Brain Health Scotland

Brain Health Scotland –

Touchpoints with Technology

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Professor Psychiatry of Ageing
University of Edinburgh
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The University of Edinburgh

Alzheimer Scotland
Action on Dementia

Scottish Government
Riaghaltas na h-Alba
gov.scot

Overview of presentation

Brain Health Scotland

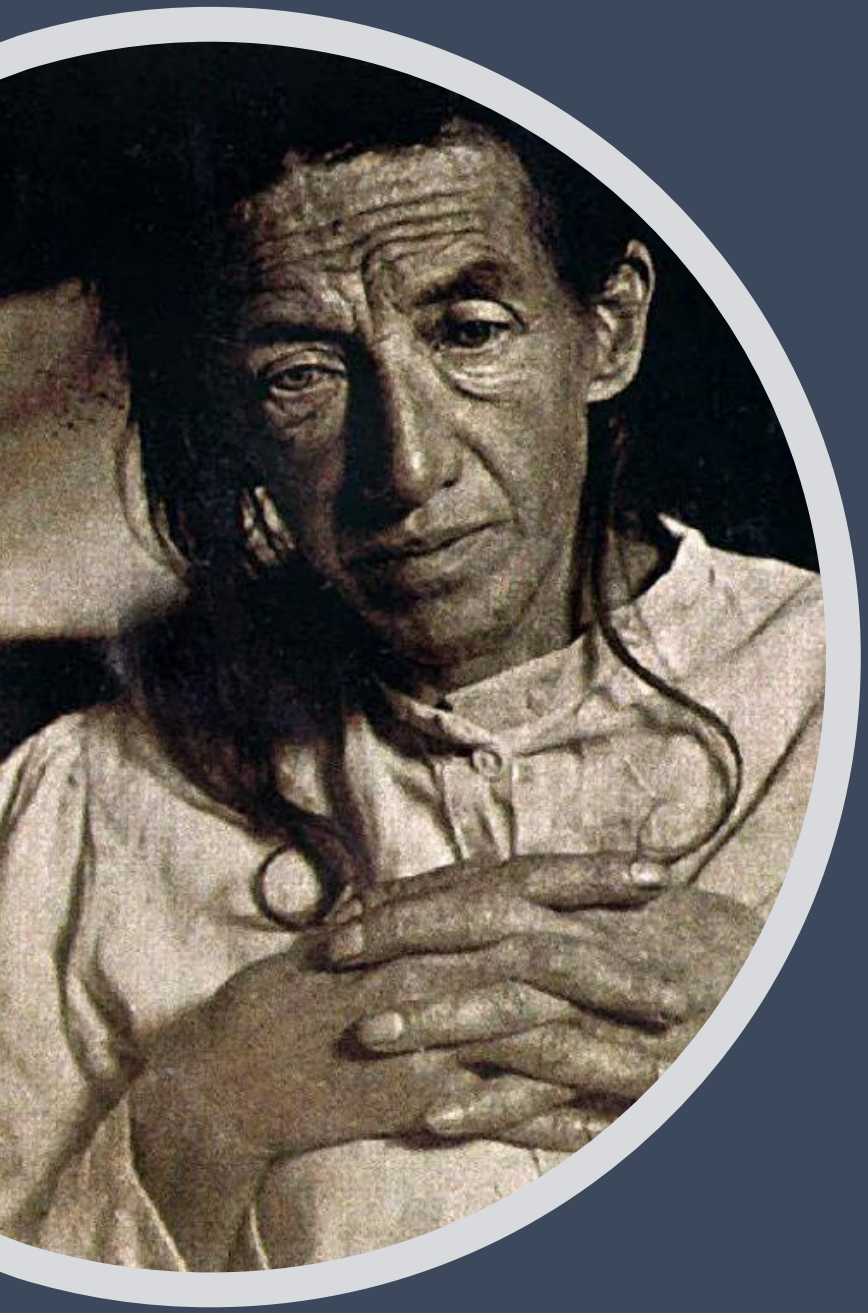
Disease before dementia

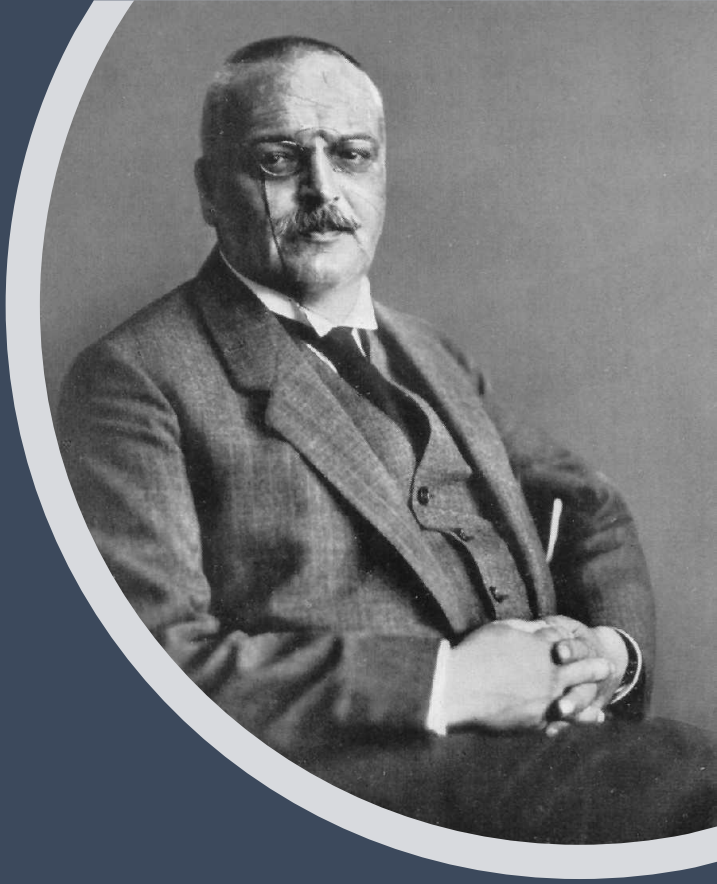
- The research direction
- PREVENT Dementia Measurement of a ‘relevant’ early pathology

Translation from Research into Practice (and back)

- The Brain Health Scotland ‘Ecosystem’

- Touch points for Technology





Alzheimer disease

Dementia

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- 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

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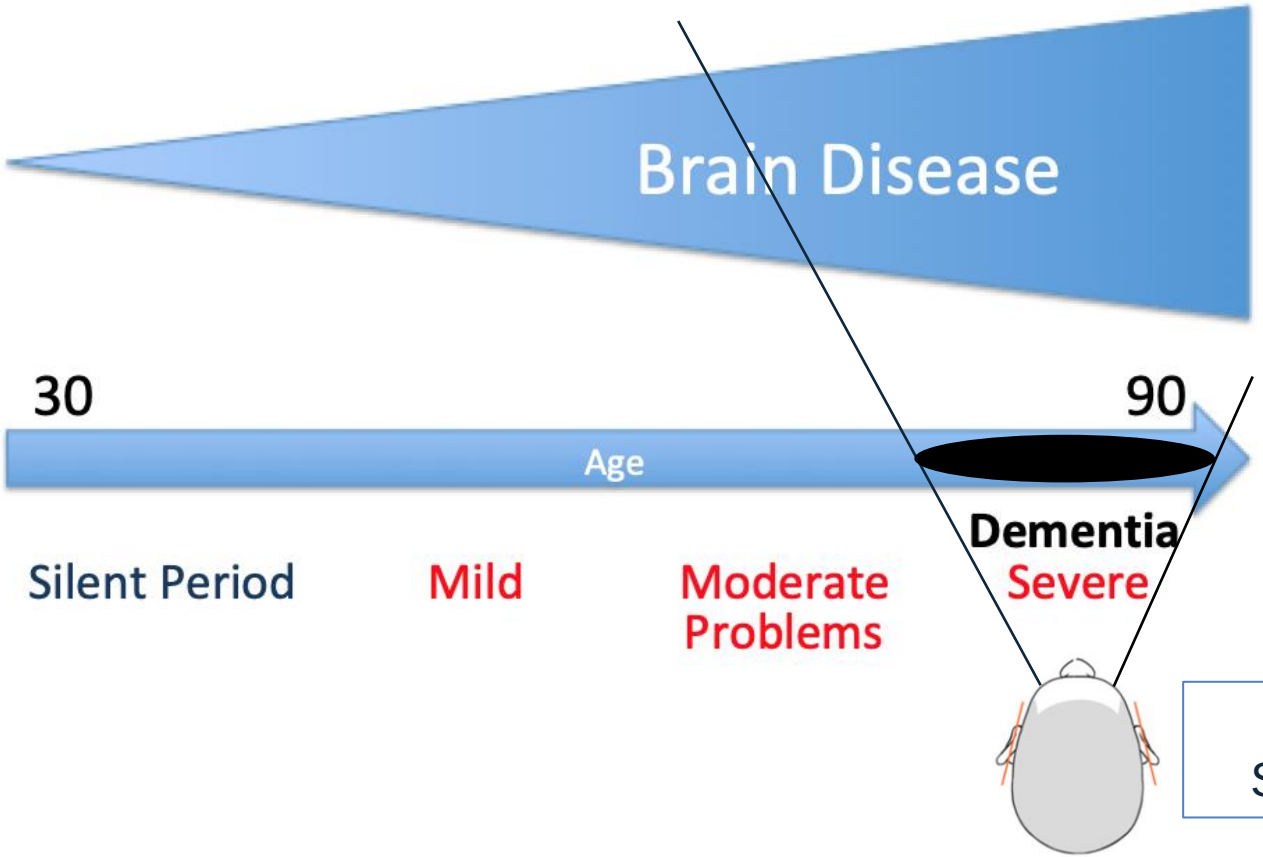
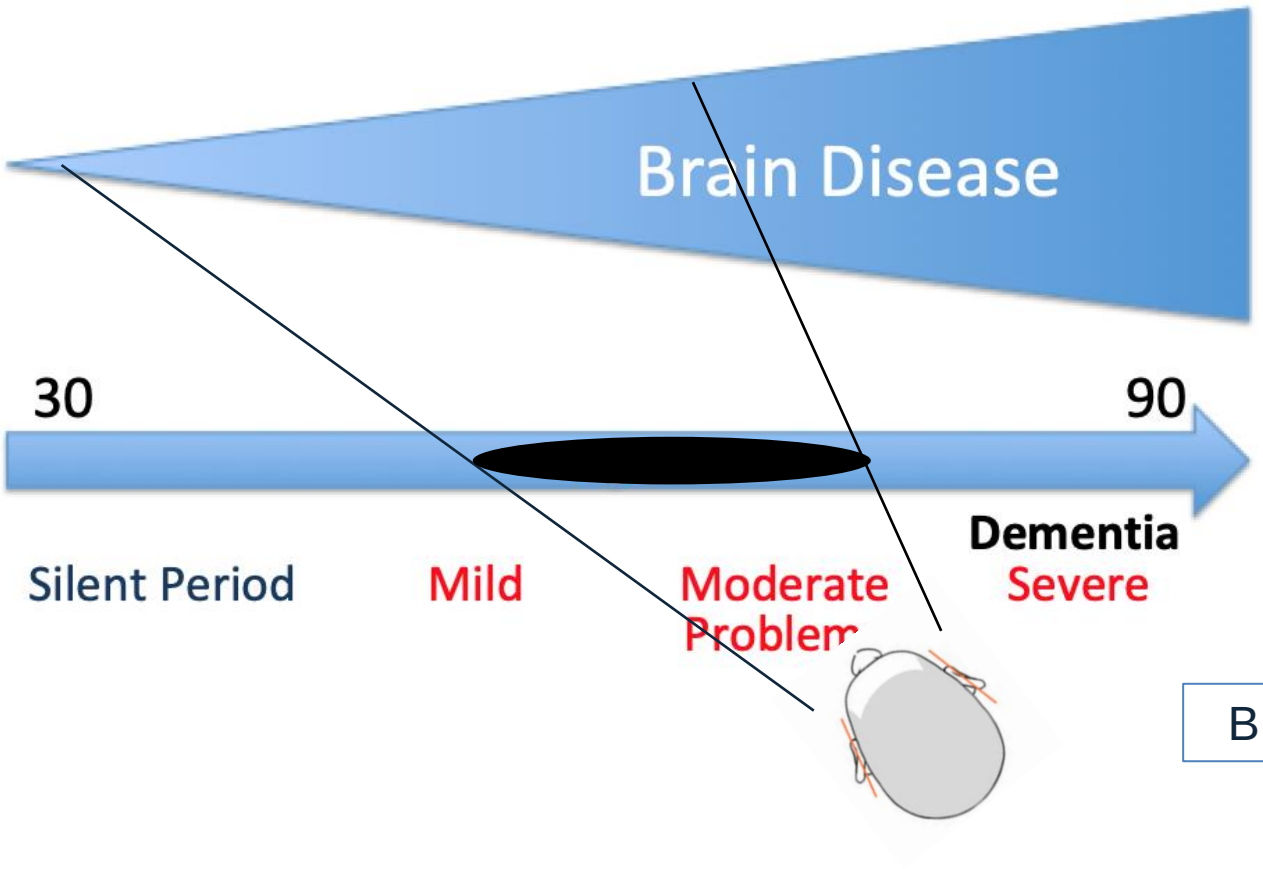
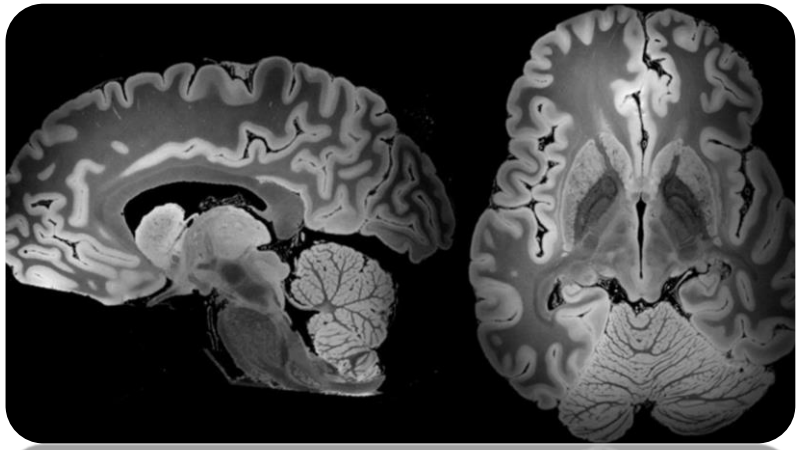


