Mount Kenya

Alzheimer's Disease: Progress in Diagnosis and Treatment

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Dementia

- **Acquired syndrome of gradual decline in memory, sufficient to affect daily life in a relatively well person.**
  - **At least deficiency in one other cognitive function:**

    Language

    Visual spatial orientation or

    Executive function

    - **Deficit not due to delirium**
    - **Not due to other medical, neurological, psychiatry condition or medication.**

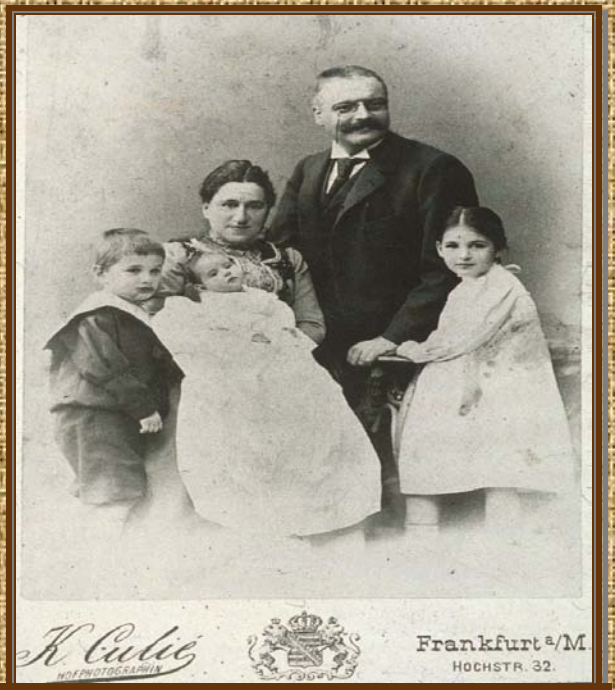
First Case:

57-Year-Old Woman with Memory Loss

Augusta D (Nov 3, 1906)

Alzheimer's Disease

Dr. Alois Alzheimer 1864–1915



Alois Alzheimer 1911

1906: 1st Case presenile dementia described

1907: Entered medical literature

Alzheimer Kraepelin Gaup Nissl

1910: Named Alzheimer's Disease

Solomon Carter Fuller, MD (1872–1953)

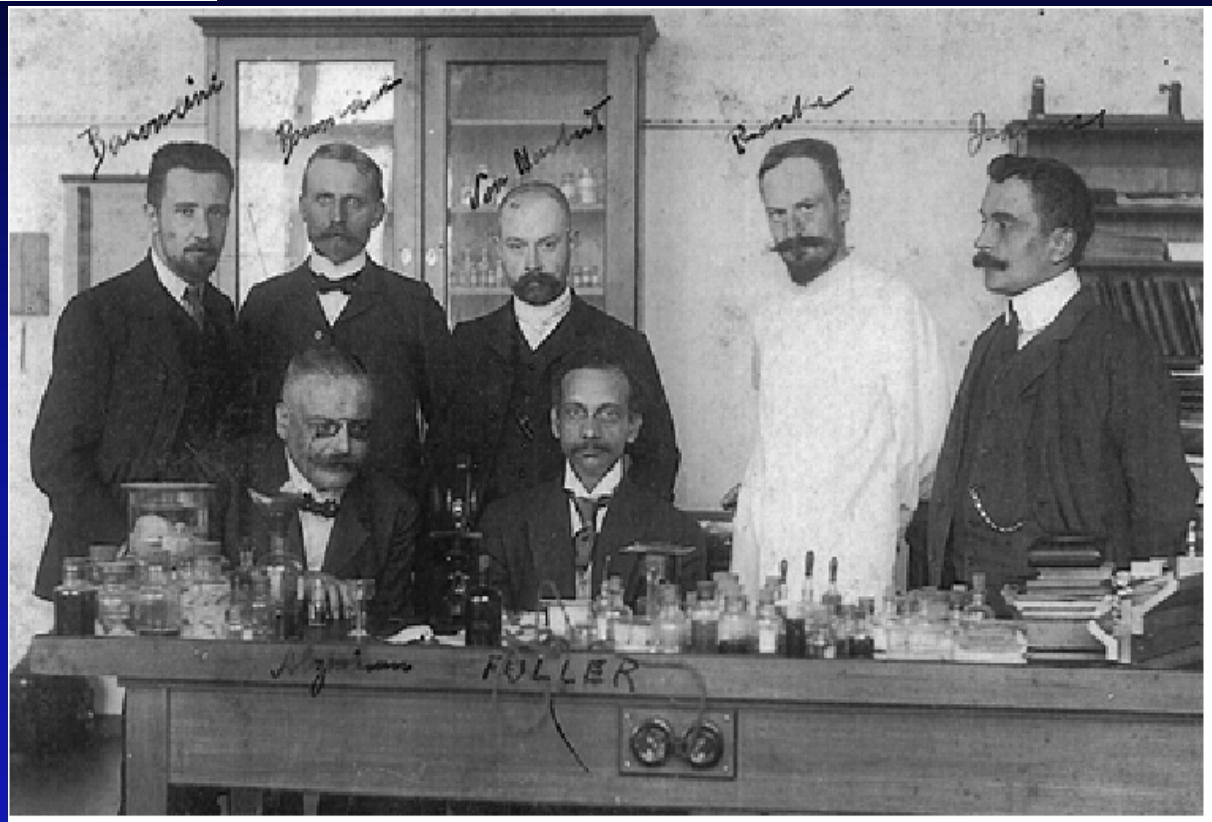
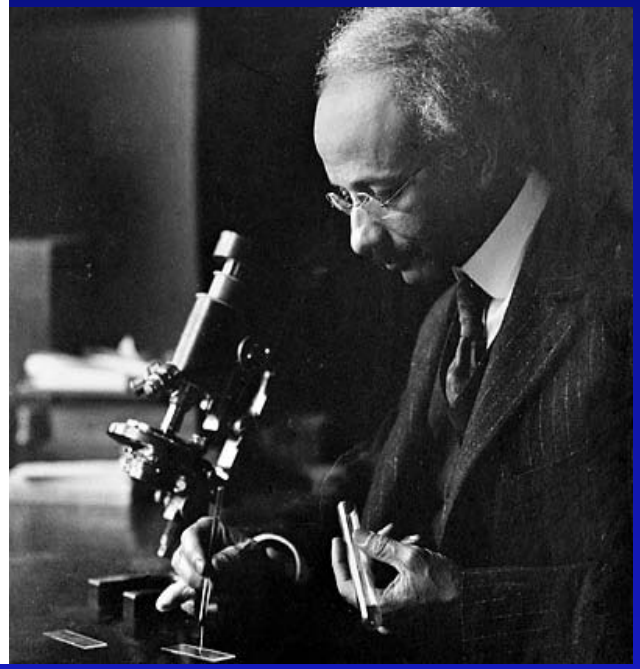


