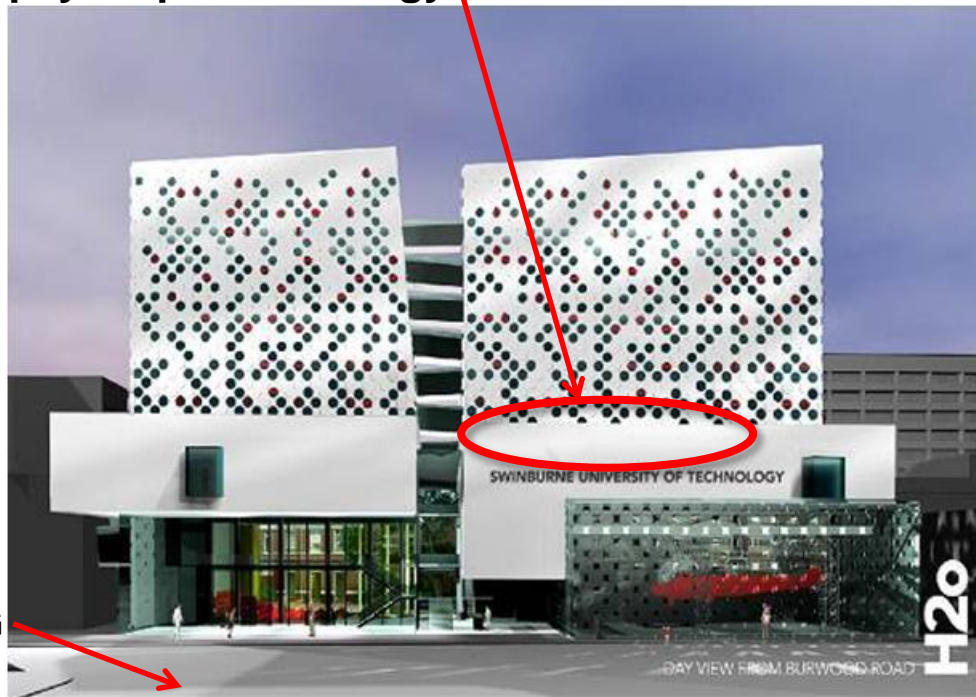


psychopharmacology

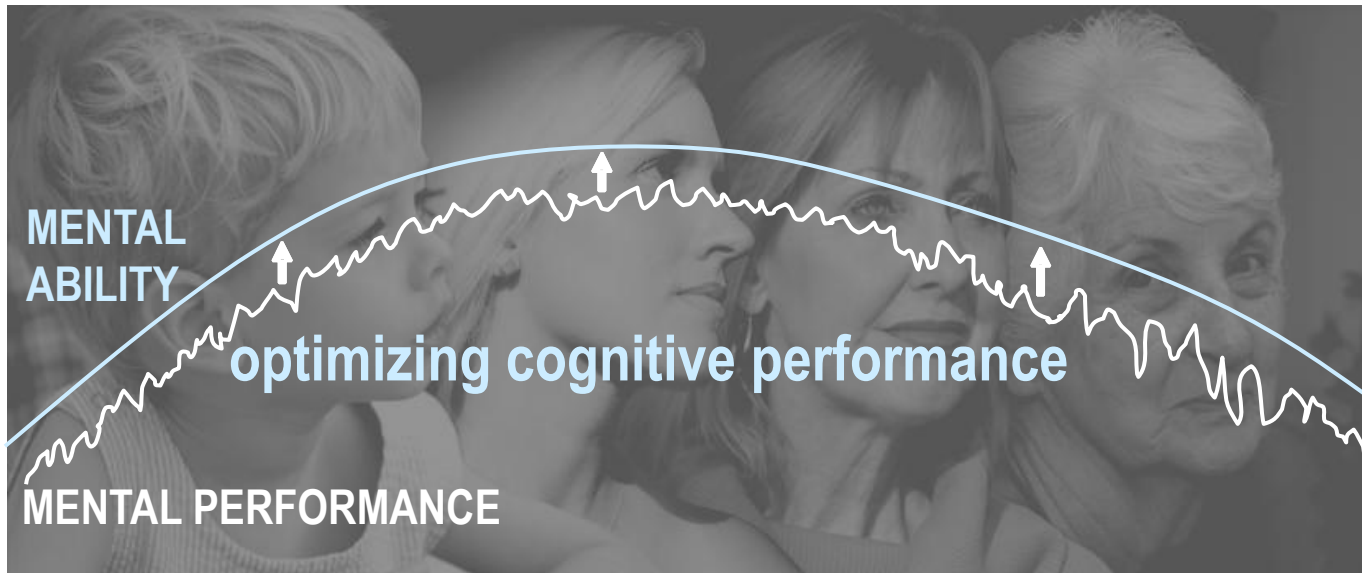


fMRI, MEG

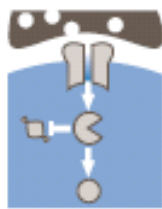
Current studies include 'ARCLI': large (N > 600) 12-month 4-arm intervention trial in elderly