Detecting the Brain Changes Early

Brain Health Scotland





BIOMARKERS

Maintaining Brain Health = Dementia Prevention

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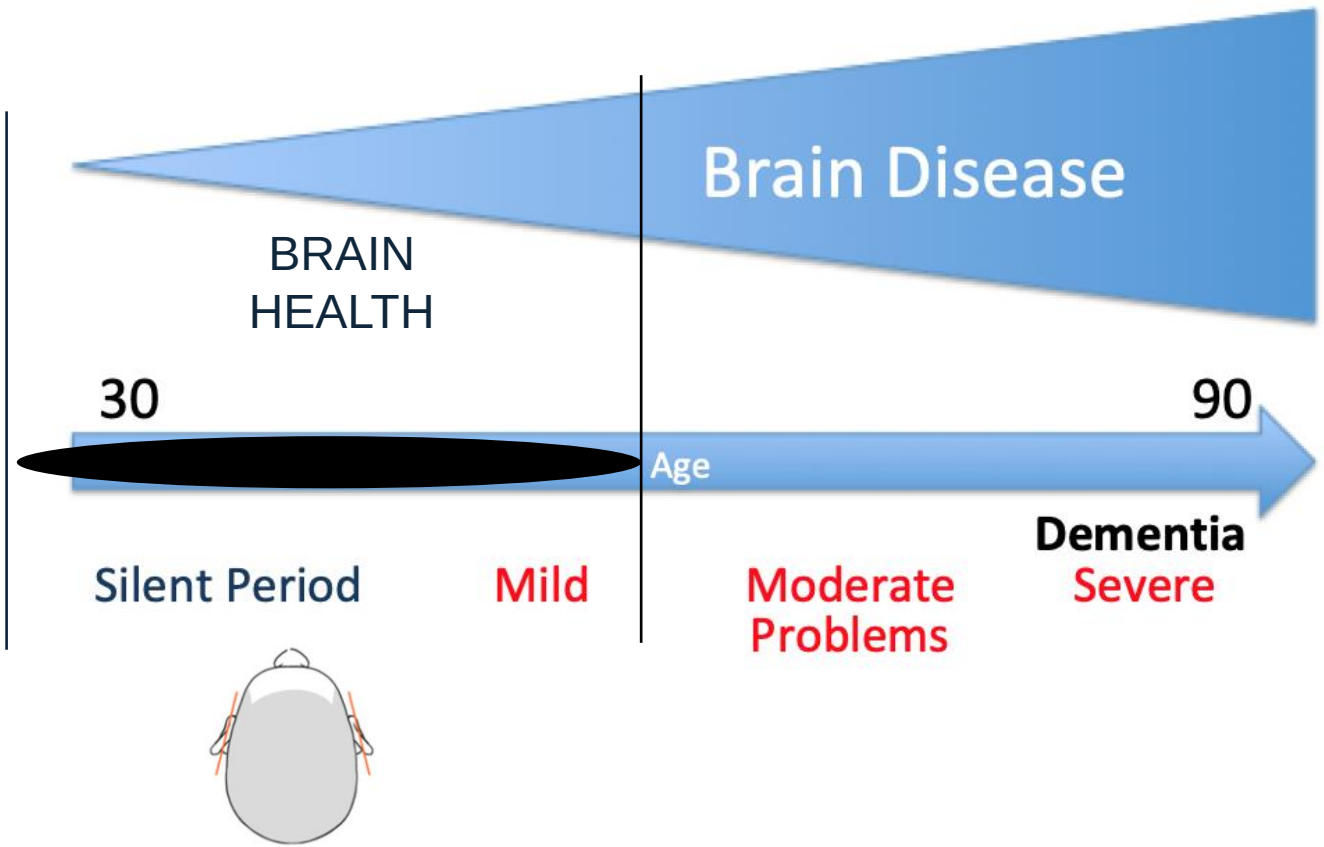
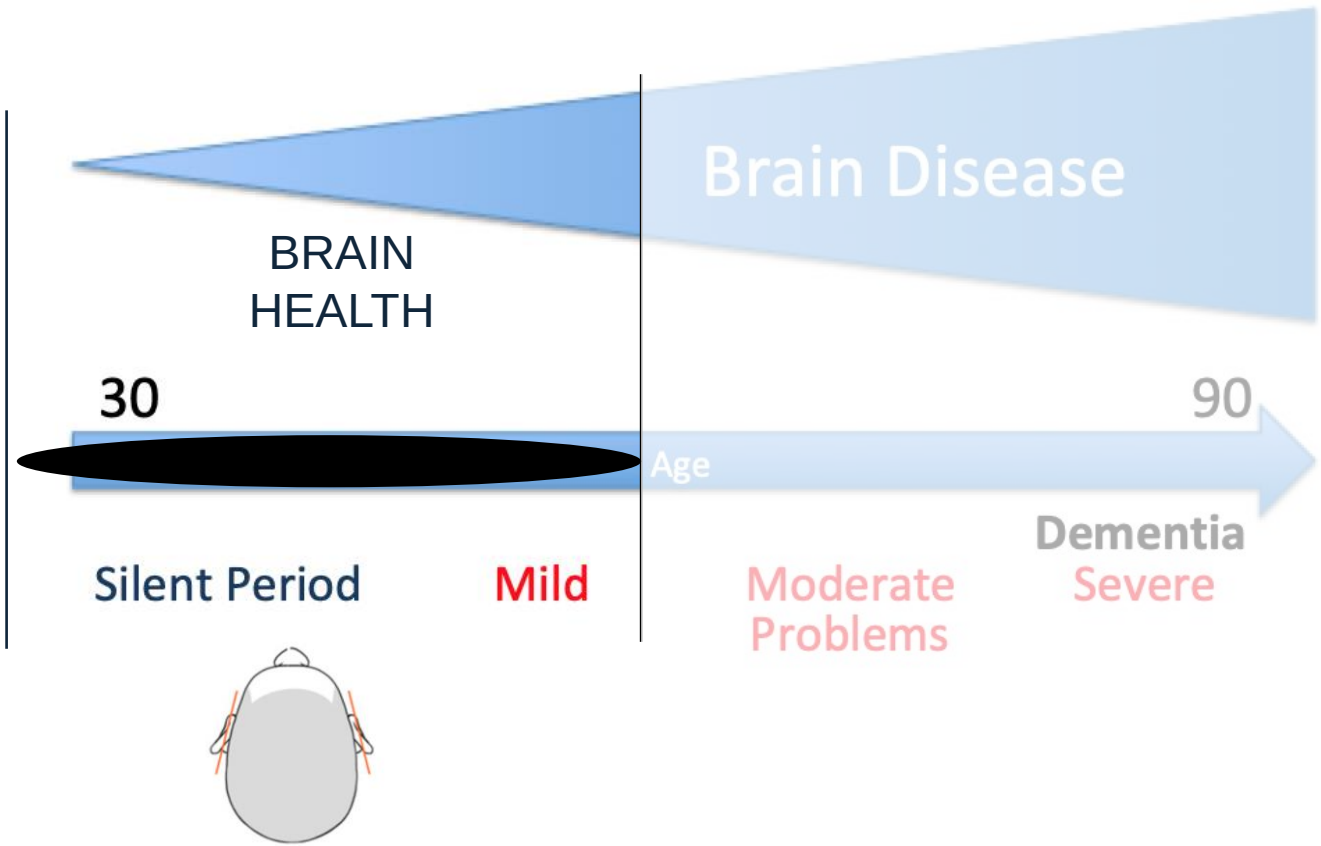


Maintaining Brain Health = Dementia Prevention

Brain Health Scotland



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

prevent dementia

UNIVERSITY OF CAMBRIDGE
Imperial College London
Inserm
THE UNIVERSITY of EDINBURGH
Trinity College Dublin
Coláiste na Tríonóide, Baile Átha Cliath
The University of Dublin
UNIVERSITY OF OXFORD

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	CED-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