Fig. 2. Alzheimer's research group, 1904, at the Neuropathology Institute, University of Munich. Solomon Fuller is seated in the center next to Alzheimer. (Courtesy: Solomon Fuller, Jr.).

Dr. Solomon Carter Fuller authored the first published paper on AD in the English Literature.



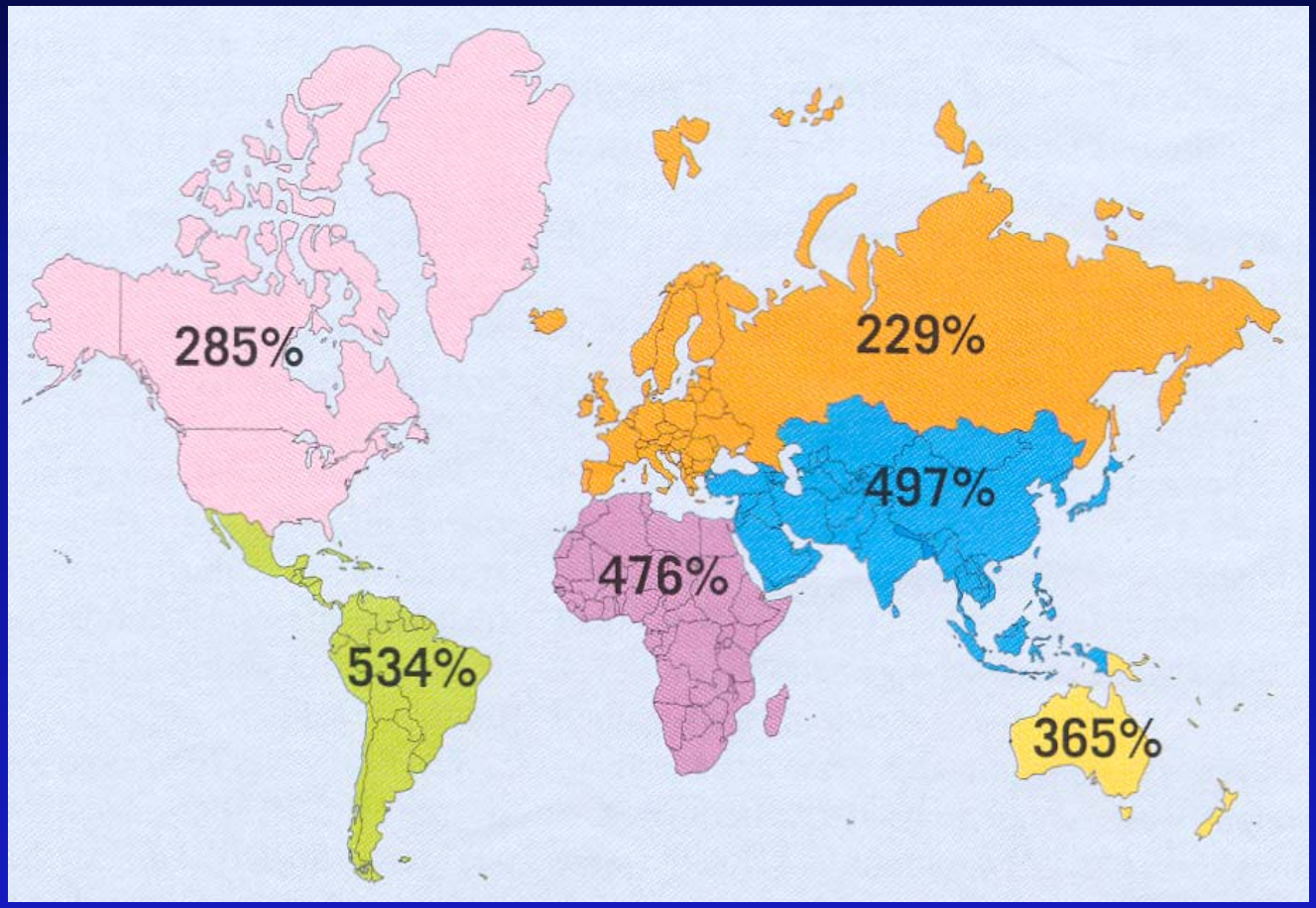
Kaplan: Solomon Carter Fuller: Where My Caravan Has Rested.
Lanham, MD: University Press of America; 2005.
Courtesy of Robert Friedland.

