-tau
- Assessment for early disease expression will consist of
 - Cognitive assessment sensitive to *early* disease
 - Behavioural and neuropsychiatric evaluation
 - Gait/power and autonomic instability
- Brain Health Services will incorporate validated emerging technologies for early disease detection

amyloid-beta plaques

neurofibrillary tangles

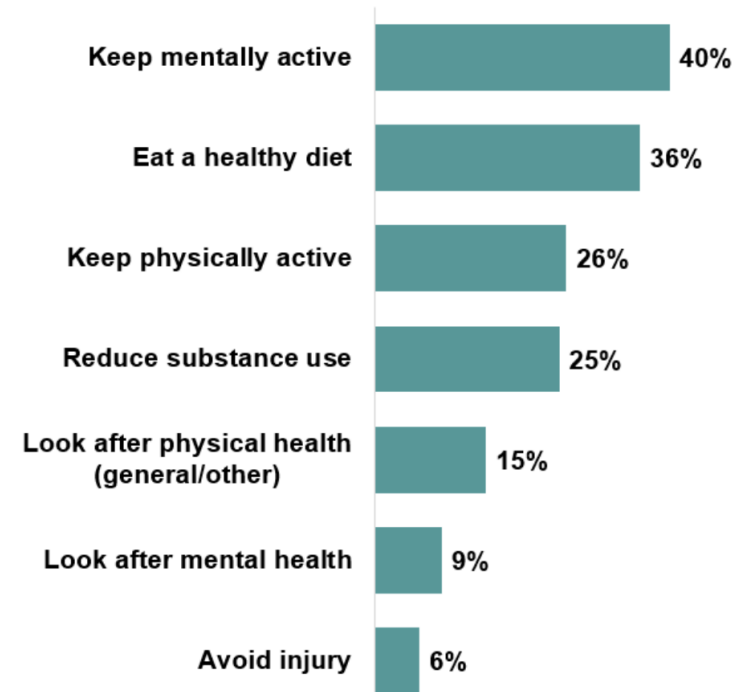
4th September 2020

Brain Health Survey 2020

**Ipsos MORI on behalf of Brain Health
Scotland**

Catriona Millar
Lorraine Murray

Figure 4 - There are several things that people can do (or avoid doing) to help protect their brain health in the future. Can you name any?



**Your brain is amazing.
Let's keep it that way.**

https://d6a732ea-0222-4f4e-bec4-6ac629ae59bc.filesusr.com/ugd/a3f95c_8826599c29c04d66b4eb266d5d887f22.pdf

Online Learning

Free Online Course

SPORT AND EXERCISE FOR BRAIN HEALTH

brainhealth.scot/sportscourse



 Brain Health
Scotland

Hosted & supported by
Alzheimer Scotland

- Free online courses
- Developed in response to calls from athletes



My Amazing Brain - Schools Programme



- **S:** Socialise and hobbies
- **T:** Tuck in!
- **A:** Active and healthy
- **R:** Rest and relax
- **S:** Safety



Education Lead
Dr Joanna Crispell



Primary Schools Programme

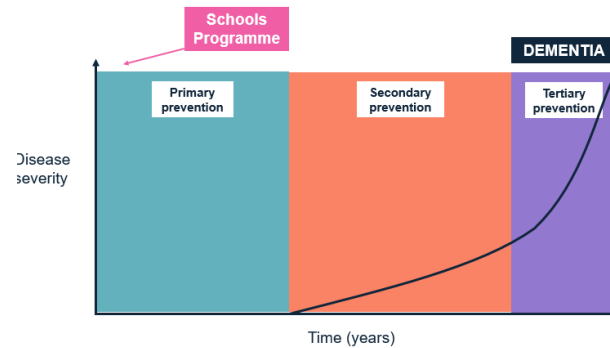
- Dedicated project with animations and supporting materials for teacher and children focussed on Brain Health.
- Launching September 2022



Earlier Brain Health Messaging



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Alzheimer Scotland





REST

Long term stress can be toxic for the brain and can make it difficult to keep on top of other things that are important for our brain health. So it's really important to make time for yourself, and the things that help you relax and switch off.

We also need to protect our sleep time. Your brain cleans itself while you sleep, flushing out waste products that build up through the day.

We should aim for a good quality 7-9 hours sleep every night. Not getting enough sleep can affect memory and thinking abilities in the short and the long term.

access practical advice and tips for improving our sleep routine. See thinkhealthy.org.uk

MEDICAL FITNESS

There are lots of medical conditions which can also have knock-on effects for the health of our brains. Such as those which affect the blood supply like high blood pressure, atrial fibrillation and diabetes. As well as conditions that can leave us more socially isolated such as hearing loss and depression.