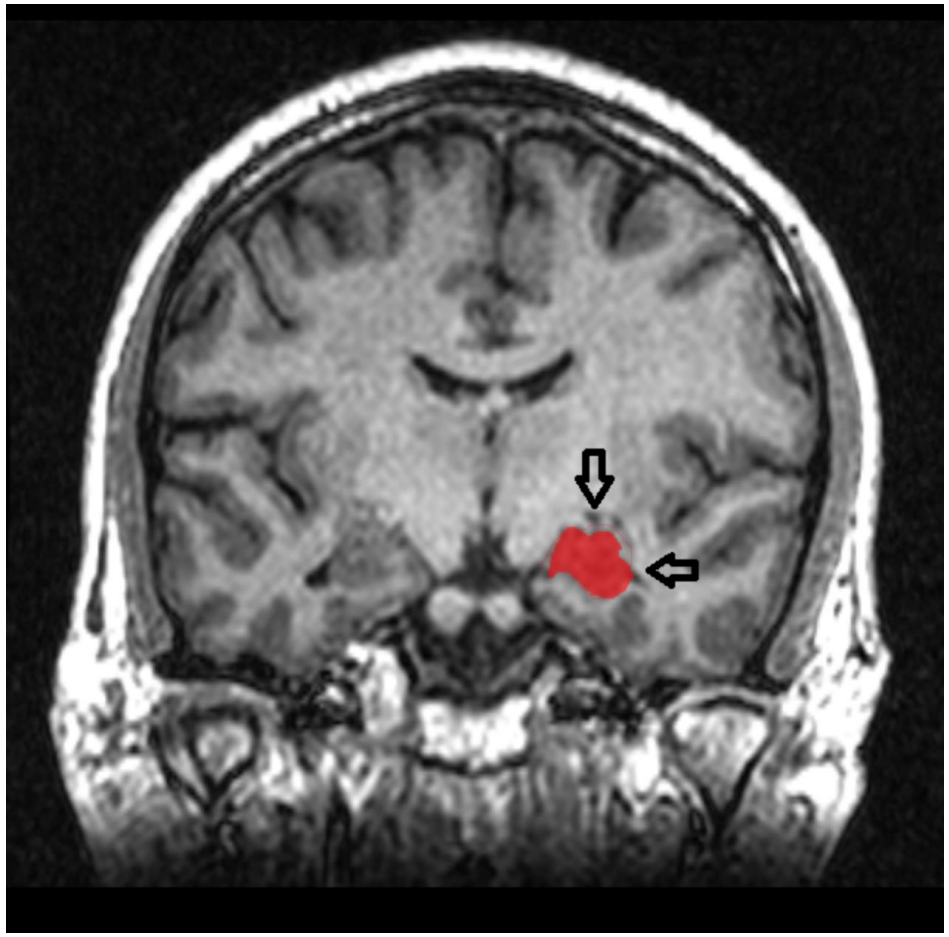
prevent dementia

UNIVERSITY OF CAMBRIDGE Imperial College London Inserm

THE UNIVERSITY of EDINBURGH Trinity College Dublin Coláiste na Tríonóide, Baile Átha Cliath The University of Dublin UNIVERSITY OF OXFORD

Alzheimer's disease 'starts' in the Hippocampus

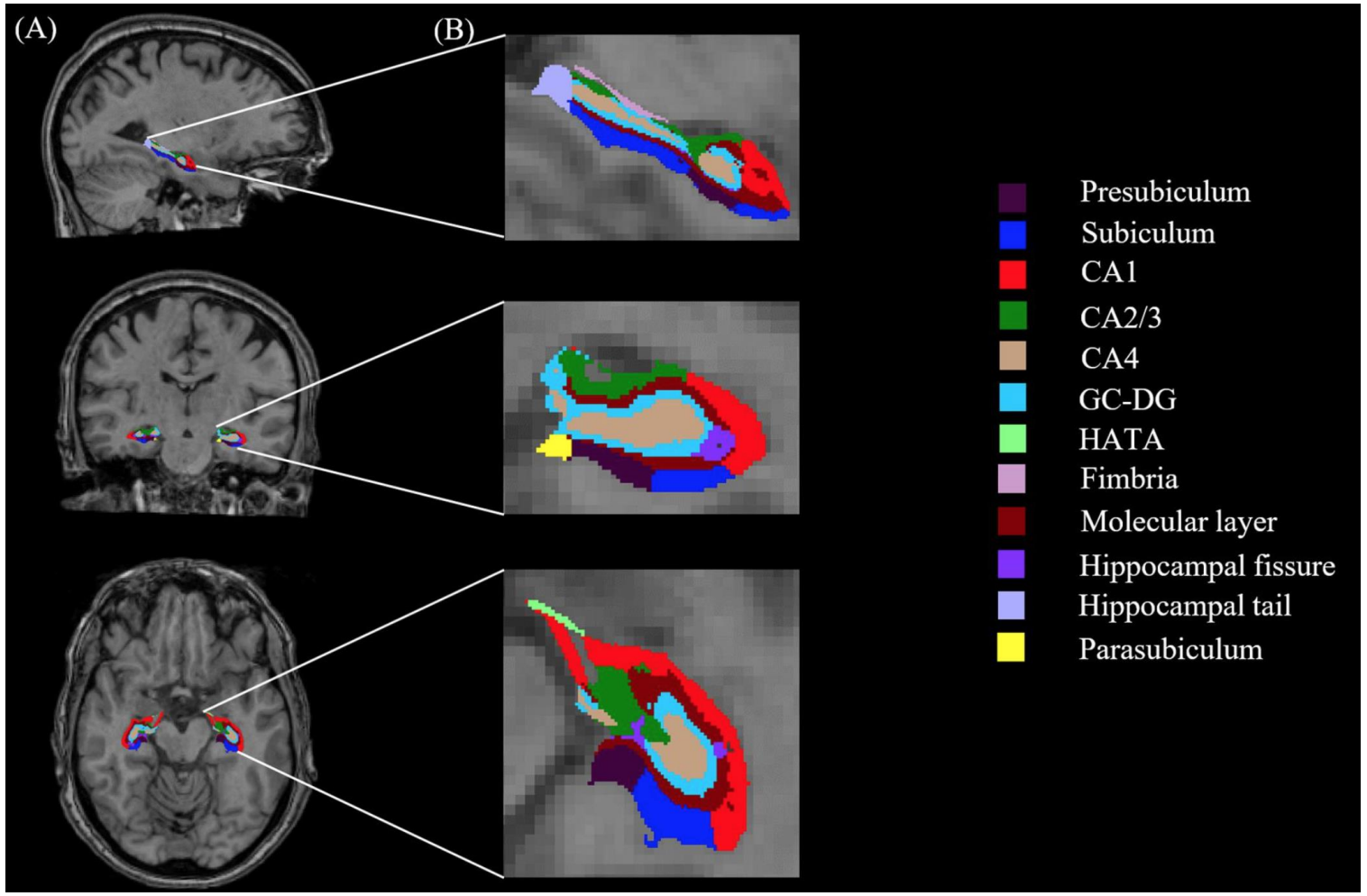
Testing the hippocampus….



Alzheimer's disease 'starts' in the Hippocampus

Testing the hippocampus….

Hippocampal Subfields….



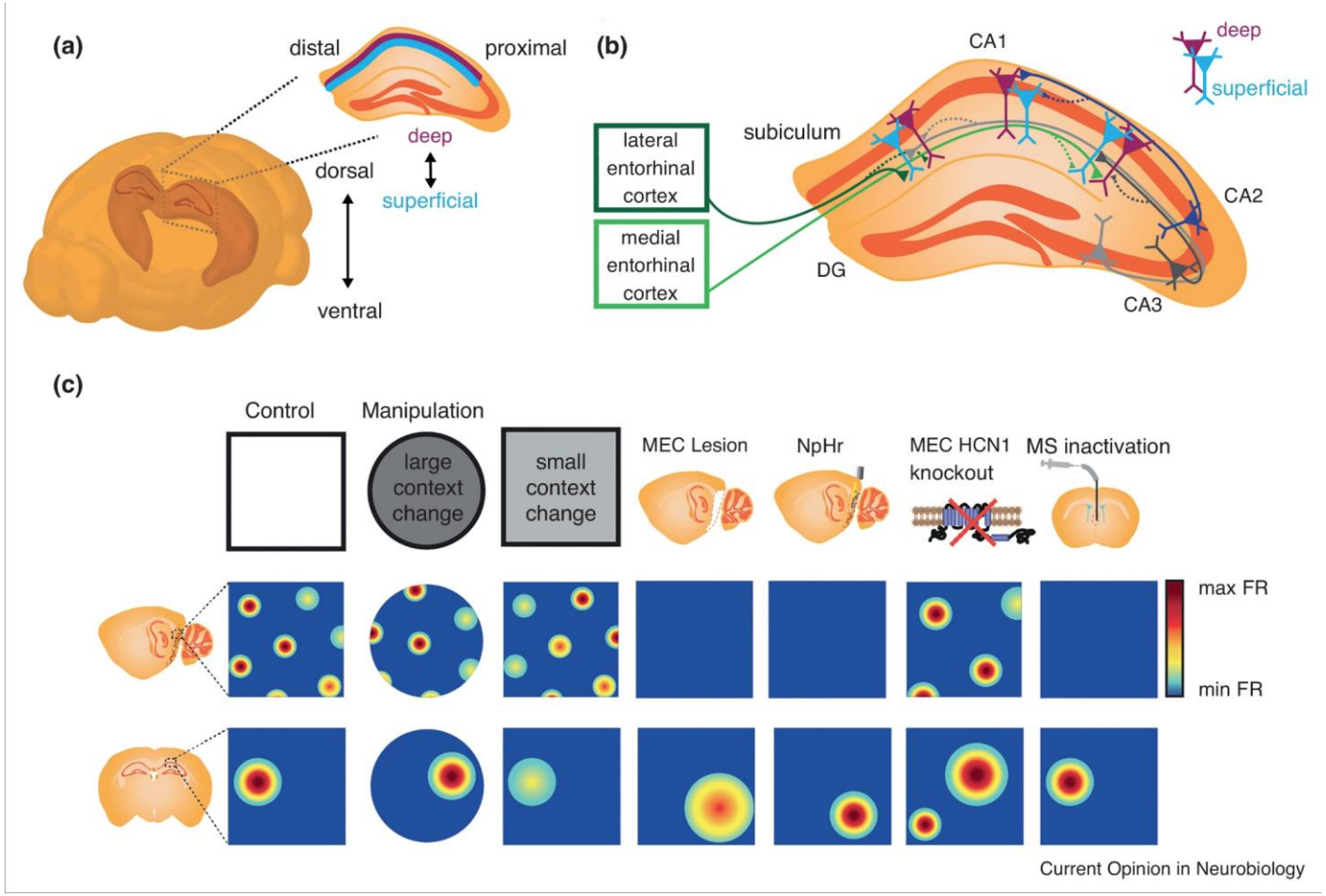
Can we detect neurodegenerative diseases at a stage their course can be impacted upon?

Alzheimer's disease 'starts' in the Hippocampus

Testing the hippocampus….

Hippocampal Subfields….

Hippocampal Place Cells….



