



Emerging Roles of Obesity and Nutrition on the Aging Brain and Cognition

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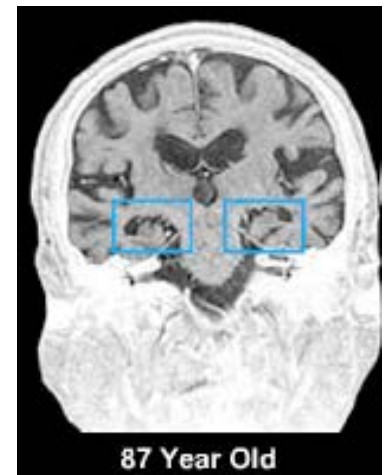
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Outline

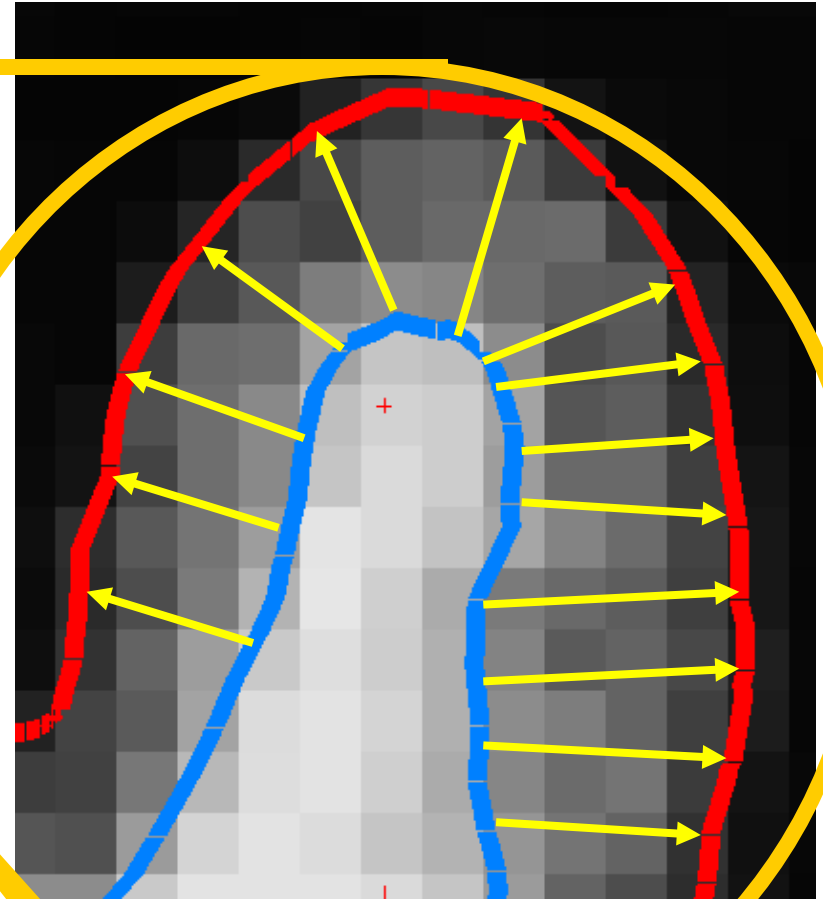
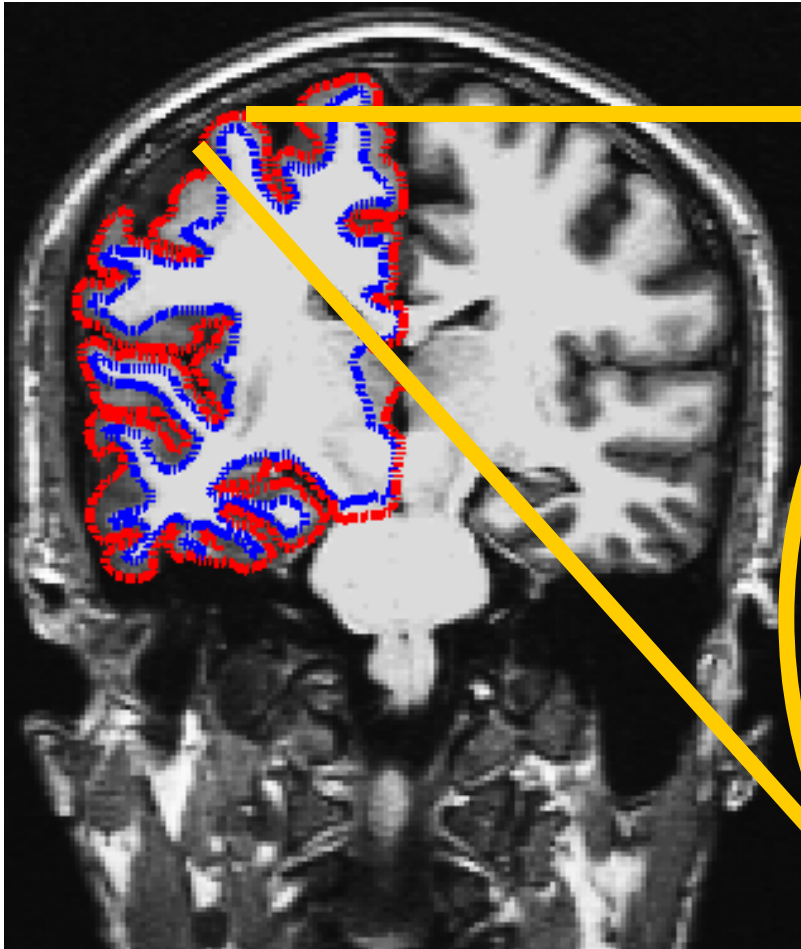
- The effect of normal aging on the brain
- Obesity and associations with brain atrophy
- Lipids and Alzheimer's disease risk
- B Vitamins, PUFAs, and brain health
- Insulin signaling, brain health, and cognition