- cognition
- brain mapping
- biomarkers
- genotyping

Optimal mental performance



Molecules



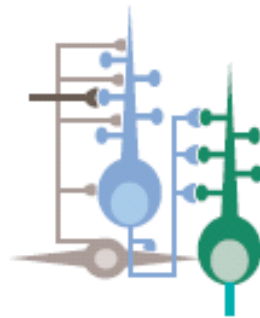
Synapse



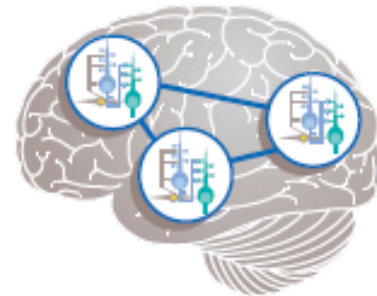
Neuron



Circuit



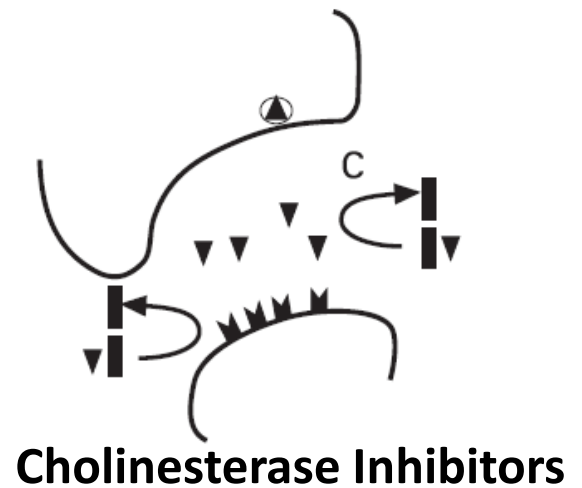
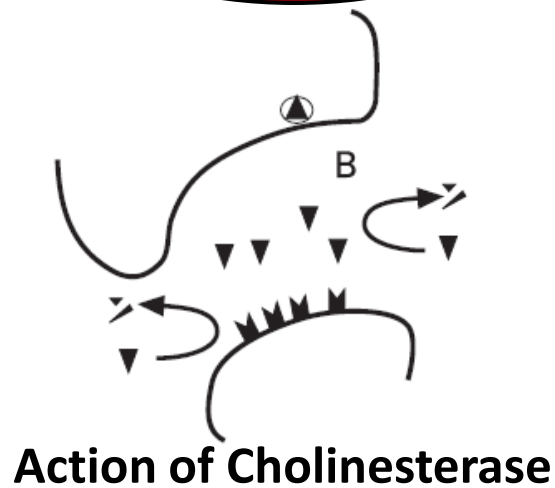
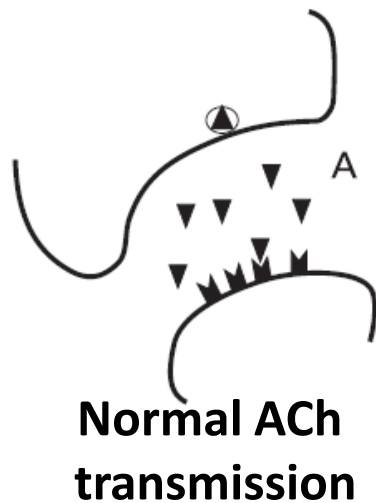
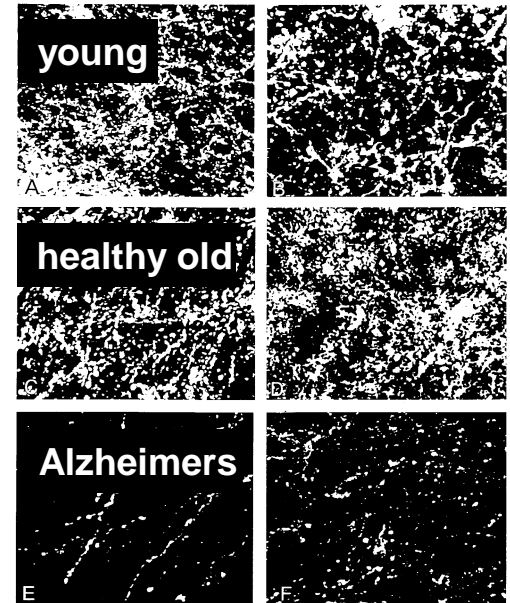
Networks



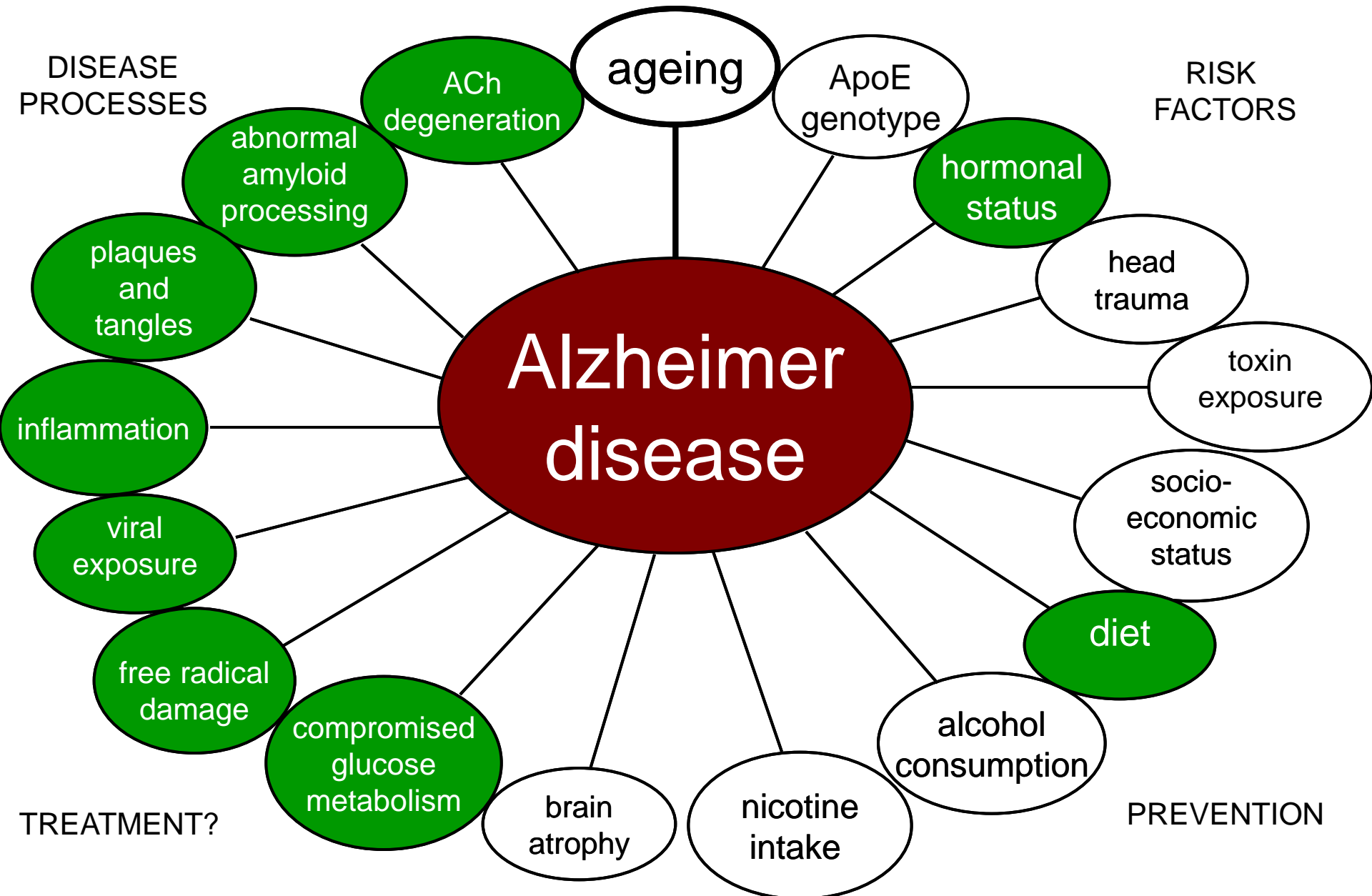
A 'magic bullet' for dementia?