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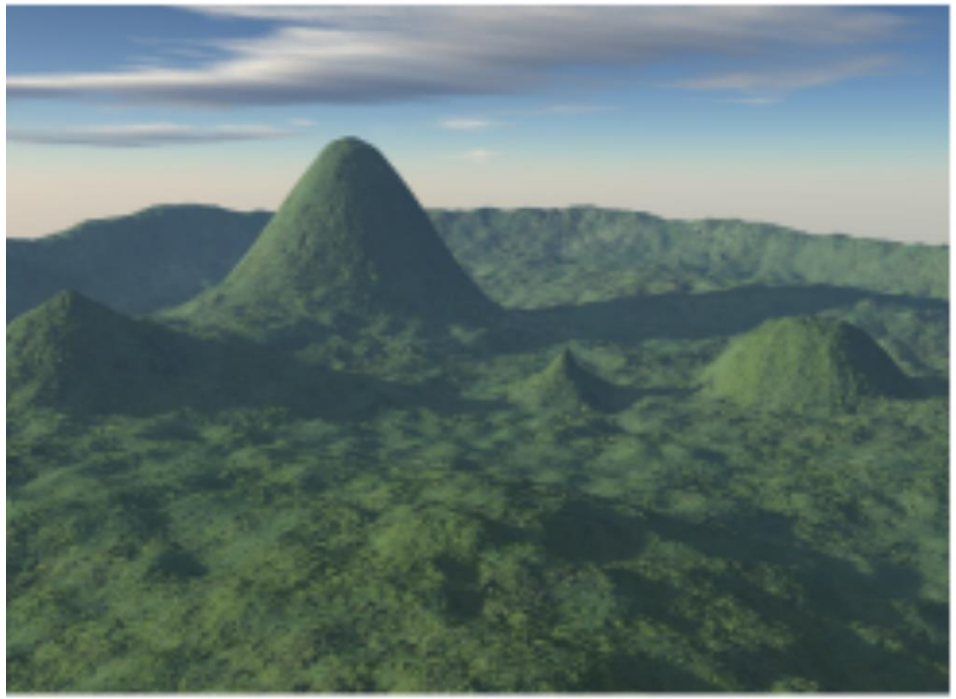

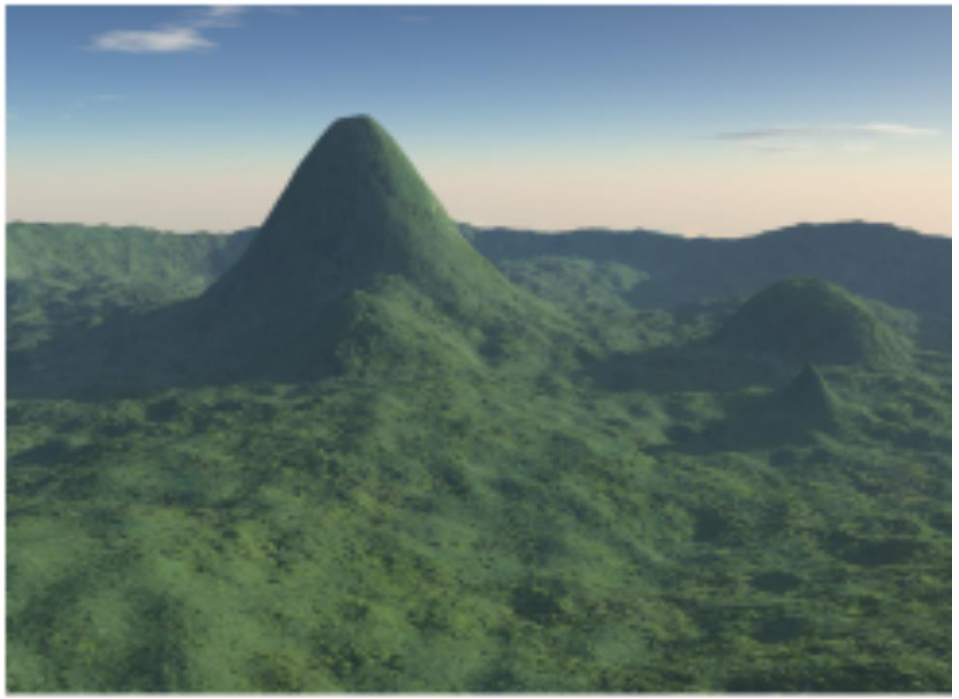

B

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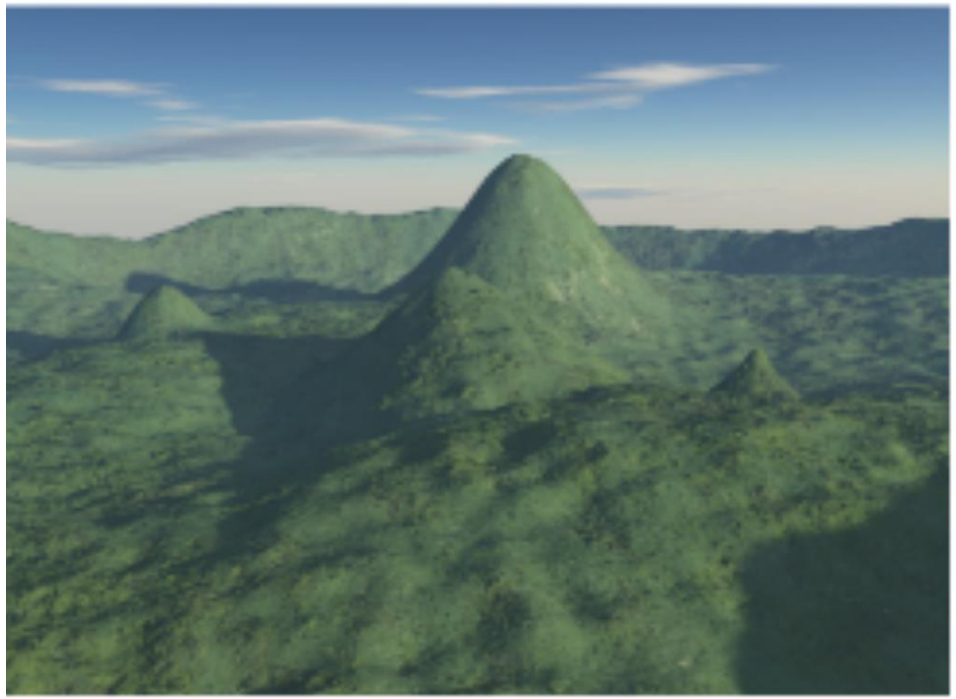
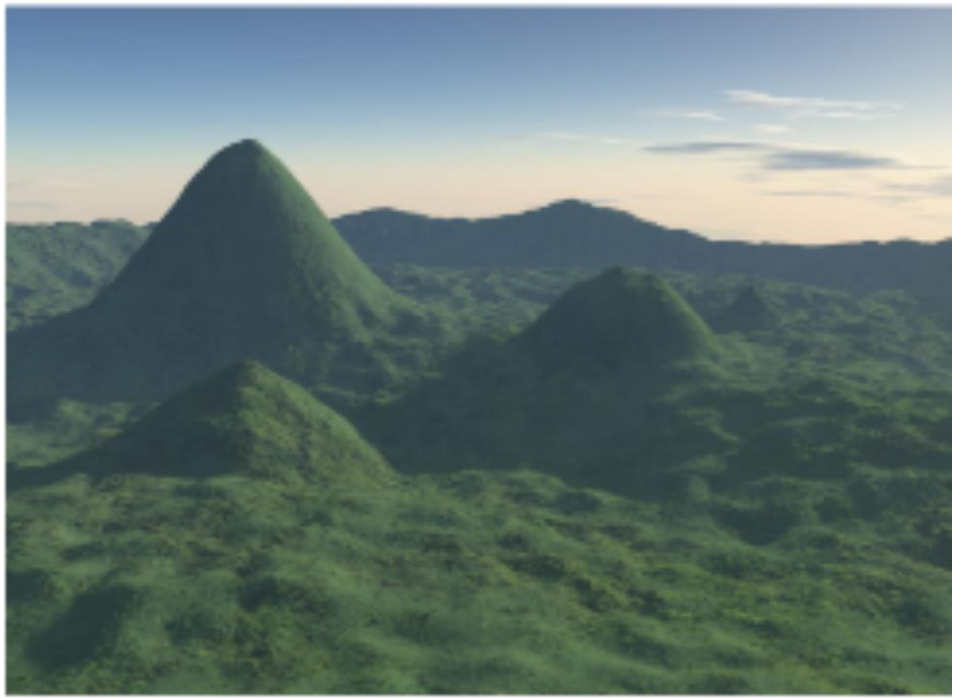
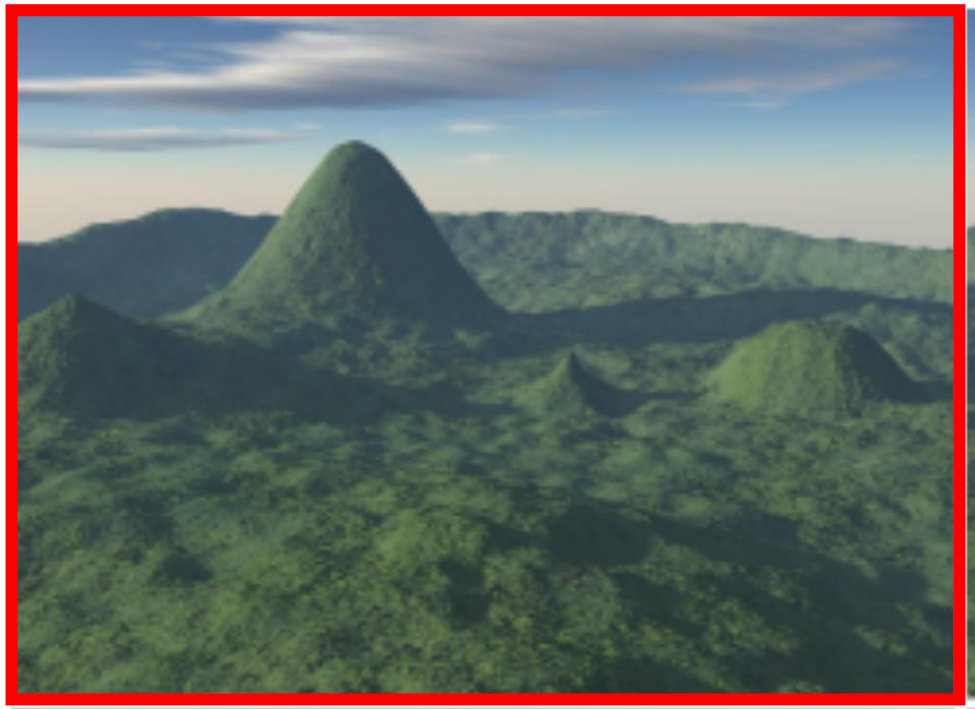




D

A



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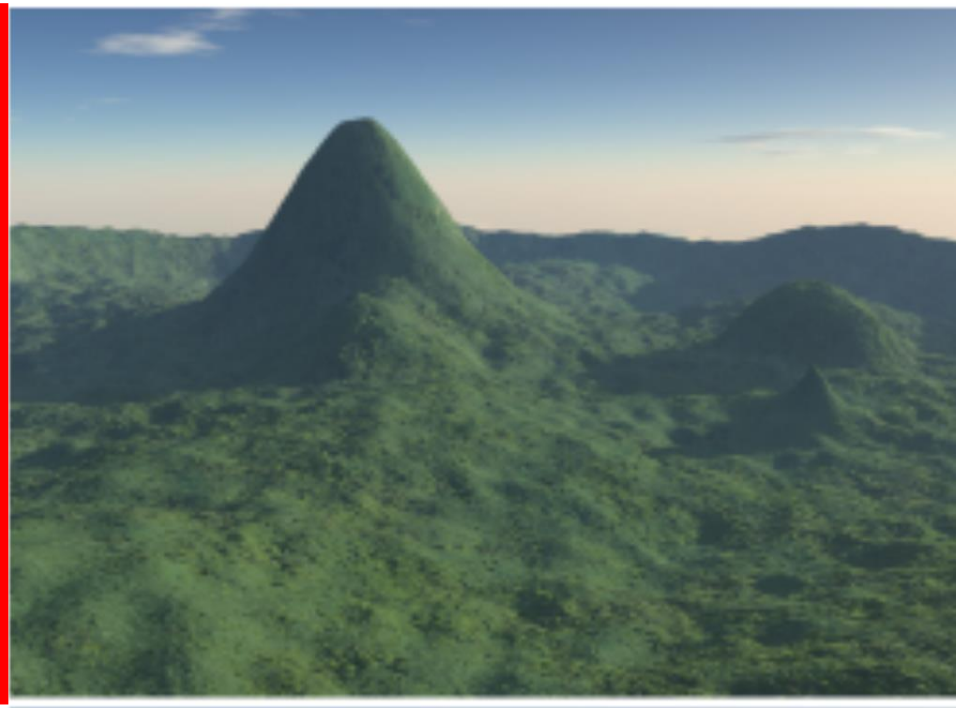