Brain Atrophy with Aging

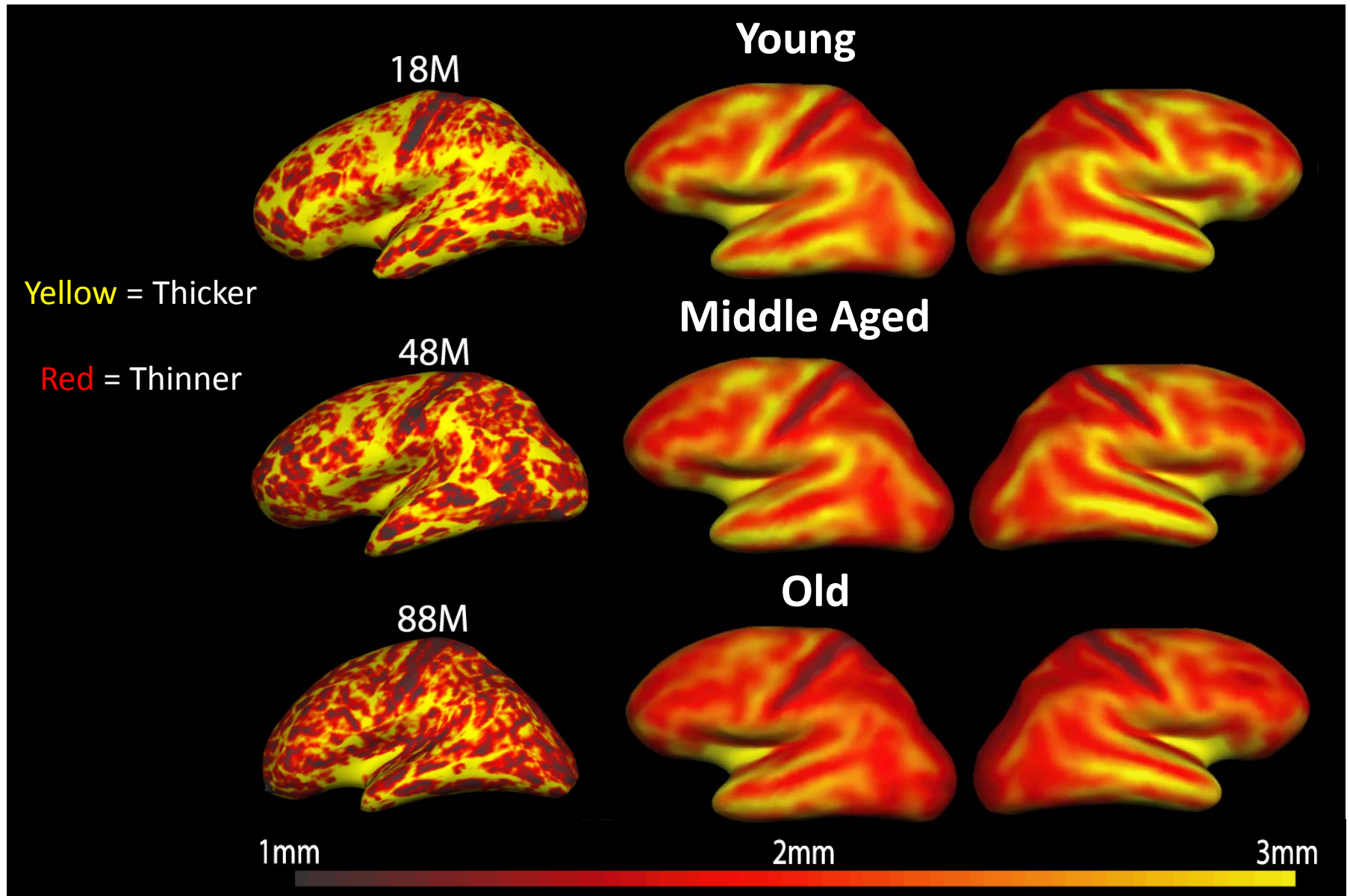
- Autopsy studies show substantial reductions in brain weight across the adult lifespan (5-10%)
- We can determine whether certain brain regions are particularly vulnerable to aging
- Prior gray matter volume studies suggest vulnerability of some prefrontal and parietal areas
- Relative sparing of sensory cortices