ACh
degeneration

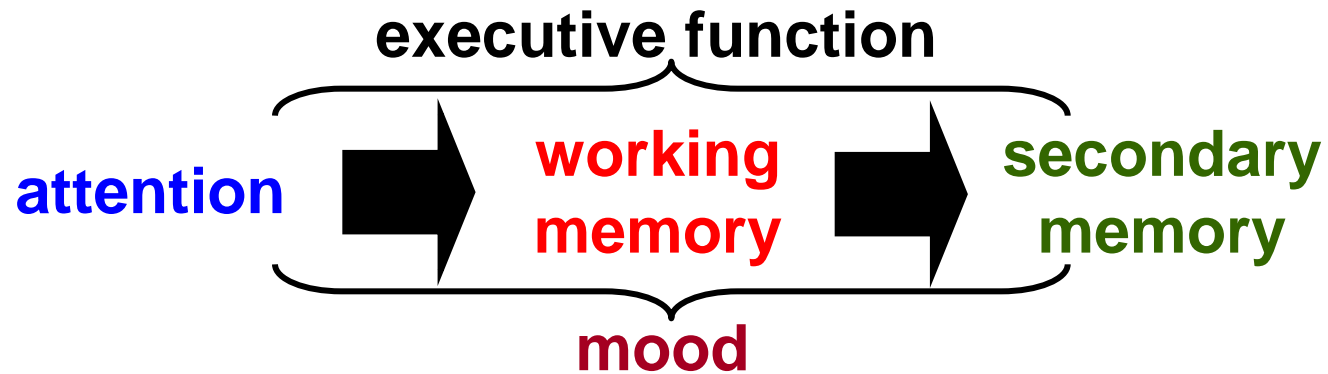
**Alzheimer
disease**



A 'magic bullet' for dementia?

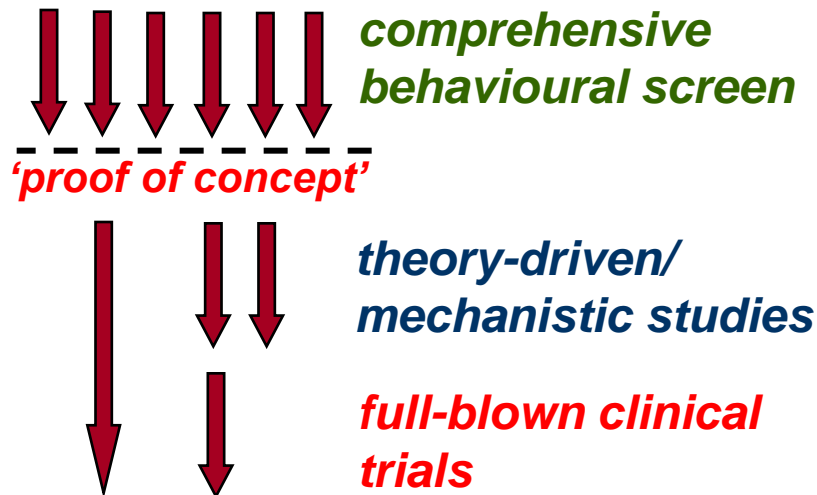


a simple model of cognition



Top down strategy: capturing behavioural effects in humans

- Focus on 'safe' treatments/interventions thought to improve mood and/or cognition from
 - history/tradition
 - anecdote
 - market



PLANT EXTRACTS

- *Ginkgo biloba*
- *Panax ginseng**
- *Ginseng quinquefolius**
- *Ginkgo-ginseng combination*
- *Melissa officinalis**
- *Salvia officinalis**
- *Salvia lavandulaefolia**
- *Valerian*
- *Guaraná**
- *Ginkgo-phosphatidylserine**
- *Cocoa polyphenols**
- *Bacopa monnieri**
- *Pycnogenol**
- *Enzogenol**
- EGCG

OTHERS

- oxygen*
- glucose
- aromatherapy oils
- caffeine
- theanine
- water
- chewing gum*
- alcohol [low dose]
- DHA
- multivitamins

*first controlled human study [11/14]