Prevalence of Alzheimer's Disease (AD)

- 100+ years later: Alzheimer's "Epidemic"
- An estimated 5 million Americans are currently suffering from AD
- An estimated 14 million by the 2050
- Most common form of dementia (60-70%)
- 4th leading cause of death due to disease for people >65 in US
- Treatment Costs: $183 billion annually

1. Murphy SL. National vital statistics reports, Vol. 48, No. 11 (http://www.cdc.gov/nchs/fastats/alzheimer.htm) Accessed Jun 2001.
2. Gutterman EM, Markowitz JS, Lewis B, Fillit H. Cost of Alzheimer's disease and related dementia in managed-Medicare. J Am Geriatr Soc. 1999; 47:1065-71.
3. Alzheimer's Disease and Related Disorders Association, Inc. (http://www.alz.org/media/understanding/fact/stats.htm) Accessed Jun 2001.
4. Brookmeyer R, Gray S, Kawas C. Projections of Alzheimer's disease in the United States and the public health impact of delaying disease onset. Am J Public Health. 1998;88:1337-42.

Predicted Percent Increase in Alzheimer's Disease by Year 2050



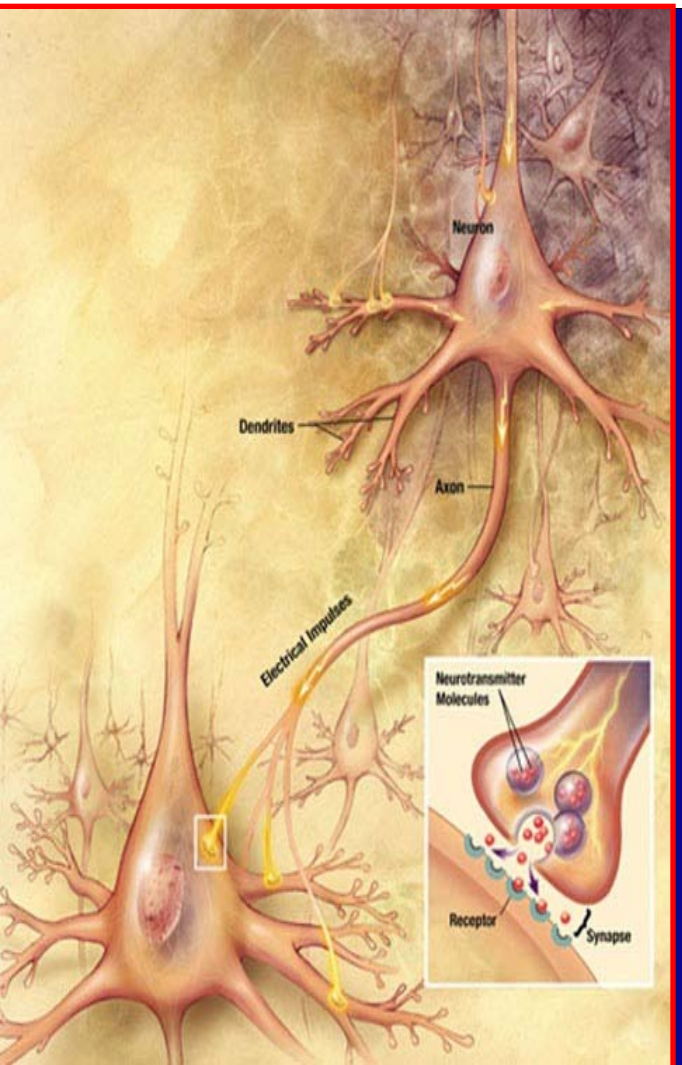
Lower rates in:
- Asia
- Africa
- India

Higher rates in:
- African Americans and Hispanics than in Caucasians or Africans

Note: Based on estimated data for 2006 and 2050.

Ziegler-Graham et al. Alzheimers Dement. 2007;3:S168-9.

Alzheimer's Disease and the Brain



- The brain has billions of neurons.
- To stay healthy, neurons must communicate with each other, carry out metabolism, and repair themselves.
- AD disrupts all three of these essential jobs.

AD and the Brain

What's the Difference Between Normal and MCI?

Normal Aging

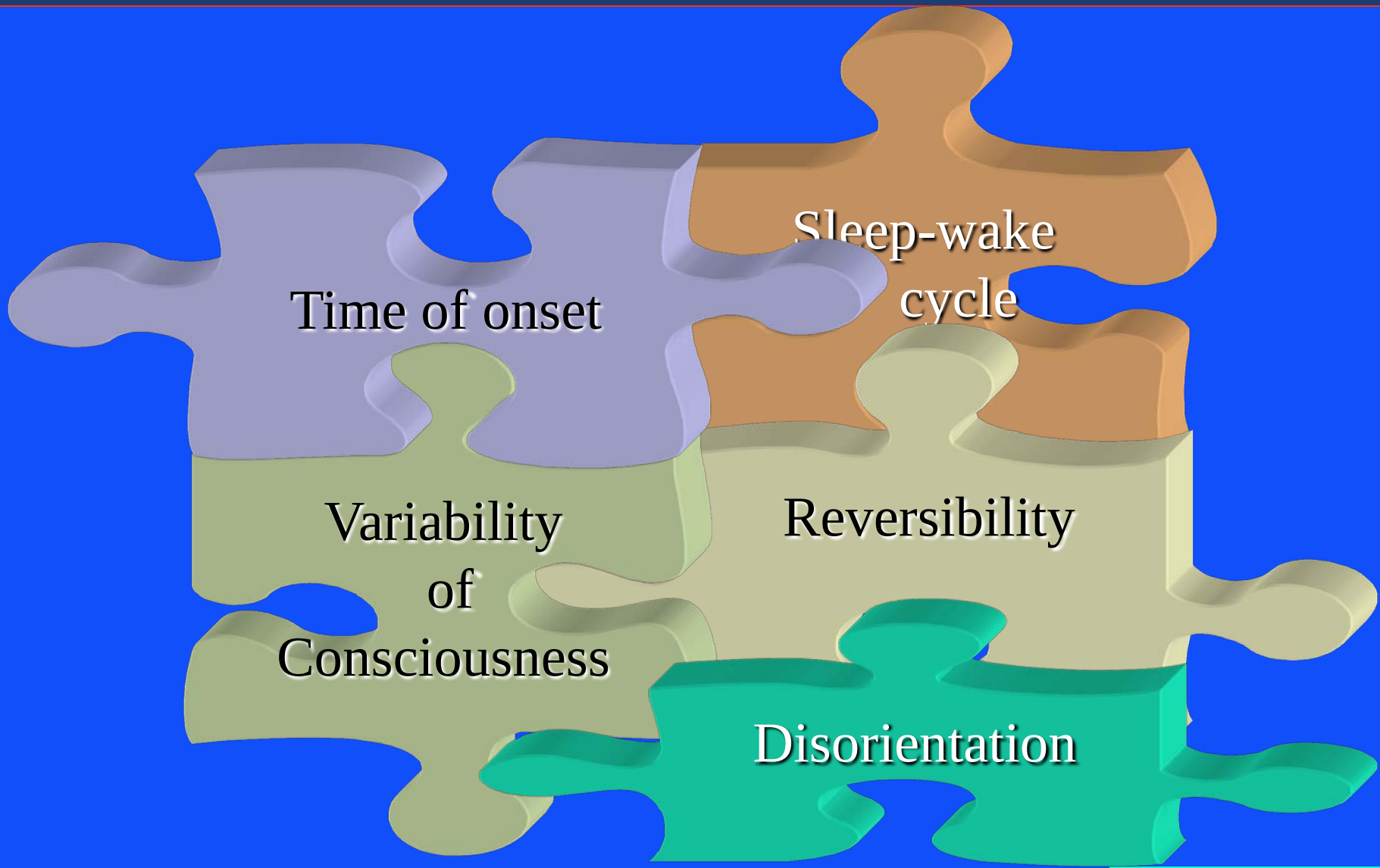
- Loss of memory for words and names
- Slowed processing speed
- Difficulty sustaining attention when faced with competing environmental stimuli
- No functional impairment