Atrophy measured with Cortical Thickness

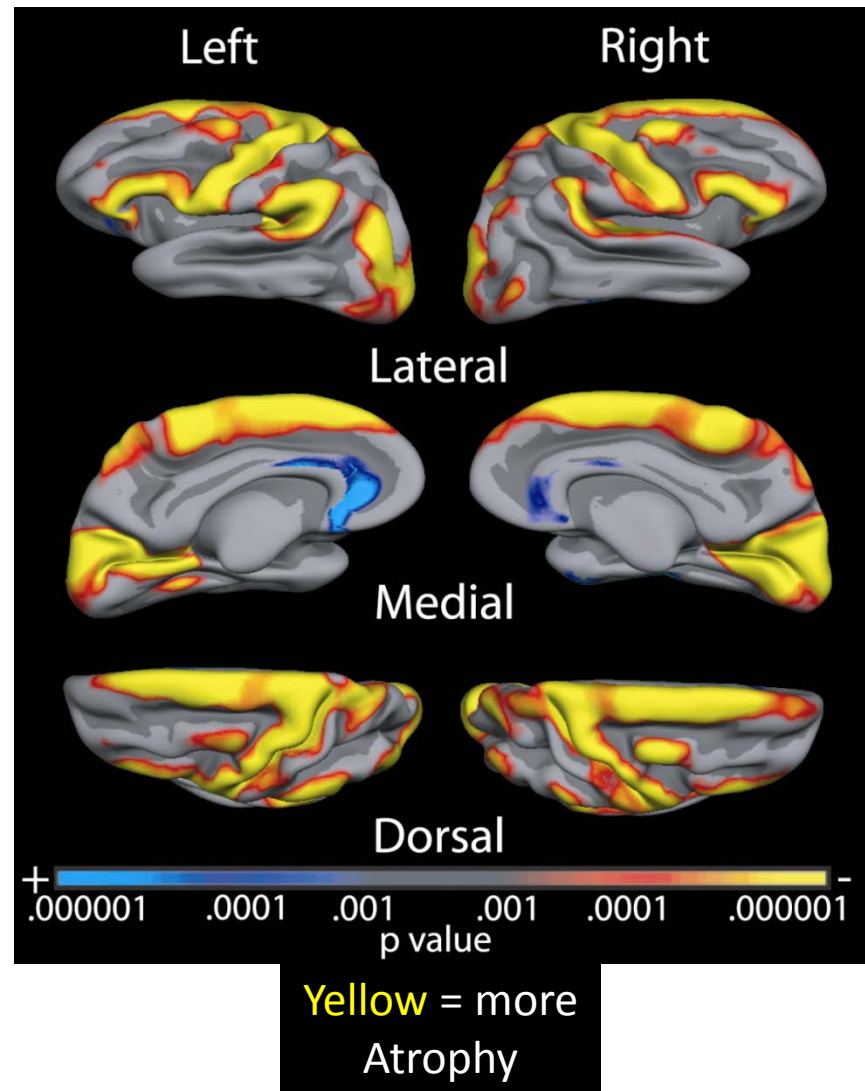


Group Mean Cortical Thickness



Age-Associated Cortical Thinning

- Regional thinning relates to cognitive performance
- Cognitive processes impacted include visual, motor, and executive function
- Mechanisms of thinning are largely unknown

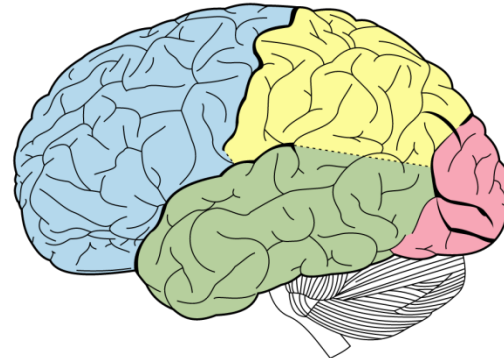


Obesity and brain atrophy in older adults

Obesity and Health Risks



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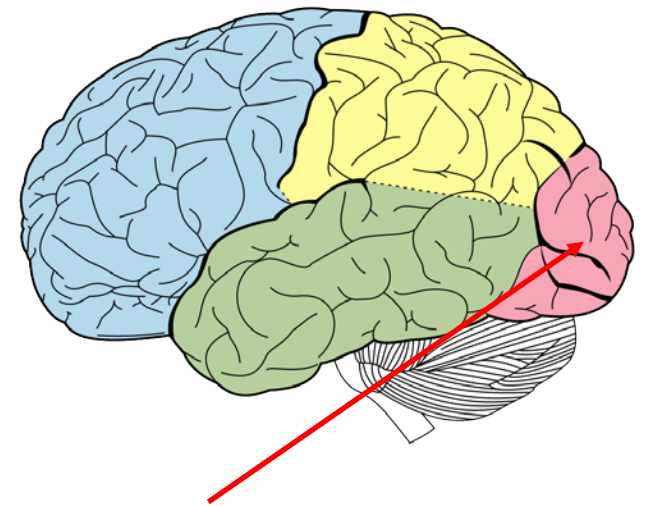
Obesity and Brain Atrophy: Review

- **Systematic review (2004-August 2013)**
- **Criteria for inclusion in review**
 - 1) At least one brain volume scan;
 - 2) One or more of the brain lobes available. Where possible, we also examined an important sub-region per lobe (e.g., hippocampus, prefrontal cortex);
 - 3) One or more anthropometric or direct measures of body fat;
 - 4) Examined weight spectrum from lean to morbidly obese