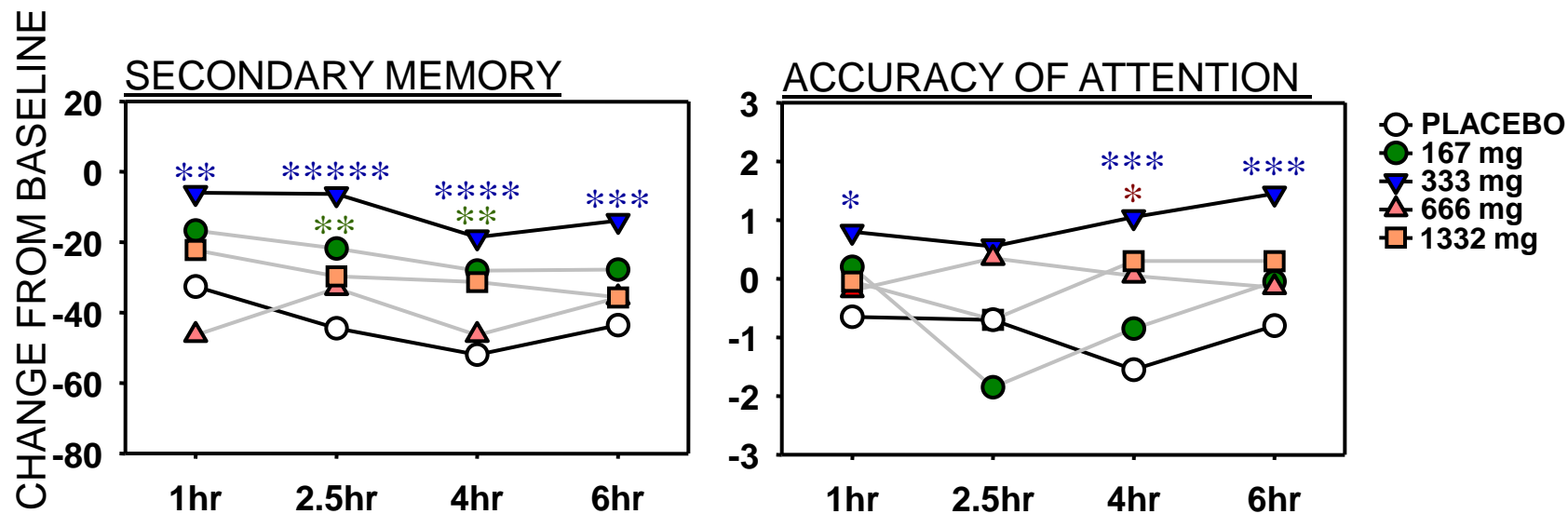


e.g. Salvia (sage)

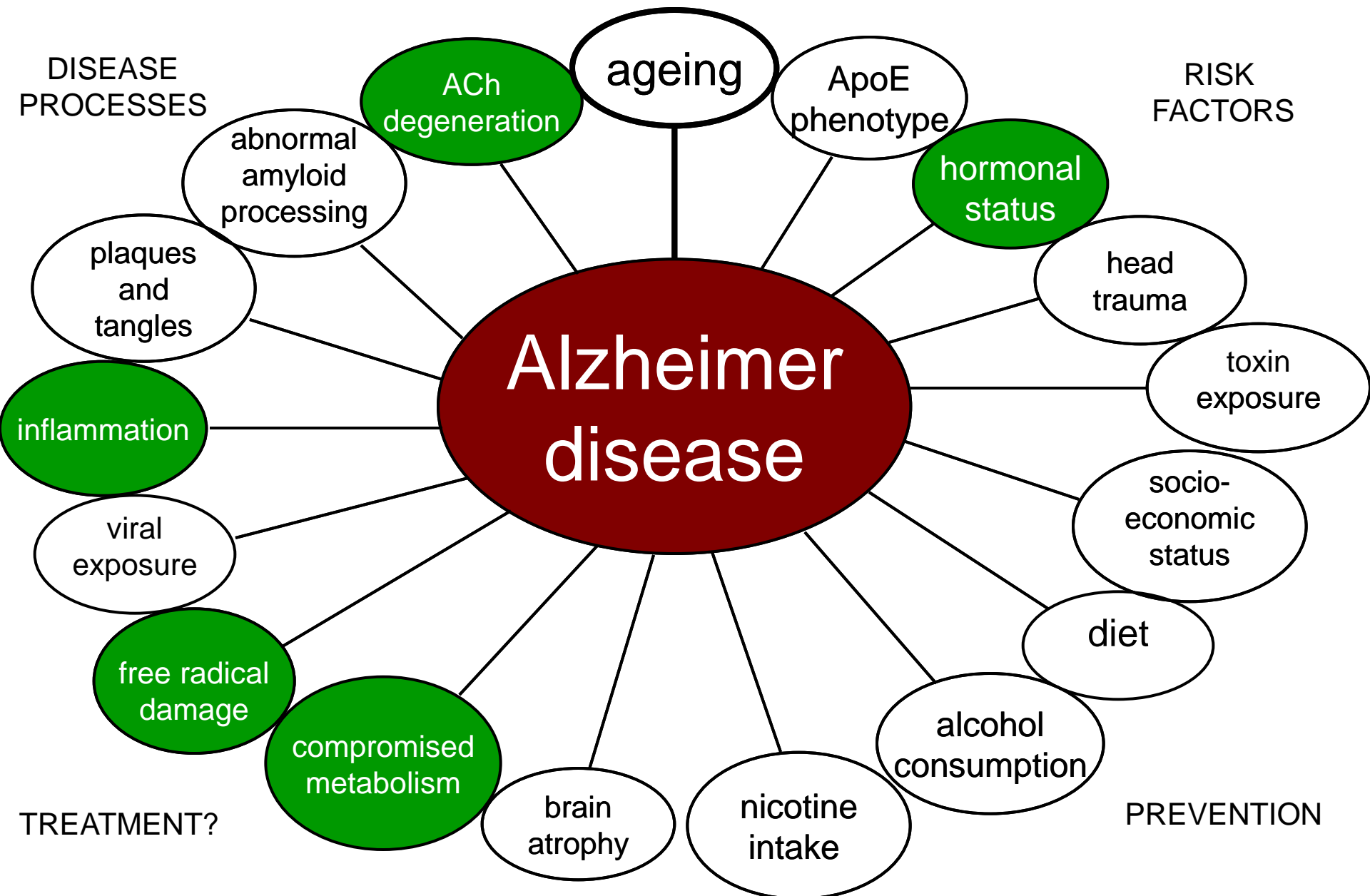
- Historical use (Ayurvedic, Chinese, European)
 - "It is singularly good for the head and brain and quickeneth the nerves and memory" (John Gerard, 1597)
 - "Sage will retard that rapid progress of decay that treads upon our heels so fast in latter years of life, will preserve faculties and memory, more valuable to the rational mind than life itself" (John Hill 1756)
- Laboratory studies
 - +ve effects on memory in young adults
 - +ve effects on memory (and attention) in the elderly
 - +ve mood effects
 - +ve 'everyday' memory performance
 - cholinesterase inhibition

An extract of *Salvia* (sage) with anticholinesterase properties improves memory and attention in healthy older volunteers

Andrew B. Scholey • Nicola T. J. Tildesley •
Clive G. Ballard • Keith A. Wesnes • Andrea Tasker •
Elaine K. Perry • David O. Kennedy