So it's really important to keep on top of your overall health by attending regular check ups, picking up on any concerns early and following medical advice closely, including taking any medications as prescribed.

SOCIALISING & LEARNING

Your brain craves company and benefits from the stimulation of social interaction. We also know that if we continue to learn and challenge our brains throughout life we can build resilience to brain disease.

Try to pick up new skills and hobbies, things you haven't tried before. Be creative - learning a new language or a musical instrument can be a great way to keep sharp. Why not take up a new activity in a group or with a friend to keep motivated while also getting that added social benefit.

HARMS

Smoking causes damage to the blood vessels that supply the brain, interrupting the delivery of vital oxygen and nutrients. Stopping smoking, even later on in life, has been shown to reduce the risk of developing dementia.

You don't need to avoid alcohol completely. But exceeding recommended weekly limits for alcohol can damage the structure of the brain and increase our risks.

Get help to stop smoking at nhs.uk/stopsmoking

Calculate your weekly units at consta.acet

EXERCISE

Being physically active is one of the best things you can do for your brain. Regular exercise helps maintain a good blood supply to the brain, improves mental wellbeing and promotes good quality sleep.

There are lots of different ways you can choose to get more active. Whatever works for you, aim to get at least 3-4 hours of moderate intensity exercise a week.

What counts as "moderate exercise"?

BRISK WALKING GARDENING
RIDING A BIKE DANCING

FOOD

What you eat is crucial for supplying your brain with all the nutrients it needs.

Your diet is also very important for maintaining a healthy weight and avoiding conditions like high blood pressure and diabetes which can damage the brain.

Following a Mediterranean-style diet has been particularly linked to good brain health. This is a diet that uses olive oil as the main source of fat and includes:

LOTS OF: vegetables, fruit, beans & pulses, fish and wholegrains
NOT TOO MUCH: meat and sweet, sugary foods

Scan here & Discover more



Brain Health Scotland
Hosted & supported by Alzheimer Scotland

HOW'S YOUR BRAIN HEALTH?

Take the following quick quiz and build your personal Brain Health Plan

START QUIZ

Your brain is amazing.
Let's keep it that way.

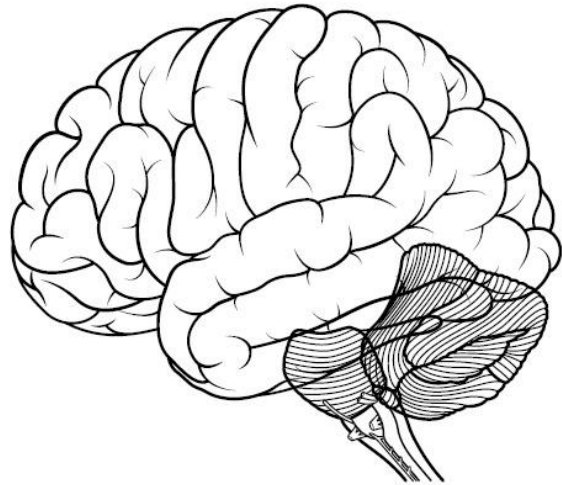
<https://brainhealthplan.brainhealth.scot/start>

Brain Health Pledges



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MY BRAIN HEALTH PLEDGE.



I WILL Get more sleep

HOW By turning off the TV
and reading in bed

WHEN Every night

WHERE At home

WITH My husband Alan

www.brainhealth.scot
www.alzscot.org

#MyBrainPledge



Step 1: Health Literacy

Step 2: Personal Pledges

Step 3: Review and observe positive feedback*

MY BRAIN HEALTH GOALS

You can use the topics covered in this guide, or other areas relevant to your brain health, to establish a series of goals.

Set goals which are realistic, timely and measurable. Completing goals along with someone else can also help keep aims fun and keep us motivated and on target.

Sharing your goals and your progress towards reaching them with others has also been shown to help!

I WILL

improve my diet

HOW

by swapping meat for fish

WHEN

three times a week

WHERE

at home

WHO WITH

my husband, John

Where do these actions take place?