Occipital Lobe and Obesity

Middle-Aged to Aged Adult

- 7 of 14 studies show more atrophy

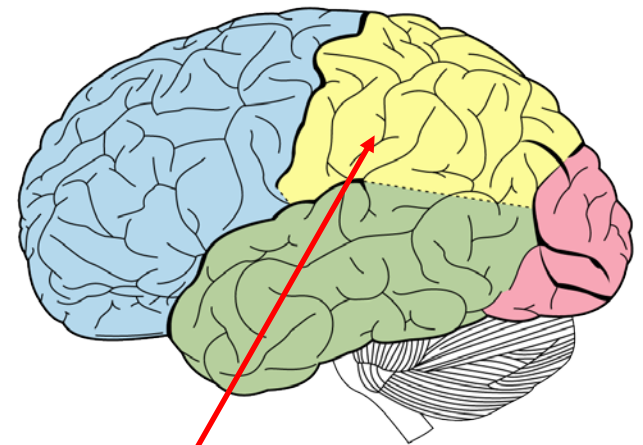


Occipital Lobe

Parietal Lobe and Obesity

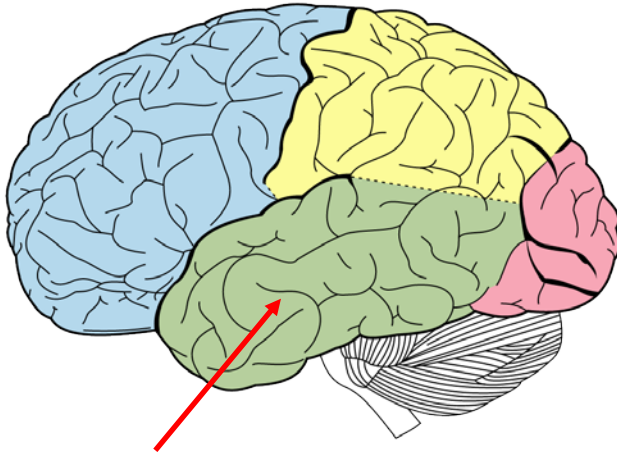
Middle-Aged to Aged Adult

- 7 of 13 studies show more atrophy
 - Only 3 studies showed this in precuneus/PCC
 - So obesity per se is not why these regions shrink