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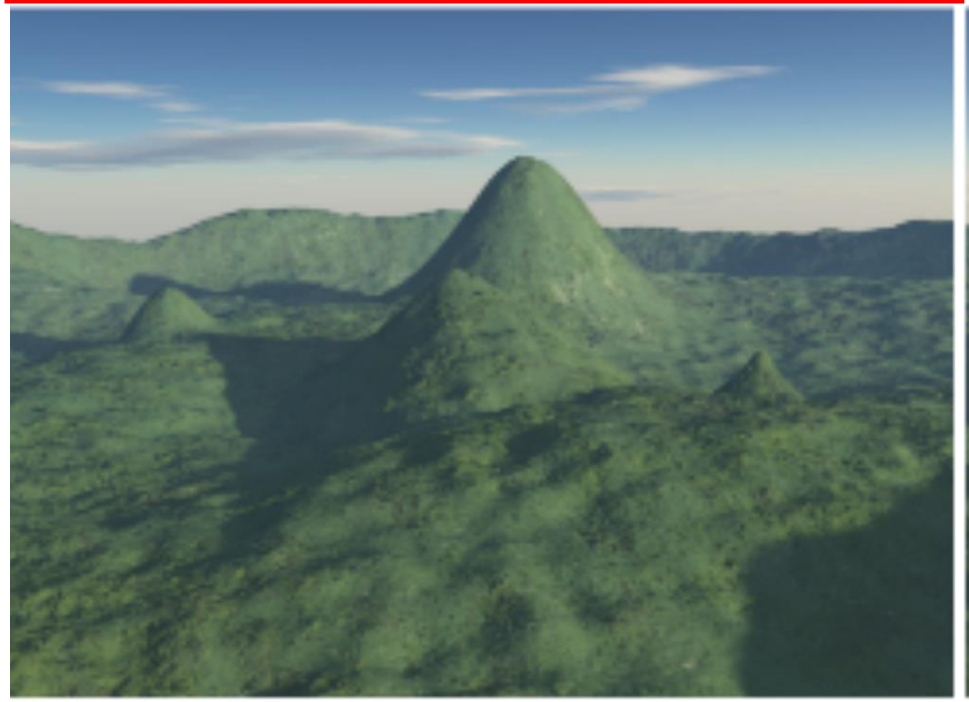

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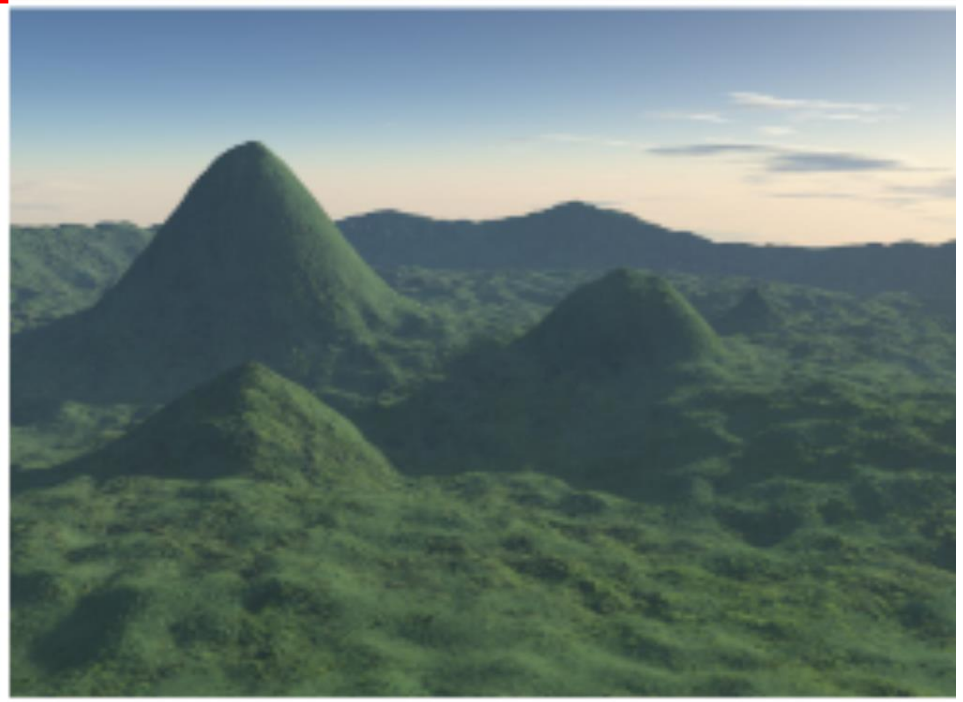


Can we detect neurodegenerative diseases at a stage their course can be impacted upon?

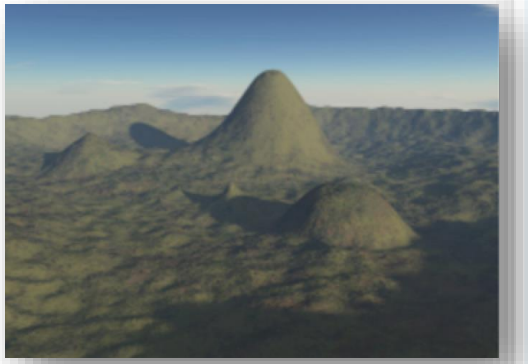
Alzheimer's disease starts in the Hippocampus

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]

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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
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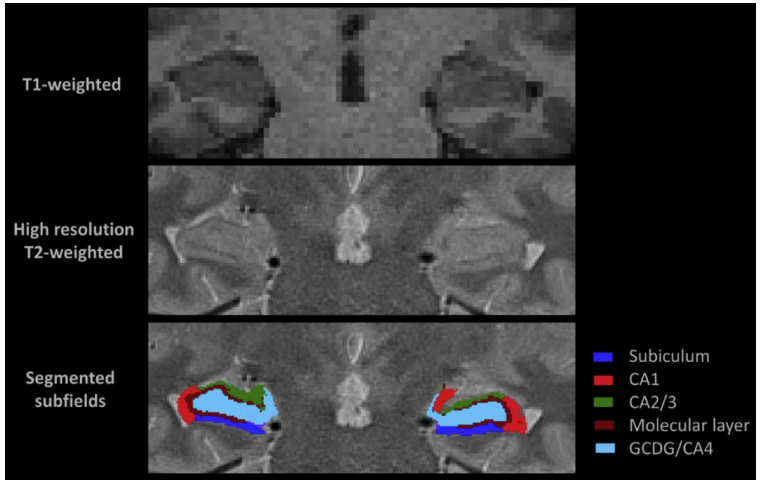
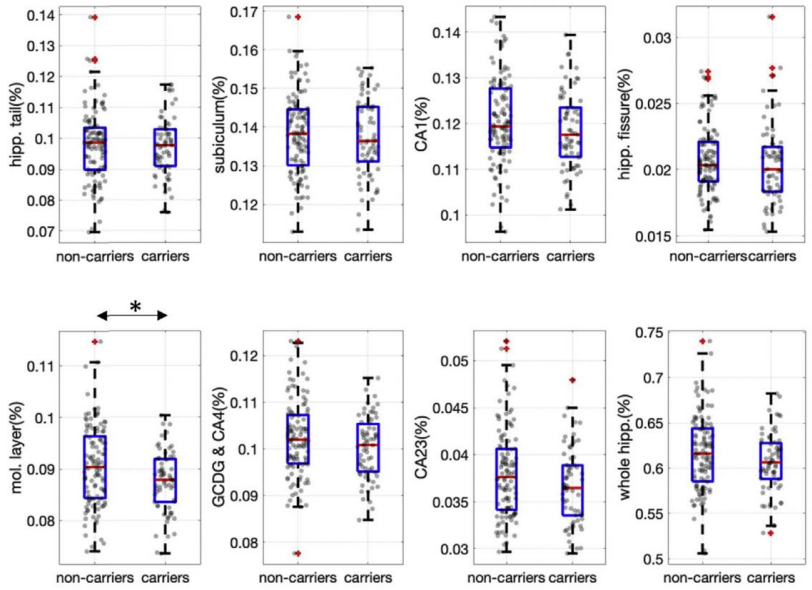
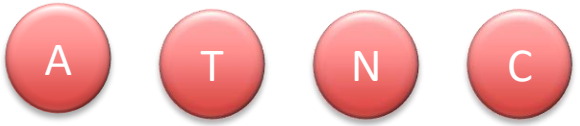


In PREVENT Dementia Cohort at Baseline (n=180) and 2-year FU (n=156): there was a significant association ($p<0.05$) between ApoEe4 status and atrophy of molecular layer of hippocampus. A region believed to be an early region for NFT build up (Braak and Braak, 1997l Thal, 2000)

APOE genotype



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 Aβ 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



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

Neurobiology of Aging 91 (2020) 36–44

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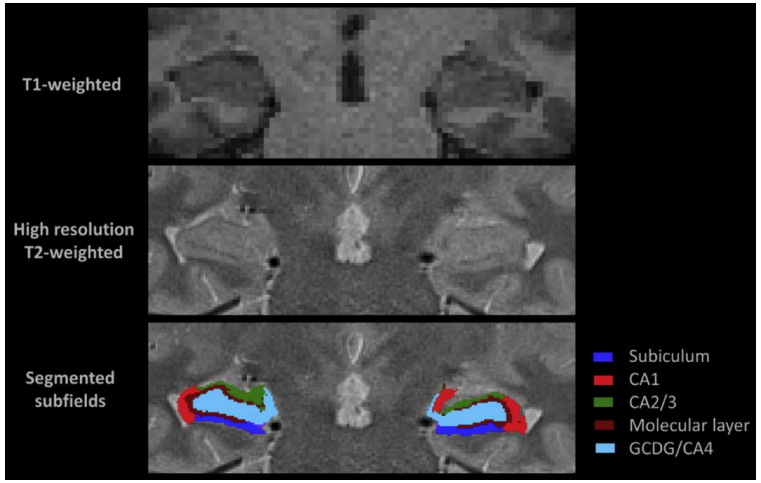

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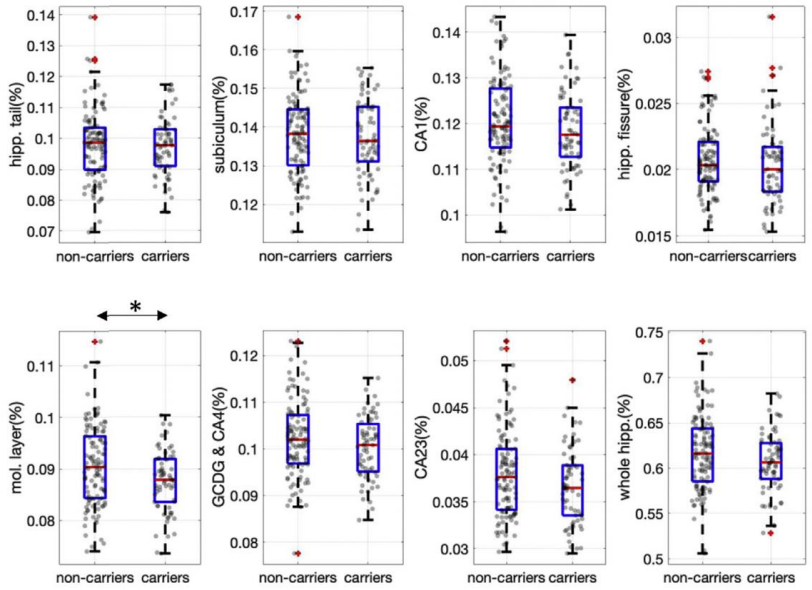