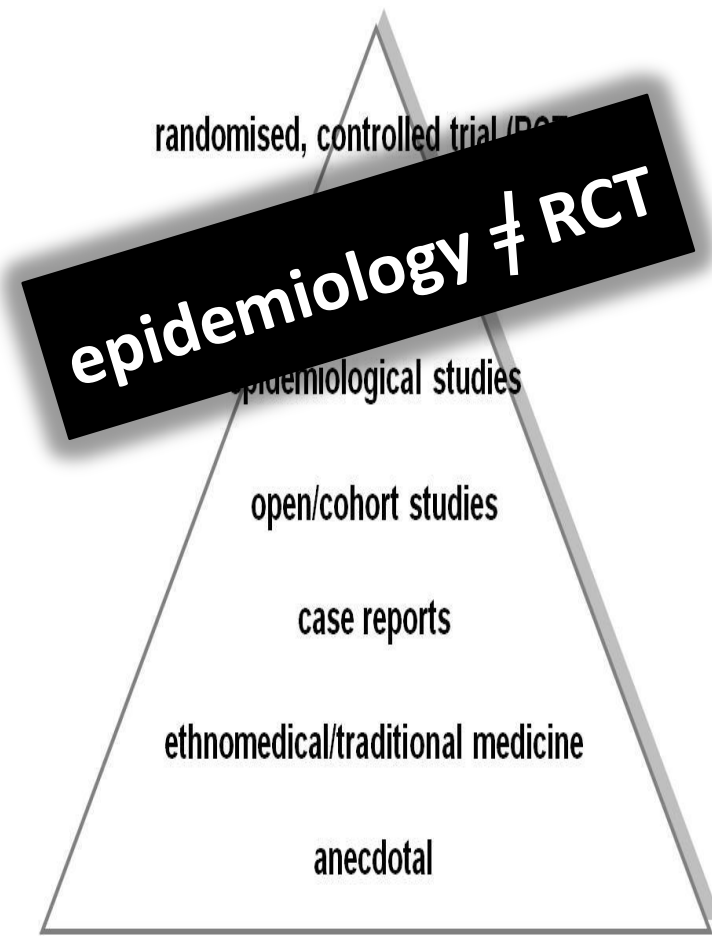
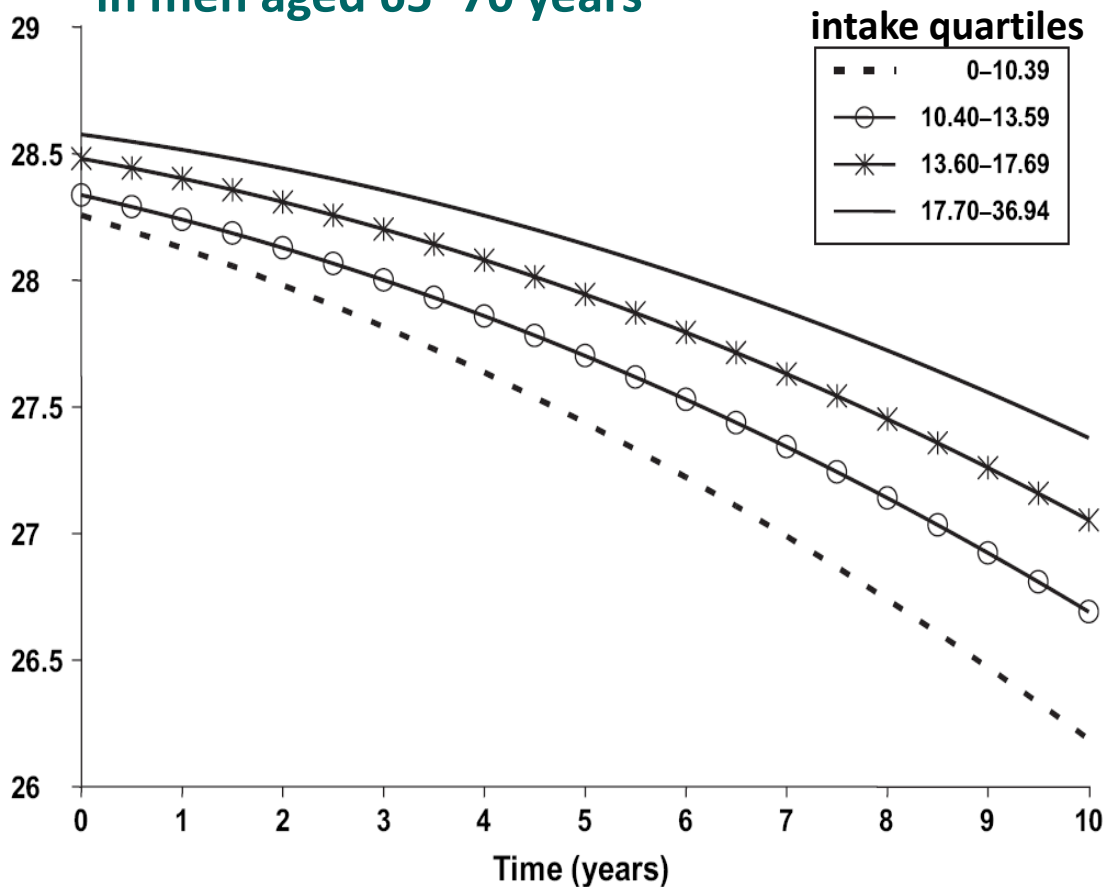