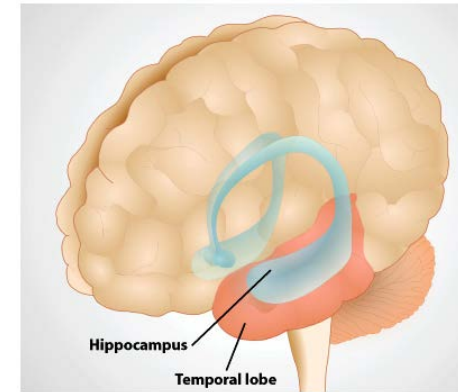
Parietal Lobe

Temporal Lobe and Obesity



Middle-Aged to Aged Adults

- 9 of 13 studies show more atrophy

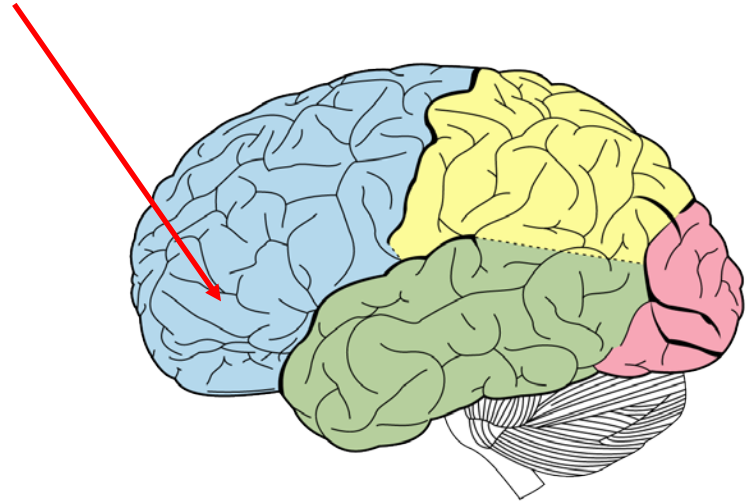


Middle-Aged to Aged Adults

- 9 of 19 of studies show more atrophy

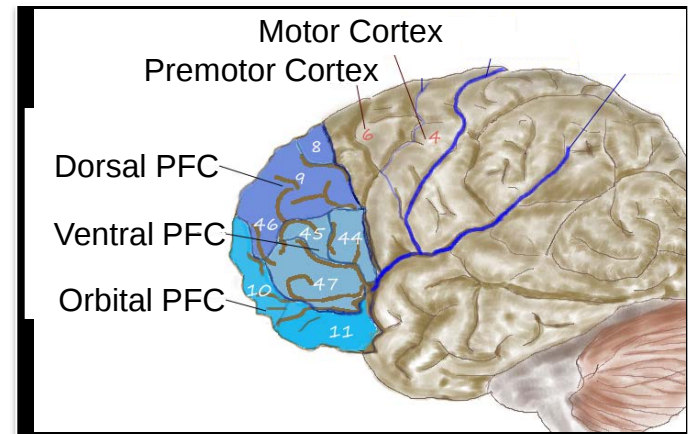
Frontal Lobe and Obesity

Frontal Lobe



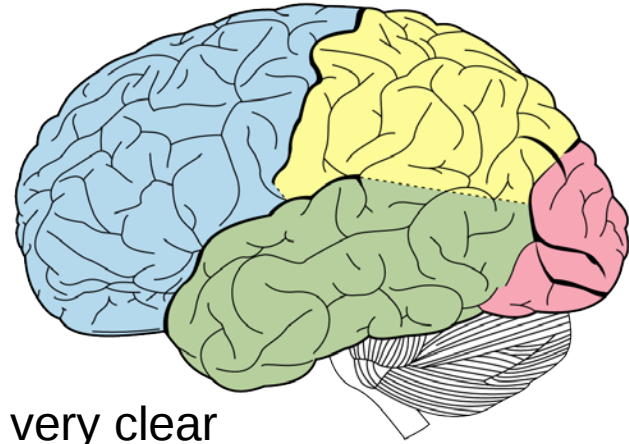
Middle-Aged to Aged Adult

- 11 of 15 studies: frontal atrophy
- 12 of 15 studies: PFC atrophy



Conclusions

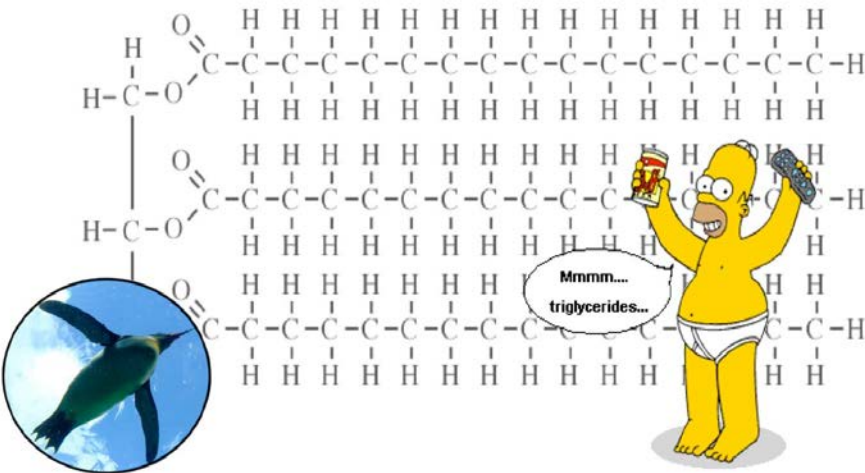
- **Medial temporal lobe, memory, and aging**
 - Obesity here shows inconsistent associations
 - Literature on obesity and memory is very mixed
- **Prefrontal cortex, executive function, and aging**
 - Obesity here shows consistent associations
 - Literature on obesity and executive dysfunction is very clear
- **What exactly does atrophy mean here?**
 - Atrophy not due to neural cell death, but shorter cell-to-cell connections
 - Weight loss may reverse atrophy and cognitive dysfunction