On-line

Community Pharmacies

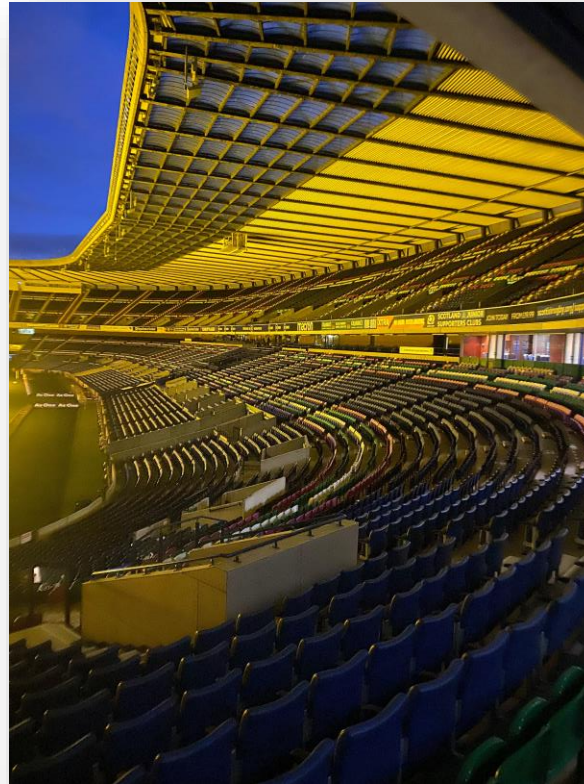
Libraries

Shopping Centers

Football/Rugby Stadiums

Workplaces

Schools



Touch Points with Sport and Exercise

- The PREVENT Research Programme
- The SPORTS and Exercise MOOC
- The BT Murrayfield Clinic

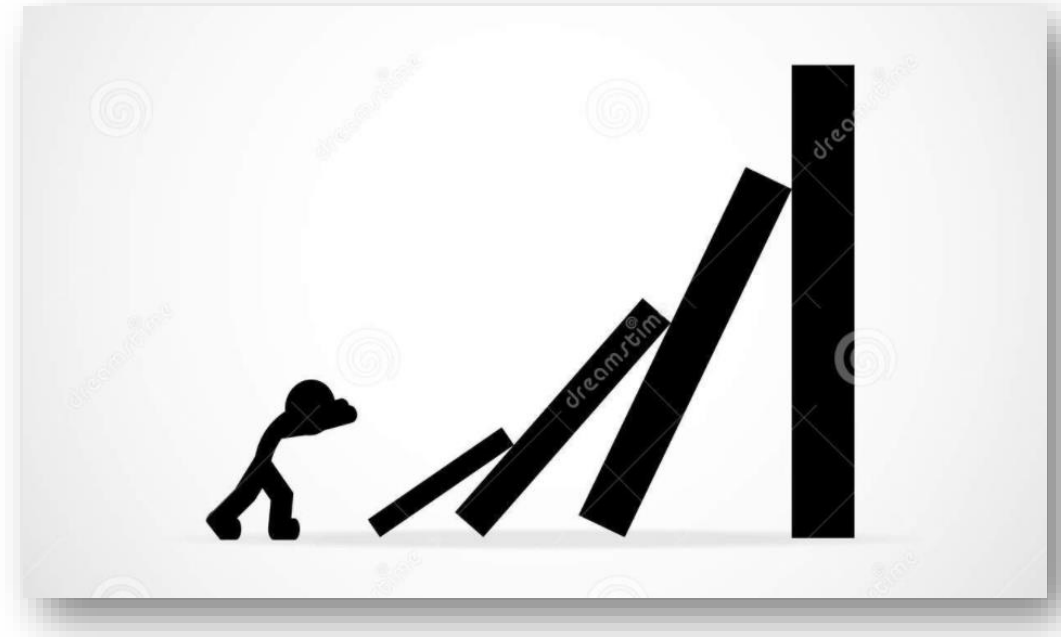


Touch Points with Technology

- Detection
 - Speech
 - Visuospatial/GPS
 - Gait/Accelerometers (Gum Shields)
 - Retinal Imaging
- Behavioural Change
 - Personal Pledges – static to dynamic
 - Health Literacy
- Interventions driven by Patient Specific Outcomes
 - Assistive technologies to maintain confidence and independence

Summary of presentation

- **Disease before dementia**
 - The research direction
- **The PREVENT Dementia Programme**
 - 700 Conversations since 2013
 - Scores now with retired elite athletes
 - Huge 'Thank You' to Alzheimer's Society for backing "Prevention" before anyone else did!!!
- **Brain Health Scotland**
 - Across Life-course and Multiple Audiences
 - Framework for clinical pathway
 - Context for specific work in Sports and Exercise Arena





Thank you