Mild Memory Loss (MCI)

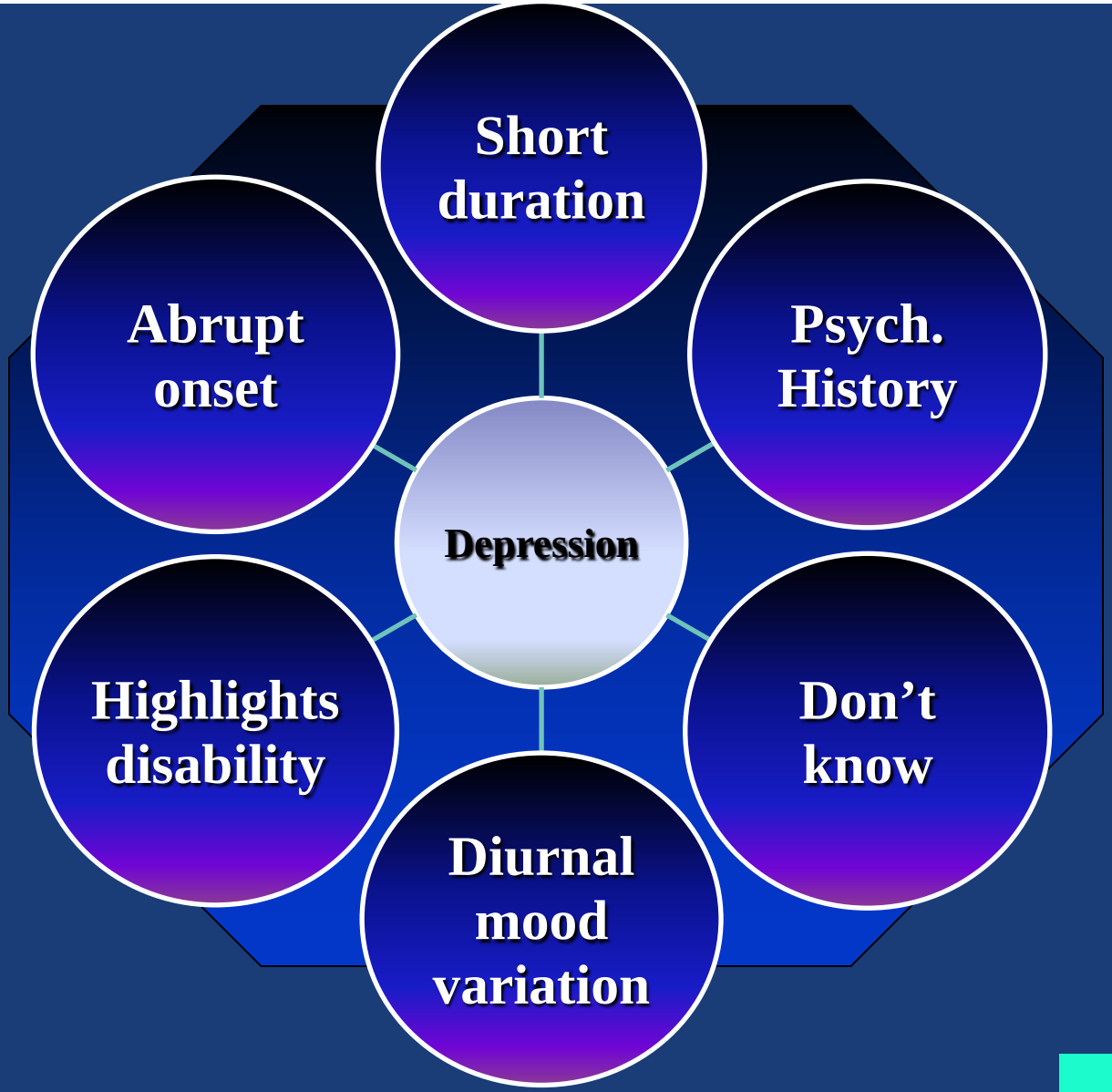
- Memory impairment beyond that expected for age, increasing over last **6 to 12 months**
- Other cognitive functions generally unimpaired
- Daily function not significantly impaired
- Not dementia

Source: Dr. Pierre Tariot, Banner Alzheimer's Disease Institute, Phoenix, AZ. What is on The Horizon for Alzheimer's Disease Research?

