

## Contributions of WHI to the Study of Cognitive Aging

Dr. Steve Rapp



#### Thanks to These Collaborators

#### Participants in WHI (WHIMS) Research Staff International Team of Scientists

National Heart Lung and Blood Institute National Institute on Aging

## What did we do in WHI (WHIMS)?

- 7474 Hormone Trials participants, <u>></u>65 yr.
- Clinic-based assessment w follow-up eval for some
- Brain scan (2) for some
- Continued follow-up by telephone still ongoing

Brain Health

Cognition





#### Terms

**'Cognitive Function'** 

#### Estimate of current overall thinking abilities

#### 'Cognitive Impairment'

- Dementia
- Mild Cognitive Impairment Mild disability
- **\_** Severe disability

#### **Brain**

- Shrinkage (atrophy)
- Damage (lesions)





## Does estrogen-based hormone therapy after menopause reduce the risk of dementia?





**Estrogen-based** hormone therapy after menopause **INCREASED** the risk of cognitive impairment in women 65 years old and older





It also produced slight shrinkage of the brain in areas related to memory (hippocampus) and other important thinking abilities (frontal lobe). Resnick et al, Neurology, 2009;72:135-142



The <u>rate</u> of shrinkage and damage to the brain did <u>not</u> change after 5 years.

Coker et al Neurology 2014;82:427-434



## What if estrogen-based hormone therapy was started around the time of menopause (50-54 years of age)?





#### Estrogen-based hormone therapy taken between 50 and 54 years of age showed <u>no</u> overall benefit or risk to cognitive function.

Espeland et al, JAMA Internal Medicine, 2013;173(15):1429-1436



Among women with heart disease, the risk of cognitive impairment <u>increased by 29%</u>

- Increased 45% for women w angina
- Doubled for women with a history of heart attack

<u>Diabetes and high blood pressure are associated with an increased</u> <u>risk of cognitive impairment in women without heart disease</u>

Women with high blood pressure (>140/90 mm Hg) had <u>more damage</u> in most brain regions than women with normal blood pressure. Kuller et al, J Clin Hypertension, 2010;12:203-212 Haring, et al J Am Heart Assoc 2013;2:e000369 INITIA Something of a paradox exists when it comes to how weight relates to cognitive function and the brain health in older women?

While midlife obesity predicts dementia, heavier weight in later life predicted <u>less</u> brain shrinkage and <u>less</u> damage.

Driscoll et al, J Gerontol Med Sci, 2016;71:1216-1222

<u>Weight loss is associated with worse cognitive</u> <u>performance</u> in older women

Driscoll et al, Obesity, 2011;19:1595-1600





#### Is diet associated with cognitive impairment?

A diet with foods that increase inflammation (e.g., red meats, saturated fats) was associated with <u>greater</u> <u>cognitive decline and earlier onset of cognitive</u> impairment

Hayden, K. et al, Alzheimer's Dementia, 2017;13:1187-1196

Adhering to a <u>low-fat diet</u> was associated a 41% lower likelihood of developing cognitive impairment compared to regular diet

Chlebowski et al, EClinical Medicine 18;2020:100240





## Cognition and the Eyes

Presence of abnormalities in the <u>retina was</u> associated with poorer cognitive function over <u>ten years</u> and <u>greater damage to the brain</u>. <sub>Haan et al, Neurology,2012;78:942-949</sub>

Women with vision impairment (<20/40) were <u>more likely to develop cognitive impairment</u> (8%) than women without vision impairment (3%). Tran et al JAMA Ophthamal, 2020







# How does air quality affect the brain and cognition?

- Greater air pollution (fine particles, traffic related pollutants) associated with...
  - More brain shrinkage
  - 81% increased the risk for cognitive decline and 92% greater risk of dementia
- Better air quality associated with....
  - 20% lower risk of dementia
  - Less decline in memory and other cognitive abilities; <u>~2.4</u> years less aging

Cacciottolo M, et al., Transl Psychiatry. 2017 Jan 7(1):e1022 Chen et al, Ann Neurol 2015;78:466-476 Casanova et al Front in Human Neurosci, 2016;10.495







#### **Cognitive Resilience**

# A sneak peak at what predicts <u>preserved</u> cognitive function?



What distinguishes women with preserved cognitive function from those with impairment?

- Lower age
- Less self-reported forgetfulness
- Better reported physical function
- Greater dispositional optimism

- Lower hemoglobin
- Lower blood sugar levels
- Less sleep disturbance
- Higher education
- Lower blood pressure
- Less depression

Casanova et al., unpublished data



What biological factors are related to preserved cognitive function among women with genetic risk for Alzheimer's disease?



#### WHI and Brain Health: The Work Continues





#### Thank you