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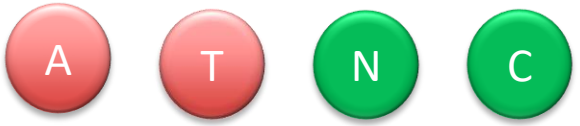


Now measurable in high-risk preclinical population in early 50's using sub-field MRI and correlated cognitive tests

Brain Health Scotland

Alzheimer Scotland
Action on Dementia

Scottish Government
Riaghaltas na h-Alba
gov.scot

Brain Health Scotland

Research into practice

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

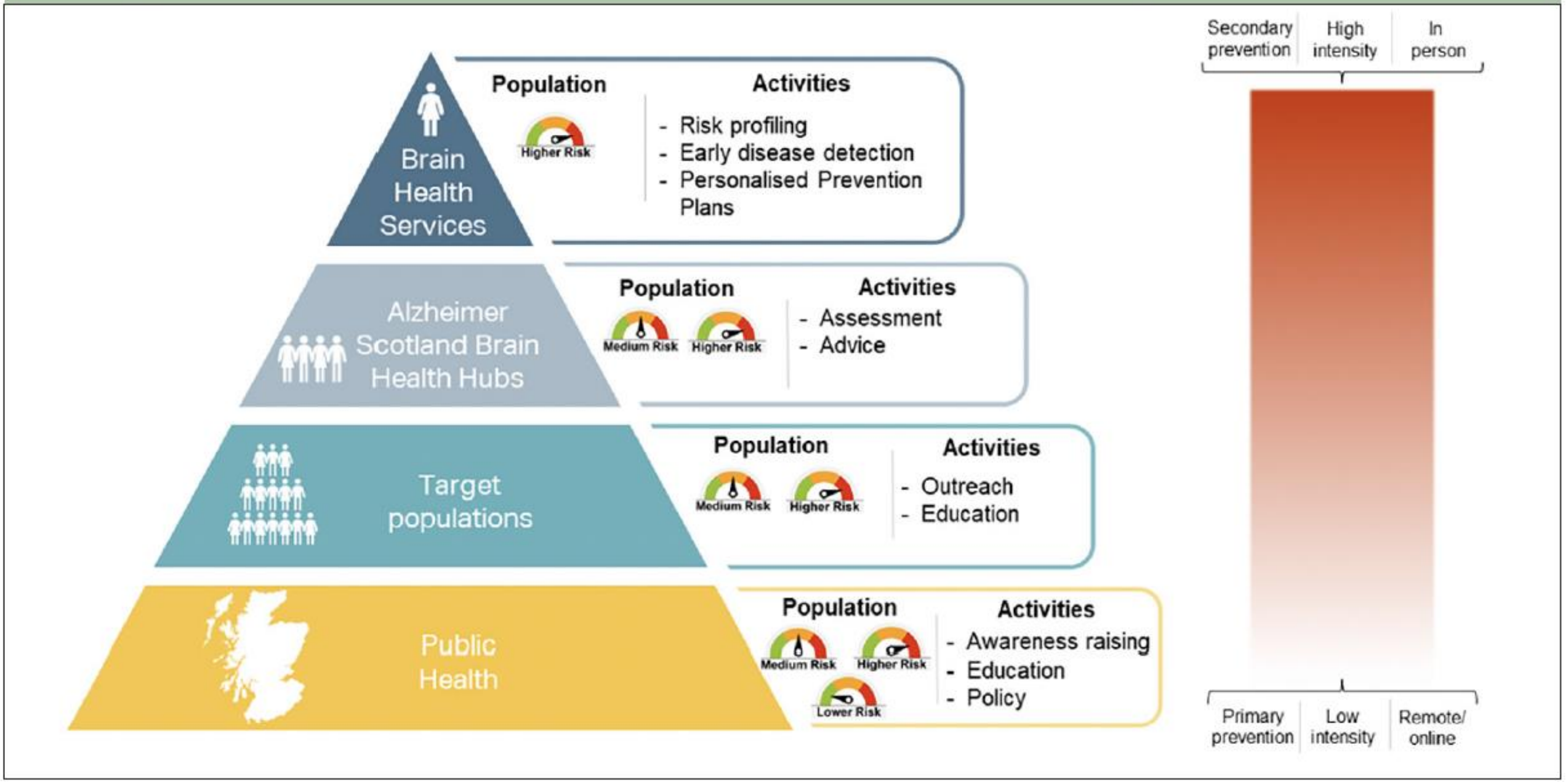
Anna Borthwick
Executive Lead
Brain Health Scotland

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

Henry Simmons
Associate Director
Brain Health Scotland
CEO Alzheimer Scotland


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

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

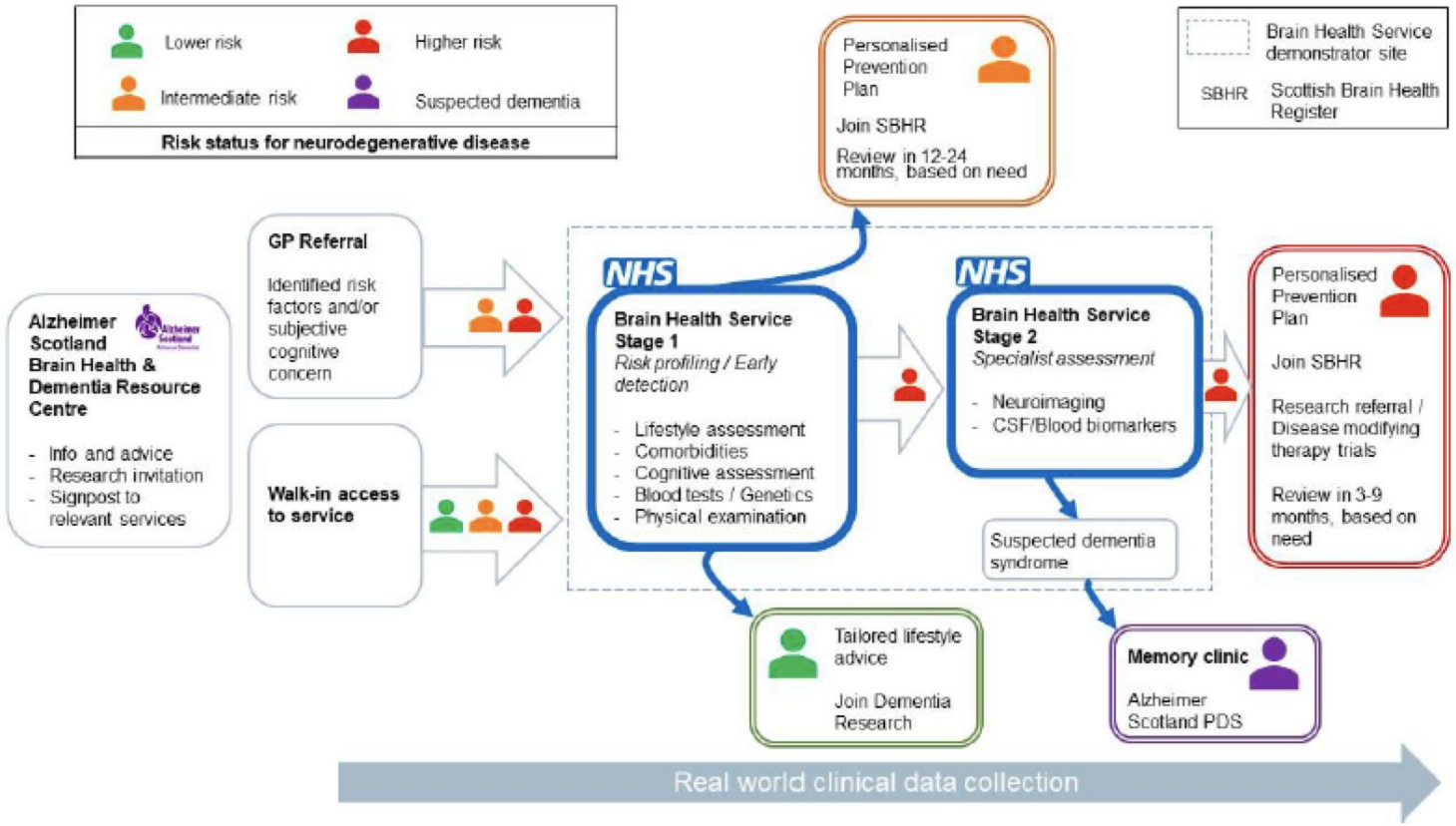
Review

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. Draper[2], A. Borthwick[2], N. Fullerton[2], M. Chantler[6], M.E. Porteous[1,3], S.O. Danso[1], A. Green[1], L. McWhirter[1], G. Muniz Terrera[1], S. Simpson[7], G. Thompson[1], D. Trépel[8,9], T.J. Quinn[7], A. Kilgour[1,2]

1. University of Edinburgh, 2. Brain Health Scotland, 3. NHS Lothian, 4. University of Aberdeen, 5. NHS Forth Valley, 6. Herriot Watt University, 7. University of Glasgow, 8. University of Dublin Trinity College, 9. Global Brain Health Institute, United Kingdom

Corresponding Author: Prof. Craig Ritchie, University of Edinburgh, United Kingdom, craig.ritchie@ed.ac.uk



Step 1
Pack
Completed

Step 2
Clinic Visit

Step 3
Brain Scan

Step 4
Review &
Personalized
Plan

NHS SCOTLAND

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

SCOTTISH RUGBY

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.