Salvia properties



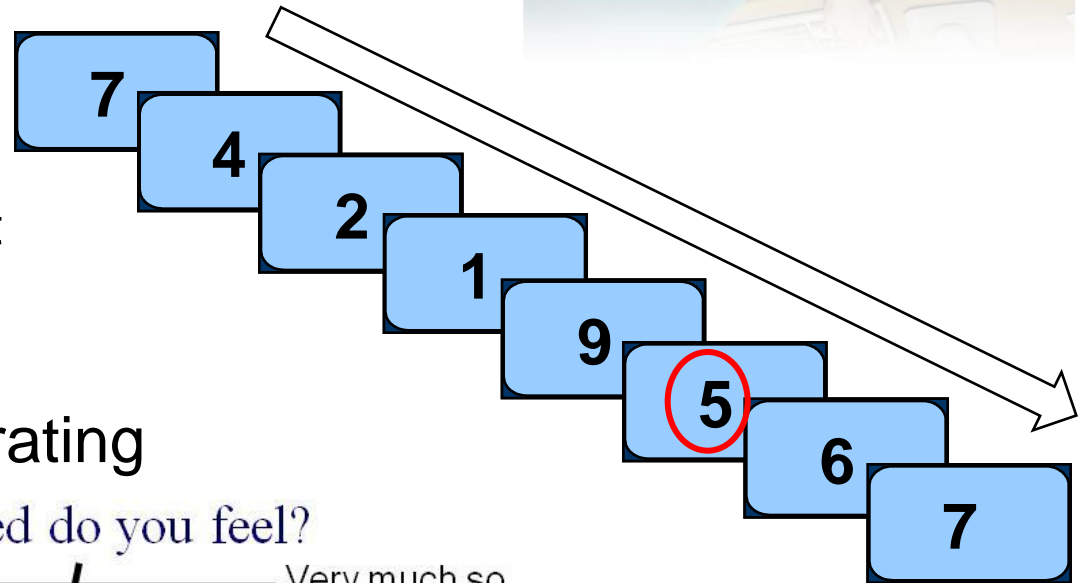
Cocoa flavanols

Flavonoid intake and cognitive decline in men aged 65–70 years



Cognitive Demand Battery

- [2 min] Computerised Serial Threes
 - repeated subtraction of 3 from random starting number between 800 and 999
 - e.g. 984-981-978-975.....
- [2 min] Computerised Serial Sevens
- [5 min] RVIP
 - Detect target string (3 odd/3 even) amongst rapid digit presentation
- [1 min] Mental fatigue rating

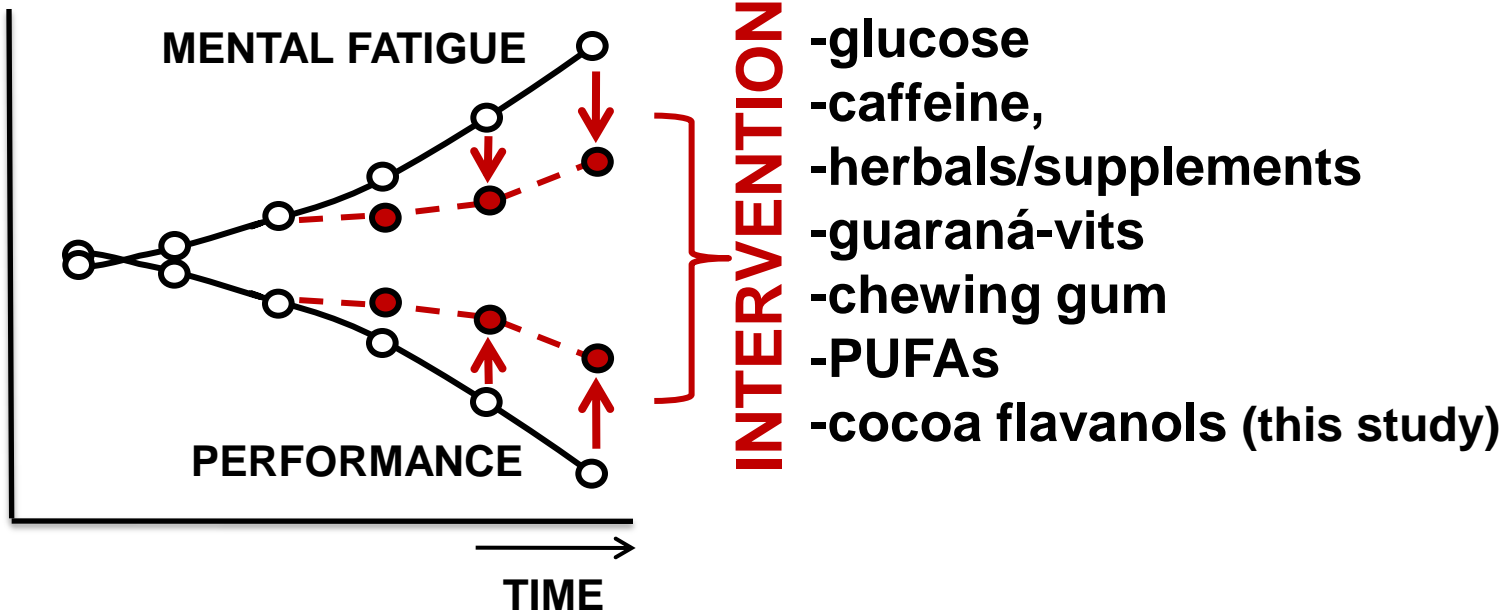


How mentally fatigued do you feel?

Not at all ————— / ————— Very much so

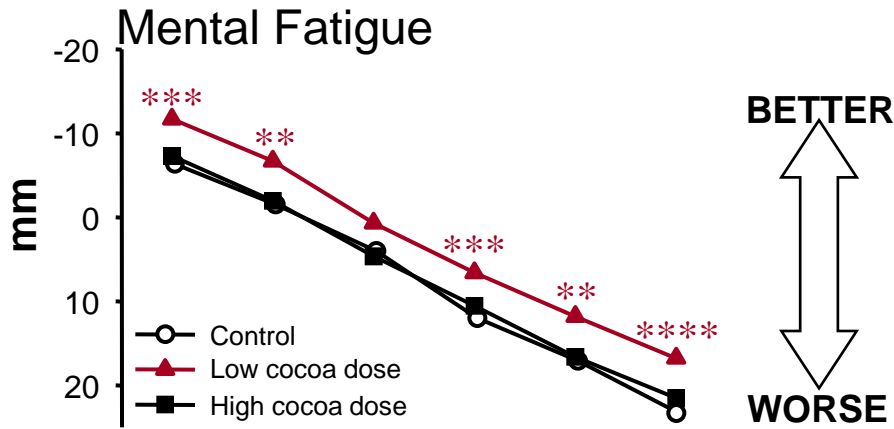
Not at all ————— / ————— Very much so

Cognitive Demand Battery



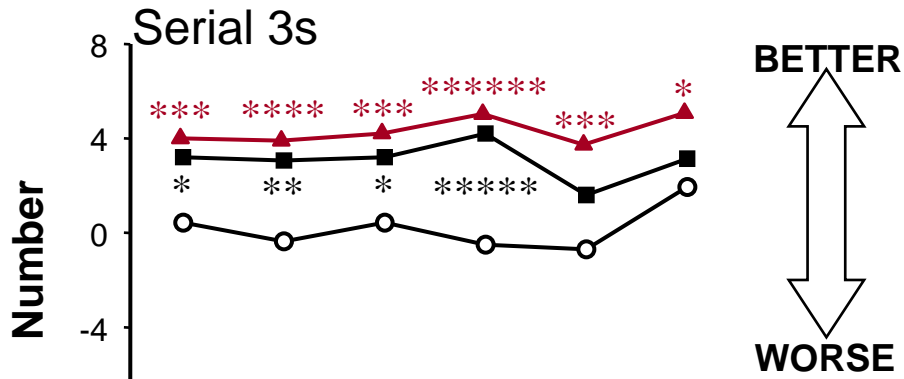
Results.