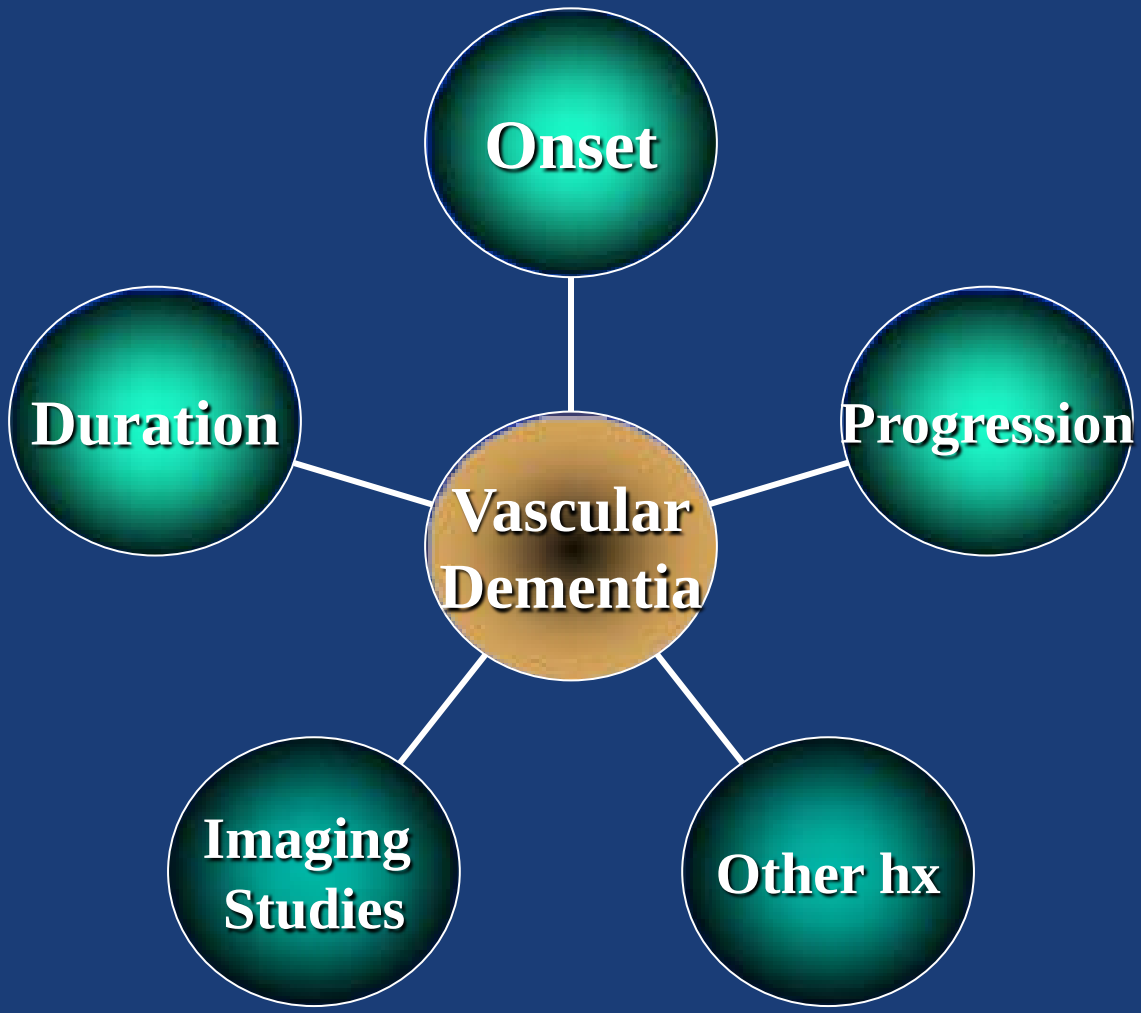
Is It Dementia or Acute Confusion?



Is It Depression or Dementia?



Is It Vascular Dementia?