Lipids and Alzheimer's Disease

Serum Lipids are Related to Alzheimer's Pathology in Nursing Home Residents

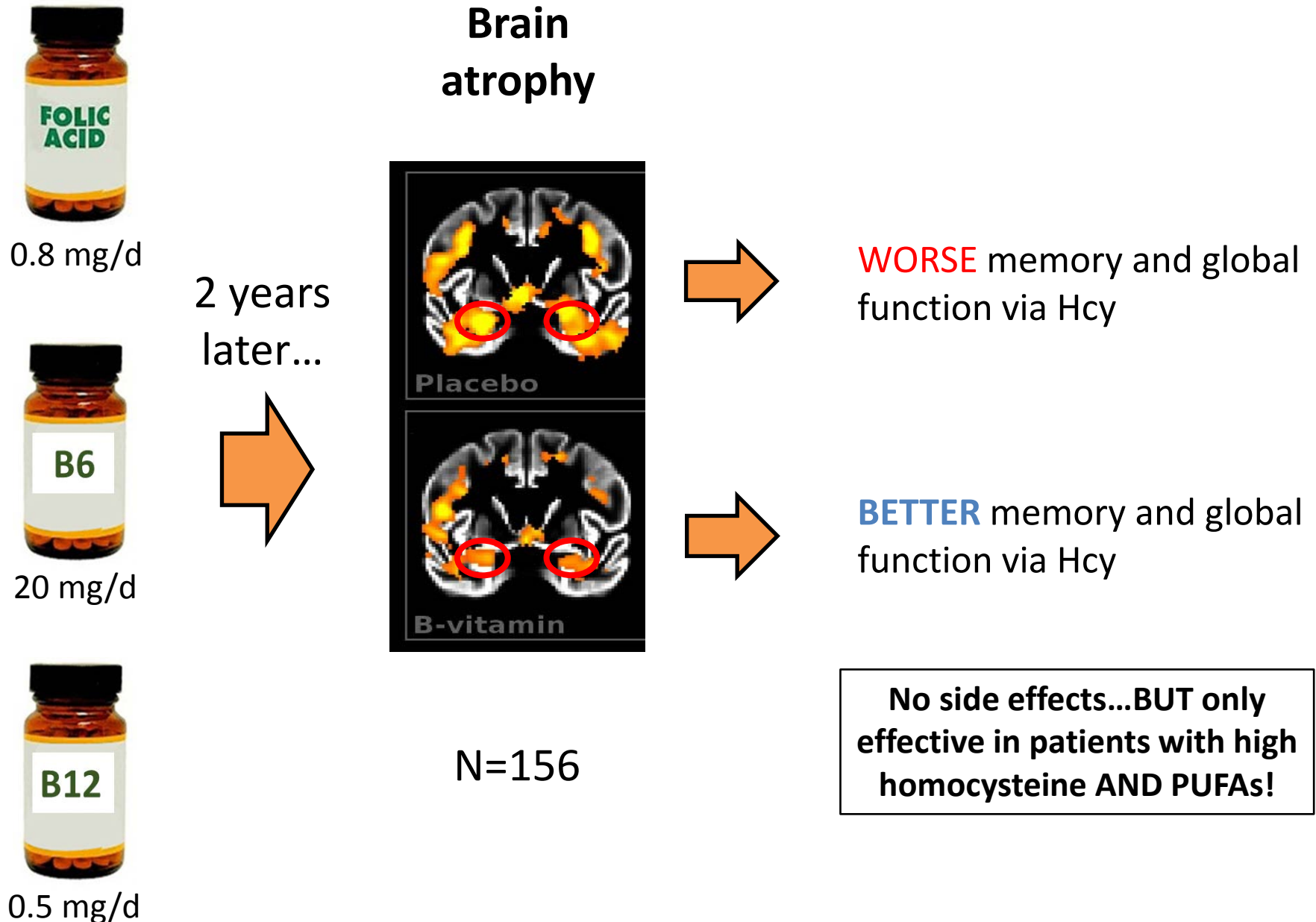
For the Love of Lipids



- A study at the Jewish Home & Hospital in NYC by Leslie Libow, MD and his group
- For 358 nursing home residents, serum lipids were determined at admission
- Neuropathologic diagnoses for AD were established at autopsy
- Residents with any AD pathology vs. those without AD pathology had higher mean serum total cholesterol ($p=0.02$) and higher mean low-density lipoprotein (LDL) ($p=0.03$)

B Vitamin Supplementation and PUFAs

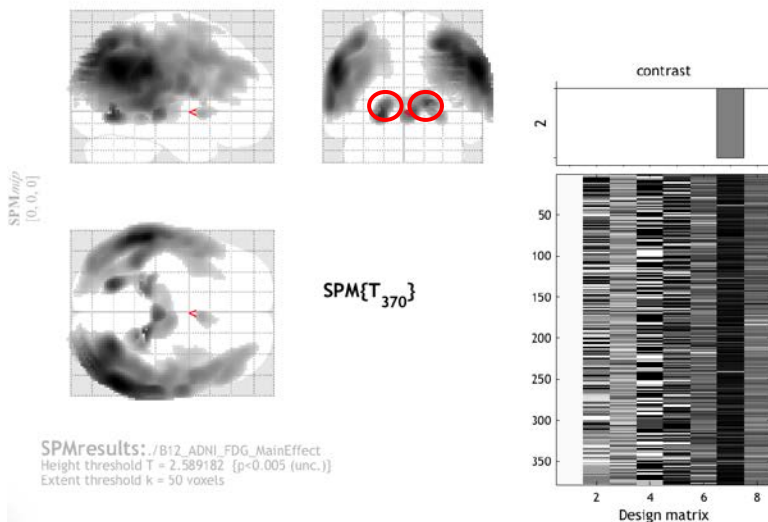
Brain Effects of B Vitamin Supplements I



Paradoxical Findings for B12 Levels and Brain Health Correlations

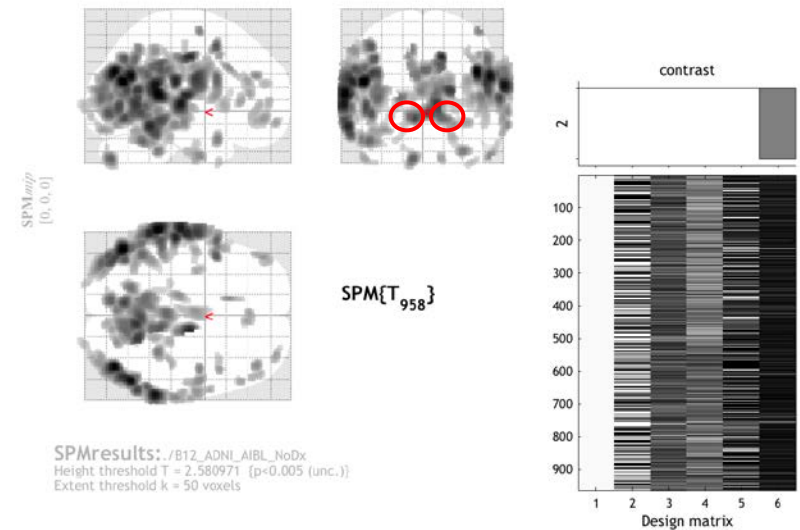
Gray Matter and Vitamin B12

B12_neg (masked [incl.] by Whole_Brain_Mask.nii)



Brain Glucose Metabolism and Vitamin B12

B12_neg (masked [incl.] by Whole_Brain_Mask.nii)



- N = 964, cognitively normal and impaired
- Higher B12 → More atrophy in hippocampus, prefrontal cortex, and parietal lobe

- N = 378, cognitively normal and impaired
- Higher B12 → Less glucose use in hippocampus and parietal lobe

Do omega-3's directly impact memory?

Tuesday, August 25, 2015

NIH study shows no benefit of omega-3 or other nutritional supplements for cognitive decline



While some research suggests that a diet high in omega-3 fatty acids can protect brain health, a large clinical trial by researchers at the National Institutes of Health found that omega-3 supplements did not slow cognitive decline in older persons. With 4,000 patients followed over a five-year period, the study is one of the largest and longest of its kind. It was published today in the Journal of the American Medical Association.

“Contrary to popular belief, we didn’t see any benefit of omega-3 supplements for stopping cognitive decline,” said Emily Chew, M.D., deputy director of the Division of Epidemiology and Clinical Applications and deputy clinical director at the National Eye Institute (NEI), part of NIH.