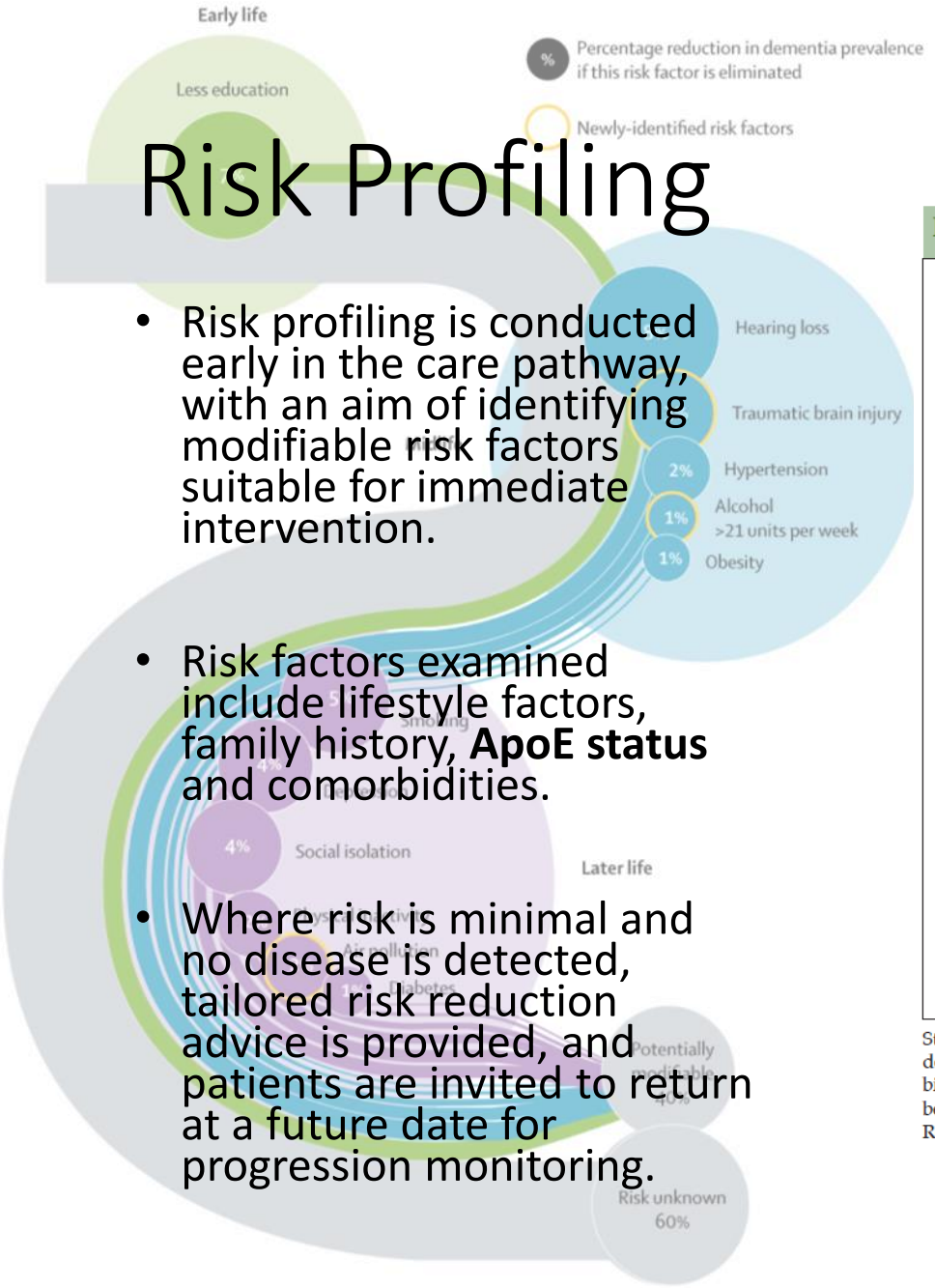
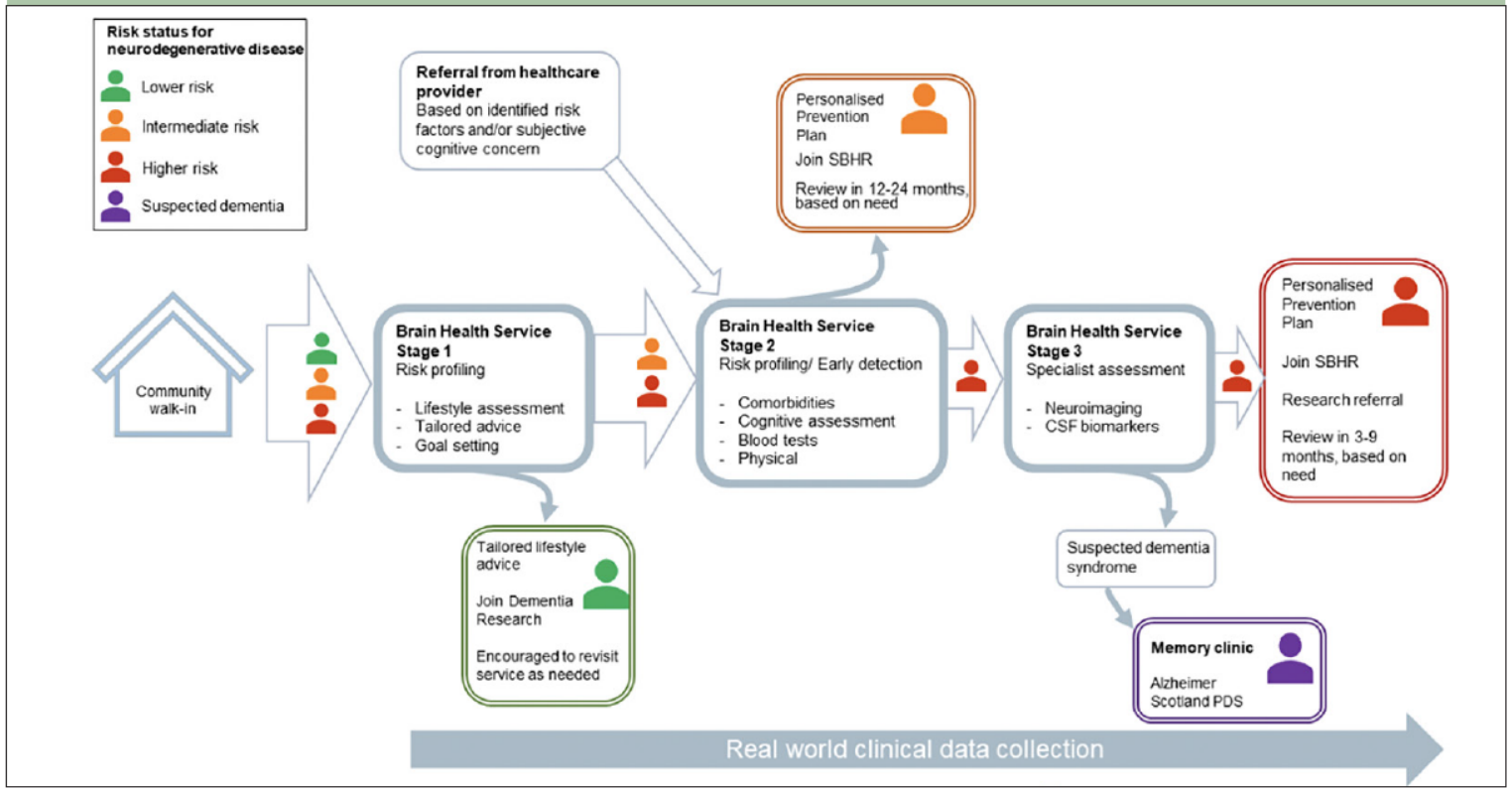


Figure 2. Care pathway for the Scottish model of Brain Health Services

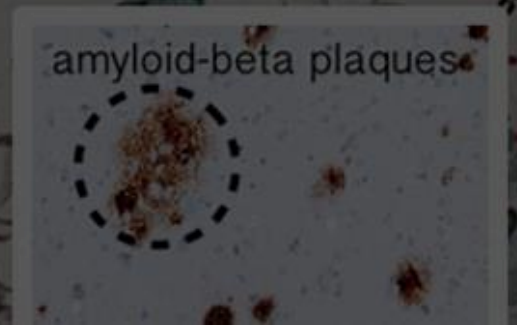


Stage 1: generic, non-clinical support (advice, light-touch lifestyle assessment, information and signposting). Stage 2: initial clinical service (risk profiling, early disease detection, personalised prevention. Parallel referral to external services for management of comorbidities where appropriate). 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

Livingston G, Huntley J, Sommerlad A, et al. Dementia prevention, intervention, and care: 2020 report of the *Lancet* Commission. *The Lancet* 2020.

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 **Aβ** 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



Brain Health Scotland

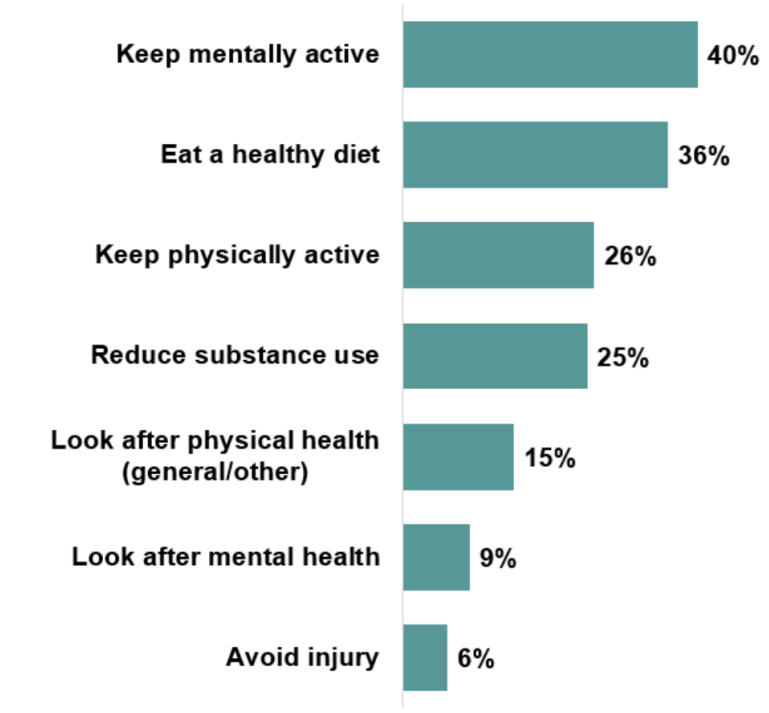
4th September 2020

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 courses
- Developed in response to calls from athletes

University of Glasgow
Trinity College Dublin
The University of Dublin
THE UNIVERSITY of EDINBURGH
GLOBAL BRAIN HEALTH INSTITUTE

My Amazing Brain - Schools Programme

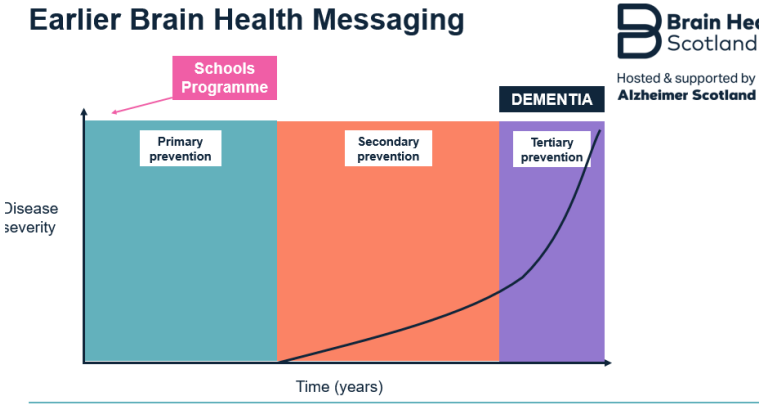
- **S:** Socialise and hobbies
- **T:** Tuck in!
- **A:** Active and healthy
- **R:** Rest and relax
- **S:** Safety