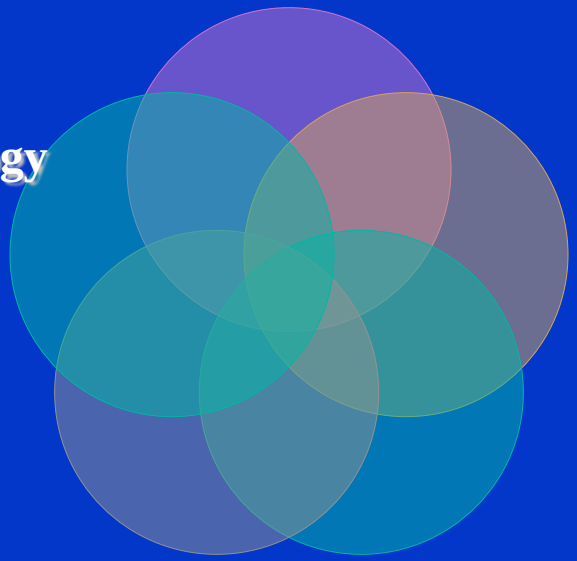


Treatment Options/Focus

Agitation and confusion

Underlying pathology

Nutrition



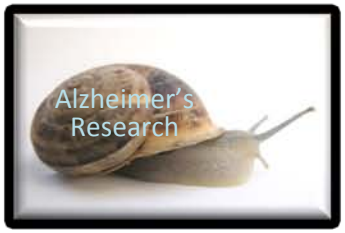
Preservation of function

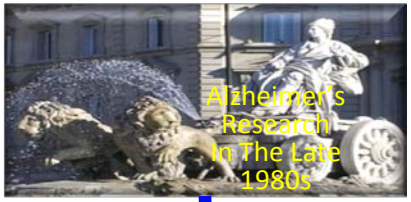
Co-morbid conditions

Obisesan et al.

Development of Alzheimer Therapy

1910-1980	1980s	1990s	2000s and Beyond
Compassion	Neurochemical Deficit (Cholinergic Hypothesis)	Systemic Deficiency (Amyloid /Inflammation)	Abnormal Folding of Protein (Refined Amyloid Hypothesis)





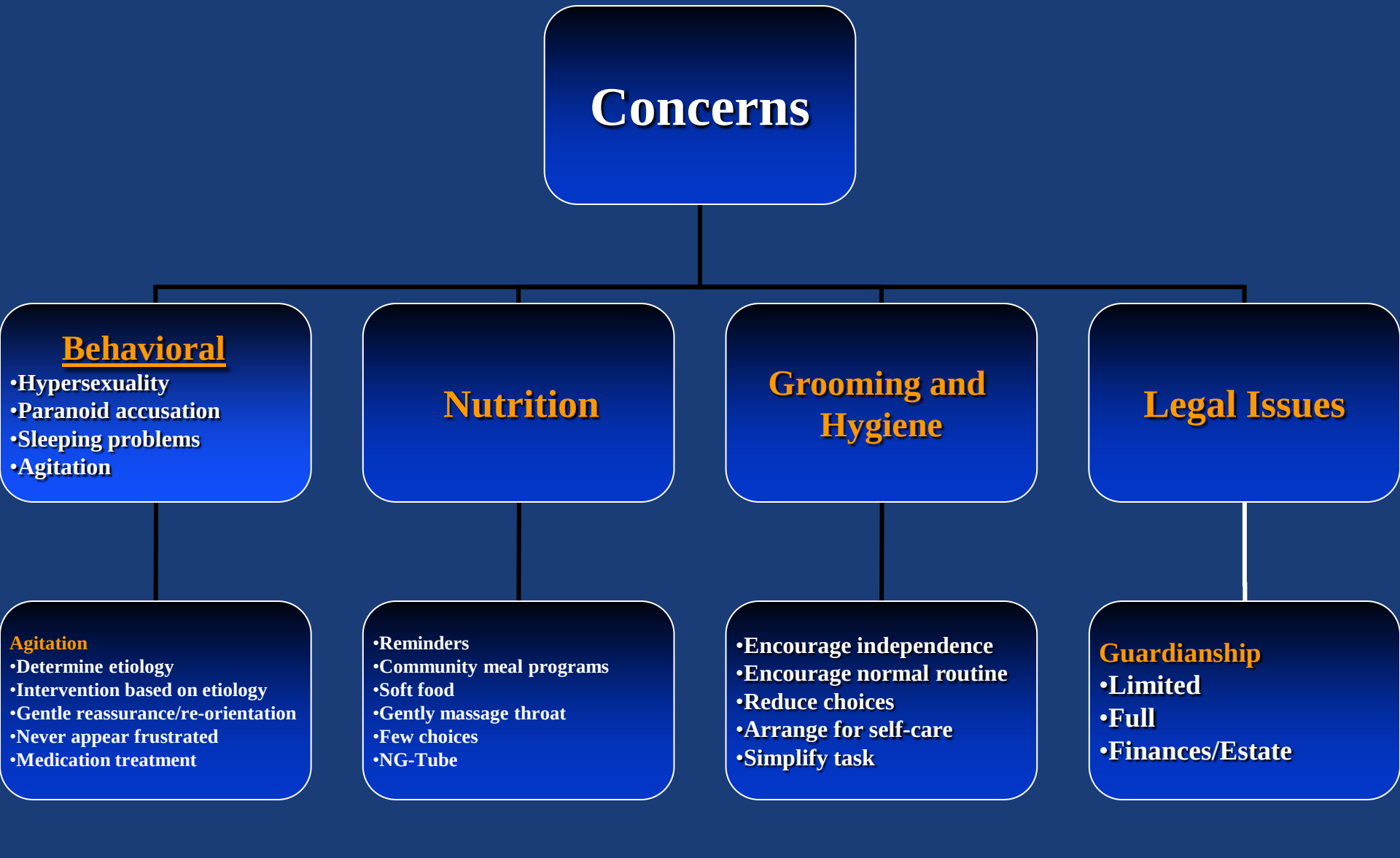
- 36 Hour Book
- Advanced Directives
- Holding