Dr. Chew leads the Age-Related Eye Disease Study (AREDS), which was designed to investigate a combination of nutritional supplements for slowing age-related macular degeneration (AMD), a major cause of vision loss among older Americans. That study established that daily high doses of certain antioxidants and minerals — called the AREDS formulation — can help slow the progression to advanced AMD.



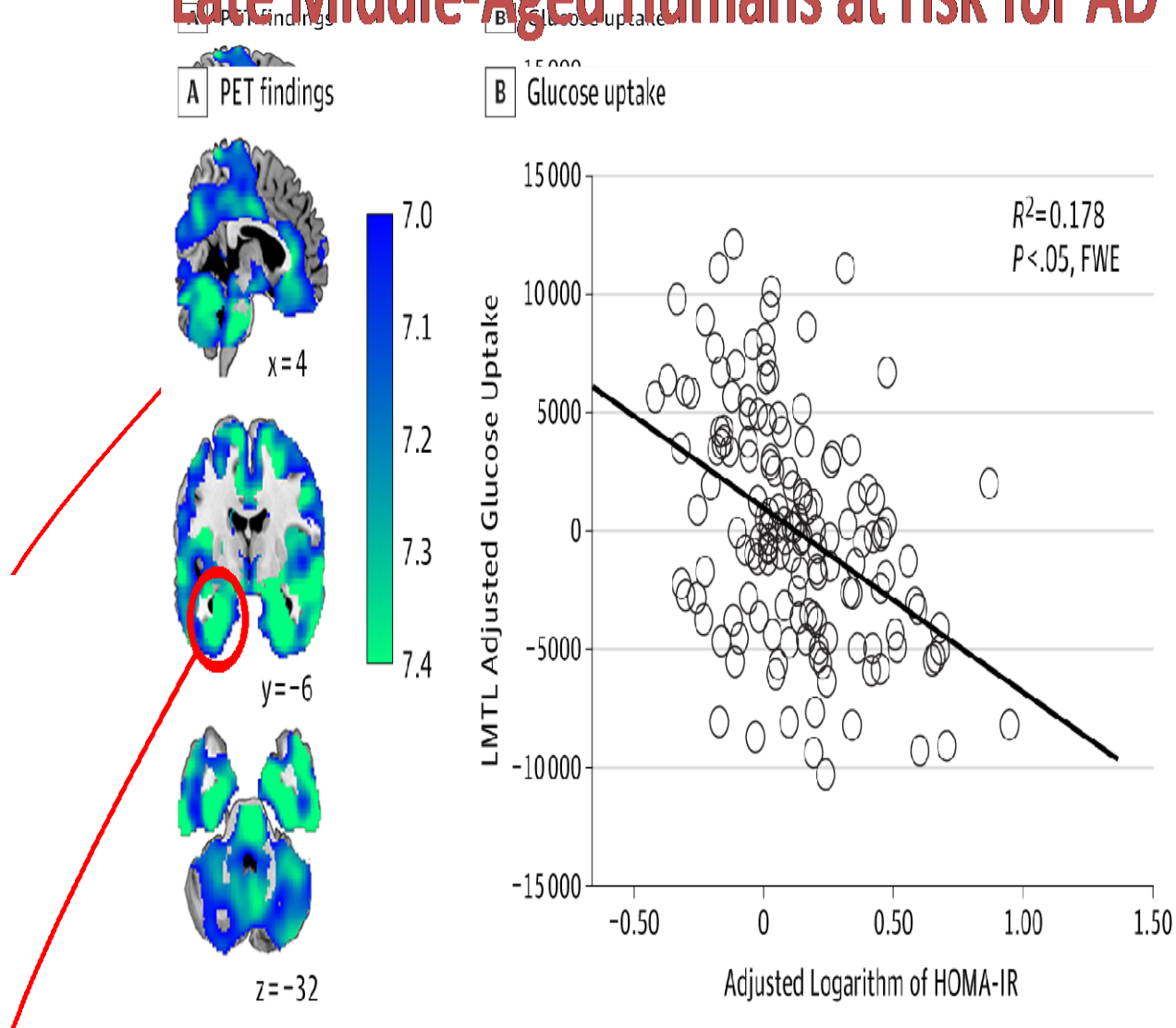
- 4,000 older participants
- 5-years of placebo vs. 350mg DHA and 650mg EPA (and other groups)
- No significant change in Cognitive decline

Conclusion: Probably not.