CHANGE FROM BASELINE

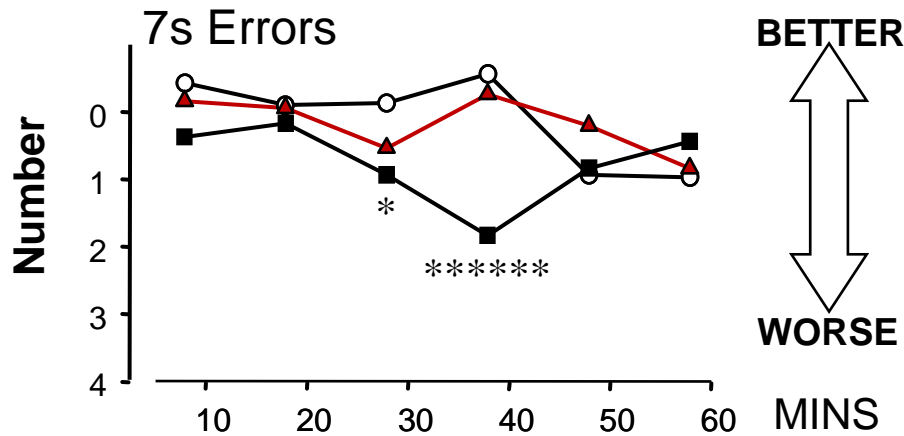


BETTER
↑
↓
WORSE

Coincides with
-peak serum flavanol
-peak FMD
-peak cerebral blood flow



BETTER
↑
↓
WORSE



BETTER
↑
↓
WORSE

Melissa officinalis [Lemon Balm]



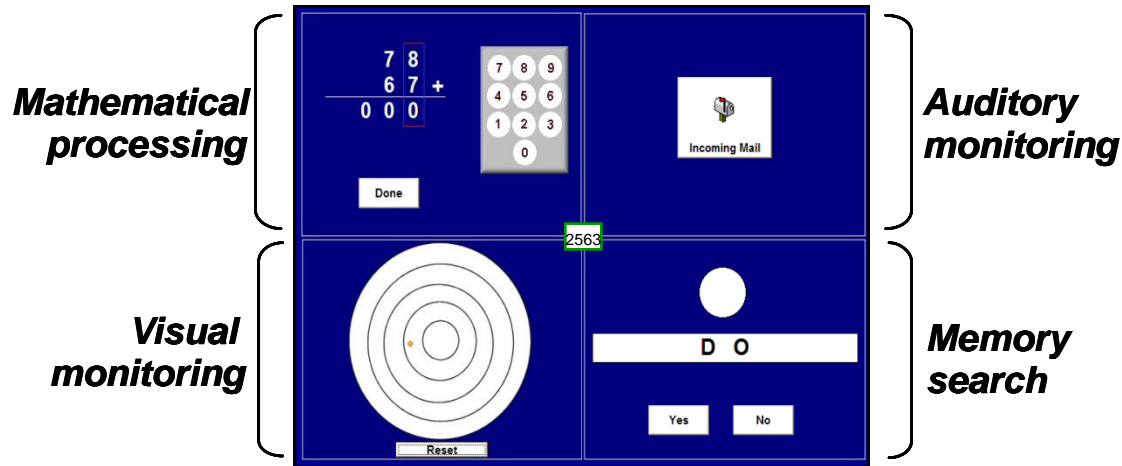
- Appears in '*Historia Plantarum*' [approximately 300 BC] and the '*Materia Medica*' [approximately 50-80 BC]
- e.g. Paracelsus [16th Century] indication for “all complaints supposed to proceed from a disordered state of the nervous system”.
- e.g. Culpepper [1616-1654]

“It causeth the Mind and Heart to becom merry.... and driveth away al troublesom cares and thoughts out of the mind arising from Melancholly...takes away grief, sorrow and care, instead of which it produceth joy and mirth”

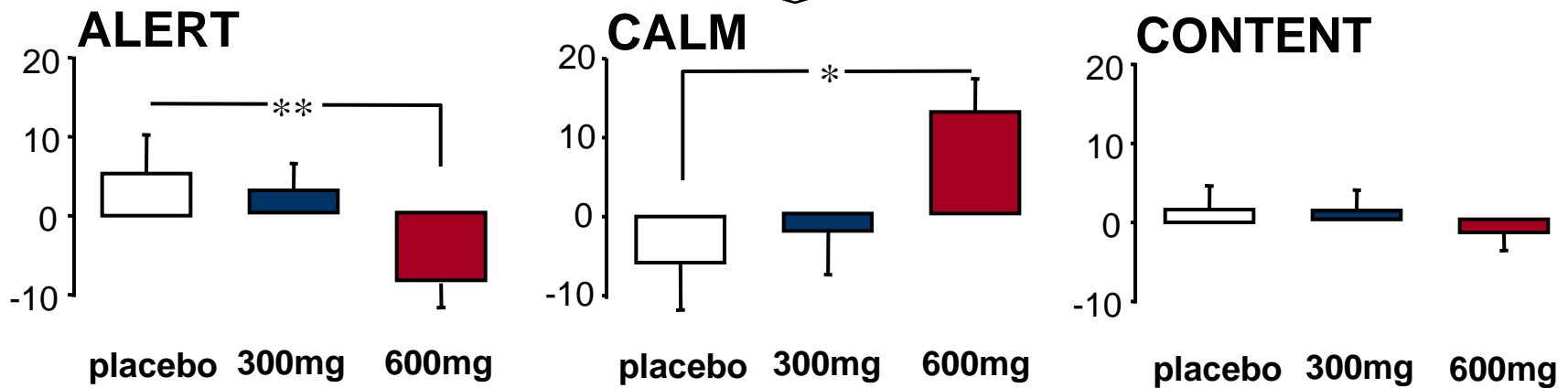


laboratory studies confirm positive mood/anti-stress effects

multi-tasking framework



CHANGE FROM BASELINE





Research report

Behavioural effects of a 10-day Mediterranean diet. Results from a pilot study evaluating mood and cognitive performance

Laura McMillan, Lauren Owen, Mami Kras, Andrew Scholey *

NICM Centre for Neurocognition, Brain Sciences Institute, Swinburne University, 400 Burwood Road, Melbourne, VIC 3122, Australia

Table 1

Effects of diet change on mood. Mean (\pm SD) mood at baseline (pre-diet) and at day 10 (post-diet) in the diet change (DC) and no change (NC) groups are shown. Probabilities associated with Group \times Time interactions are shown (**** $p < .001$).