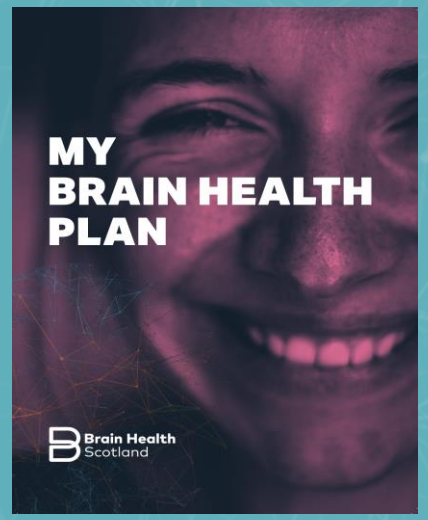
Education Lead
Dr Joanna Crispell

BRODIES LLP

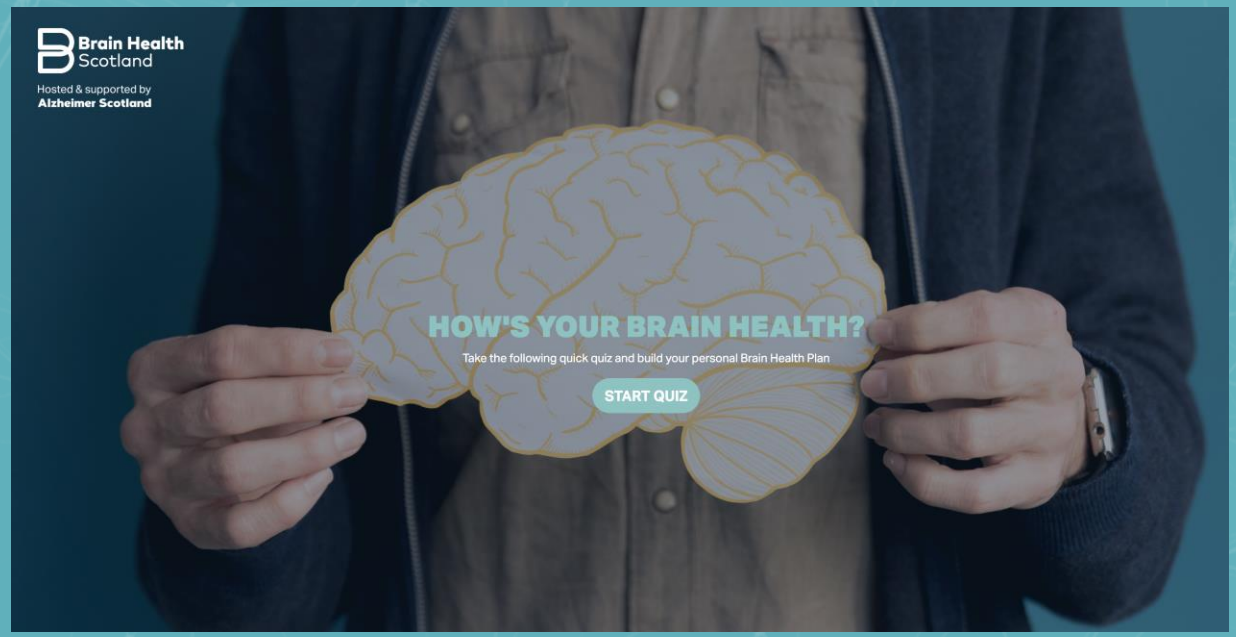
Primary Schools Programme

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





Brain Health Scotland



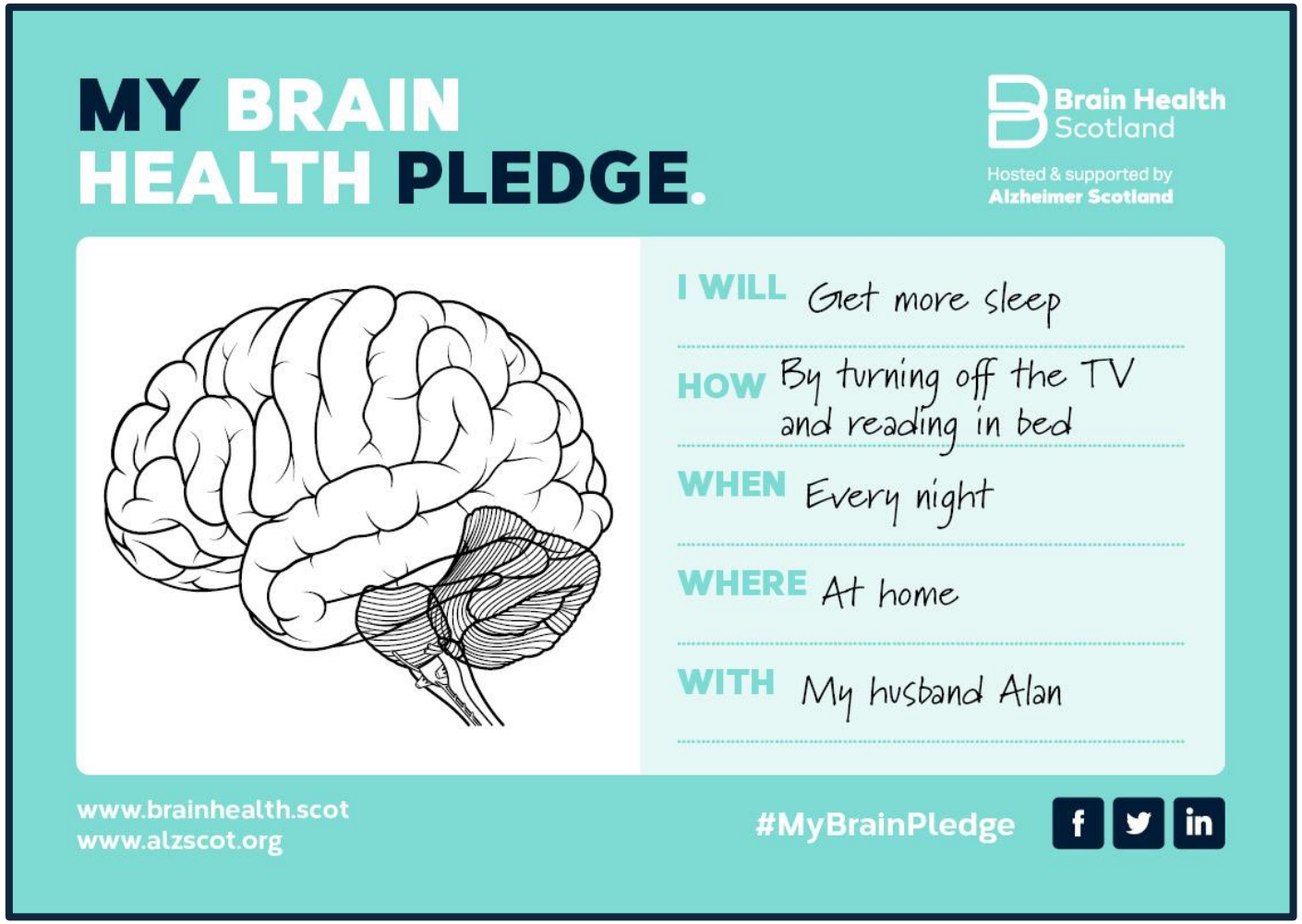
Your brain is amazing. Let's keep it that way.

https://brainhealthplan.brainhealth.scot/start

Brain Health Pledges

Brain Health Scotland

Hosted & supported by
Alzheimer Scotland



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

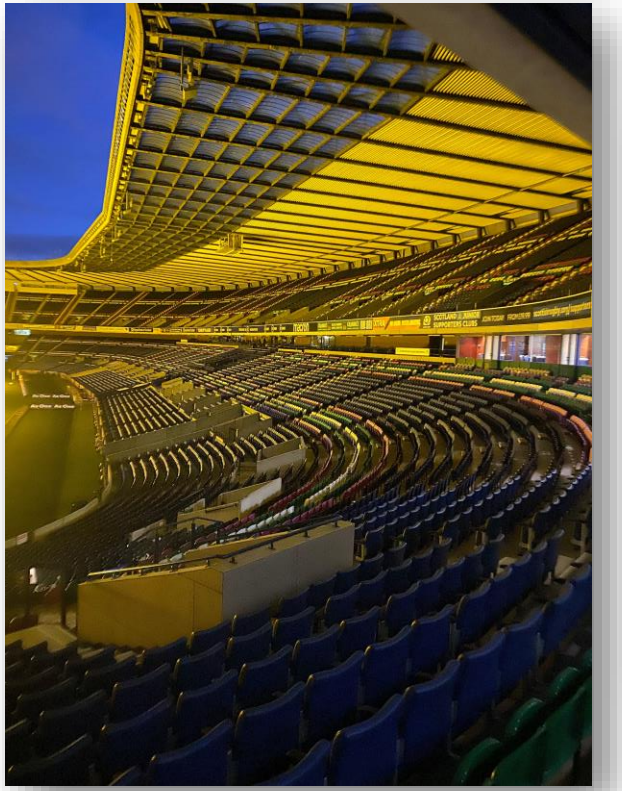
WHEN three times a week

WHERE at home

WHO WITH my husband, John

Where do these actions take place?

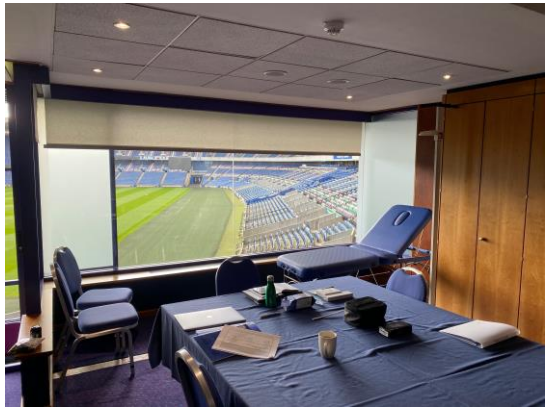
- On-line
- Community Pharmacies
- Libraries
- Shopping Centers
- Football/Rugby Stadiums
- Workplaces
- Schools



Touch Points with Sport and Exercise

Brain Health Scotland

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



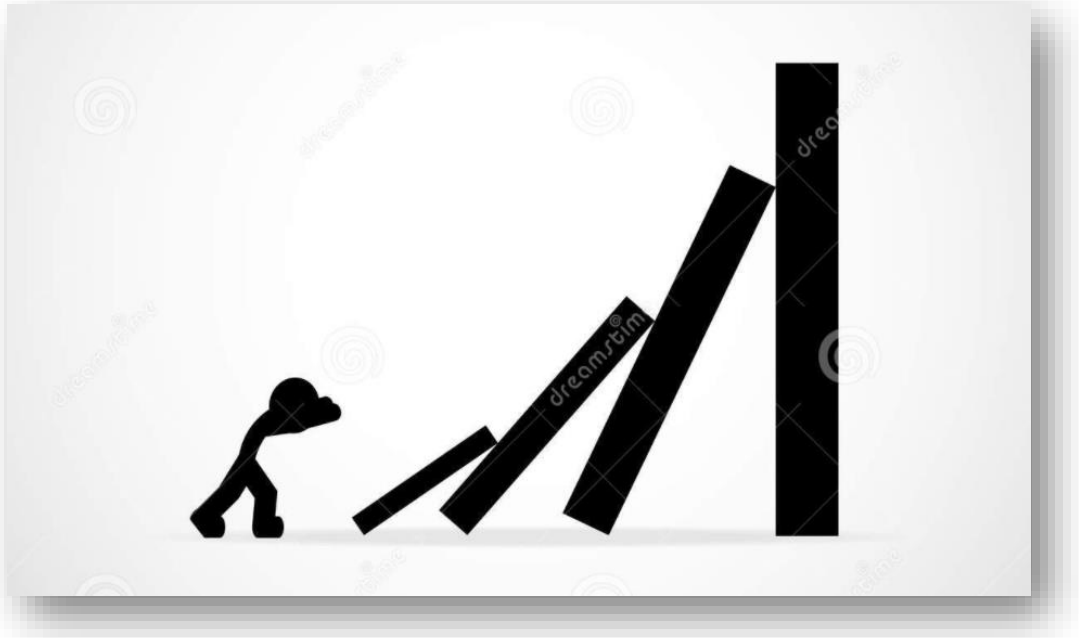
Touch Points with Technology

Brain Health Scotland

- 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