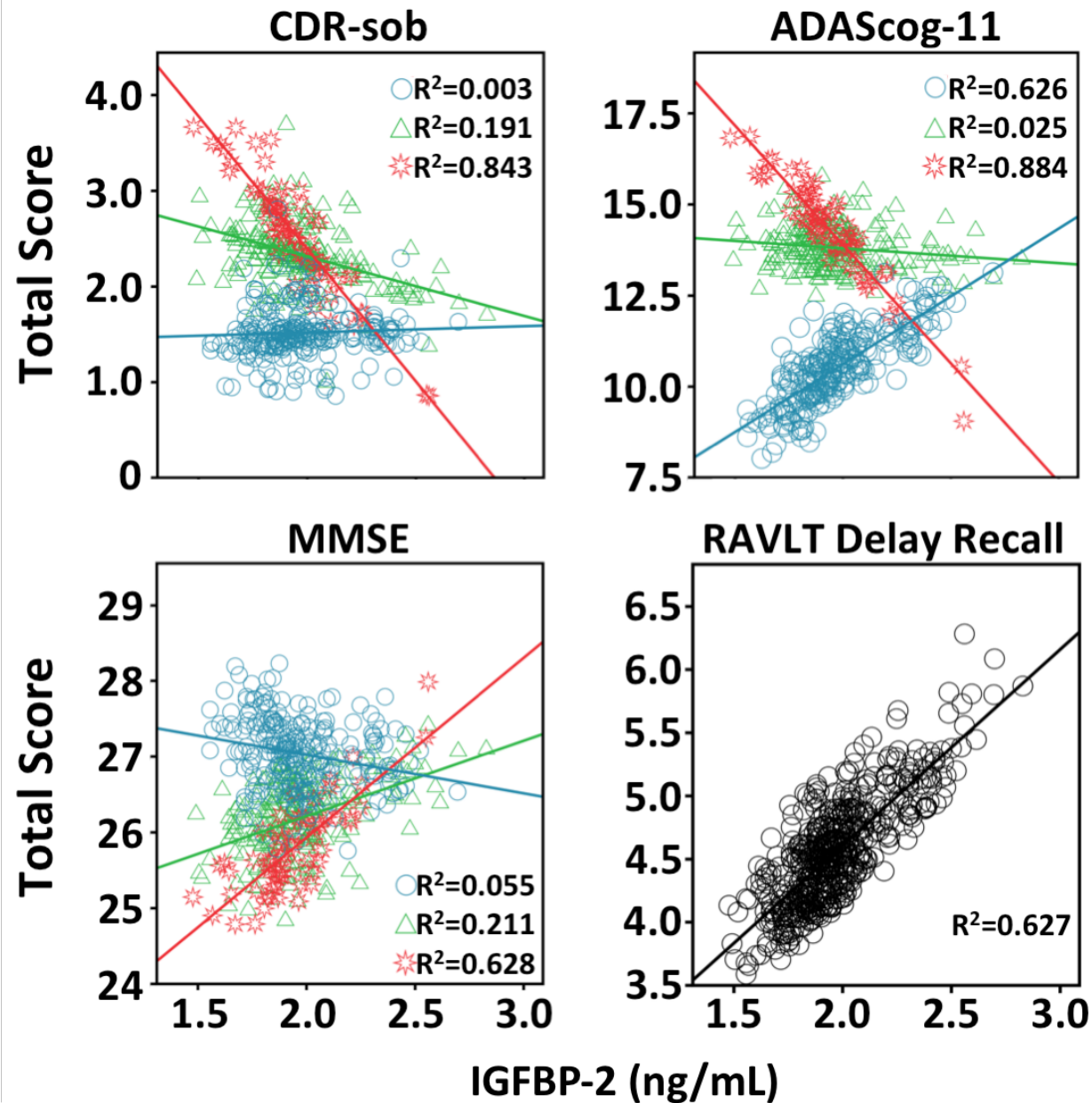
Insulin Signaling and the Brain

Insulin Resistance, Glucose Uptake, and Memory

Late Middle-Aged Humans at risk for AD



IGF-1 and Cognition



Circle = Normal
Triangle = Pre-AD
Asterisk = AD

Take-Homes

- The aging brain shows atrophy most in prefrontal cortex and occipital lobe
- Obesity is strongly related only to frontal lobe/prefrontal cortex in elders
- High LDL and total cholesterol, and other metabolic syndrome factors, increase risk for Alzheimer's disease
- B vitamin supplementation works only if clients have high PUFAs AND high vascular risk factor biomarkers
- Maintaining optimal insulin sensitivity in the periphery is very important for maintaining cognitive health in normal aging and across the Alzheimer's spectrum

Acknowledgements



External Collaborators

Laura Baker	Michael Lutz
Barbara Bendlin	Michelle Mielke
Suzanne Craft	Stephanie Rainey-Smith
Robert Dantzer	Allen Roses
Richard Davidson	Carol Ryfe
Natalie Denberg	Andrew Saykin
Sterling Johnson	Daniel Tranel
	JoAnn Tschanz

Lab

Joseph Webb
Kelsey McLimans
Brandon Klinedinst
Jonathan Cerna

Funding



Moderate Alcohol Intake is Associated with Lower Dementia Incidence I

- 3,069 community dwelling adults aged 75 or above without dementia in the Ginkgo Evaluation of Memory (GEMS) study were followed for 6 years
- 2,587 were cognitively normal at beginning of study
- 482 had Mild Cognitive Impairment (MCI)
 - Precursor to Alzheimer's
- Goal: To determine the relationship between alcohol intake and people who developed AD
 - Intake determined by self-reports as:
 - ❖ Light = 1-7 drinks/week
 - ❖ Moderate = 8-14 drinks/week
 - ❖ Heavy => 14 drinks/week



Moderate Alcohol Intake is Associated with Lower Dementia Incidence II

- Moderate alcohol intake (1-2 drinks/day) associated with a 37% lower risk of dementia in participants with normal cognition at baseline, but not in MCI patients
- For those with MCI at baseline:
 - Any alcohol intake was associated with a faster rate of cognitive decline
- Heavy drinkers (> 14 drinks/week) were nearly twice as likely to develop dementia compared to non-drinkers with MCI
- These results support current recommendations to drink in moderation