	DC		NC		Group \times Time Interaction (p)
	Pre-diet	Post-diet	Pre-diet	Post-diet	
<i>Profile of Mood States</i>					
Depression	21.92 \pm 7.23	18.83 \pm 5.44	23.18 \pm 10.99	21.17 \pm 7.59	.58
Anxiety	18.00 \pm 5.10	14.50 \pm 2.94	16.91 \pm 14.75	14.75 \pm 2.90	.51
Anger	17.33 \pm 6.34	14.42 \pm 3.70	17.09 \pm 8.38	15.3 \pm 5.37	.32
Vigour	20.00 \pm 4.24	23.67 \pm 5.60	22.64 \pm 7.38	17.58 \pm 4.21	.00****
Fatigue	16.17 \pm 5.20	12.17 \pm 4.41	14.18 \pm 6.98	14.08 \pm 3.63	.16
Confusion	11.83 \pm 4.57	10.75 \pm 4.09	10.55 \pm 4.32	9.73 \pm 2.49	.67
Total disturbance	65.25 \pm 27.06	47.00 \pm 17.13	59.27 \pm 37.32	57.91 \pm 22.09	.06
<i>Bond-Lader Visual Analogue Scale</i>					
Alert	53.63 \pm 9.76	70.06 \pm 7.35	60.72 \pm 14.16	51.70 \pm 17.48	.00****
Content	66.08 \pm 12.49	78.97 \pm 8.59	70.21 \pm 14.91	59.81 \pm 15.14	.00****
Calm	58.38 \pm 14.52	60.04 \pm 17.32	62.82 \pm 15.85	55.87 \pm 19.89	.38

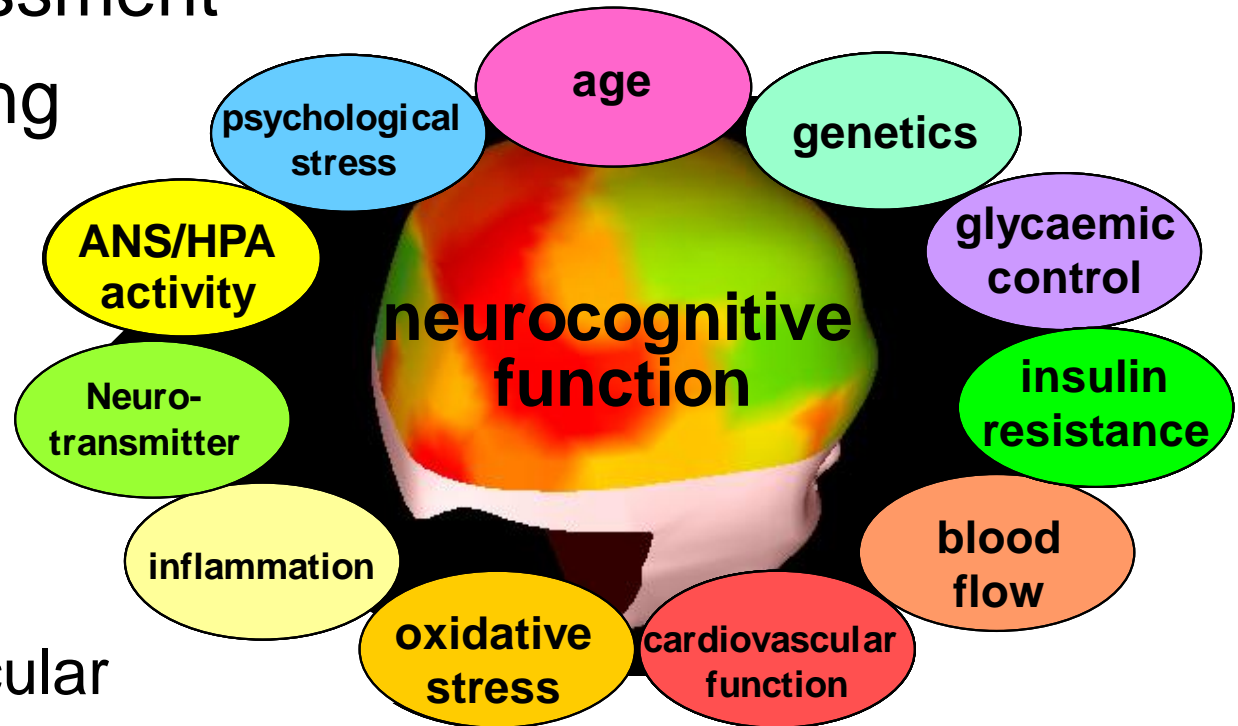
follow-up study confirms results and suggests effects may emerge after 5 days

Summary and issues

- complex dose-time-task interactions
- Acute/chronic effects can be dissociated
- what about combinations?
 - e.g. sage + melissa + bacopa + ginseng +?
- mechanisms?
 - full receptor/enzyme screening
 - co-monitoring physiological activity/biomarkers
 - In vivo receptor blocking studies
- refinement
 - sometimes better effects from less 'refined' products?
- standardisation
 - GMP
 - GLC/MRI fingerprinting
- standardisation
- standardisation

Human Psychopharmacology capabilities

- cognitive testing
- mood assessment
- brain imaging
 - EEG
 - fMRI
 - MEG
 - TMS
- biomarkers
 - cardiovascular
- field testing
 - internet
 - mobile phones



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Christina Kure [heart and brain health]

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Matt Pase [heart-brain axis]

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Karen Nolidin [genetic determinants]

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