- Anti-inflammatories
- Hormone Replacement
- Anti-oxidants (e.g. Vit. E)

- Immunotherapy
- HOPE Era: Prevention and CVD Risk

Tacrine	Donepezil	Rivastigmine	Galantamine	Memantine
1993	1997	2000	2001	2003

Caregiver Directed Management?

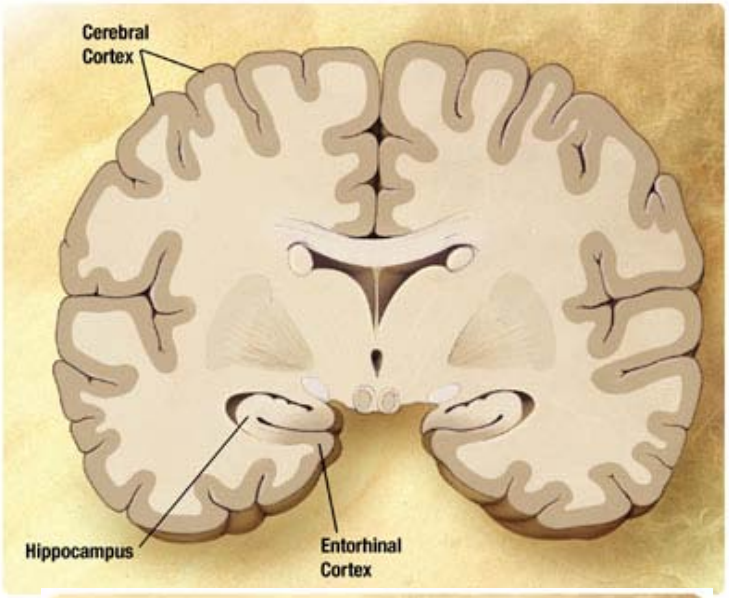


Progress in Diagnosis

(?Autopsy Vs Early Diagnosis)

AD and the Brain: MCI

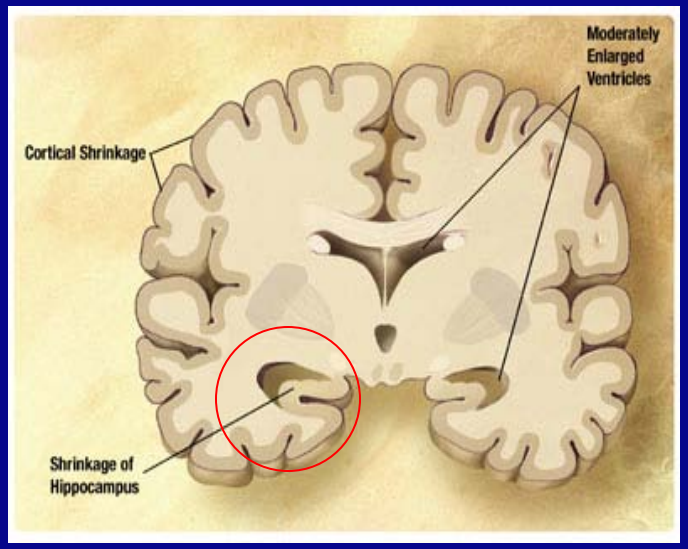
Preclinical AD (MCI)



- Affected regions begin to shrink as nerve cells die.
- Changes can begin 10-20 years before symptoms appear.
- Memory loss, the first visible sign, is the main feature of mild cognitive impairment (MCI).

Alzheimer's Disease and the Brain (Mild Stage)

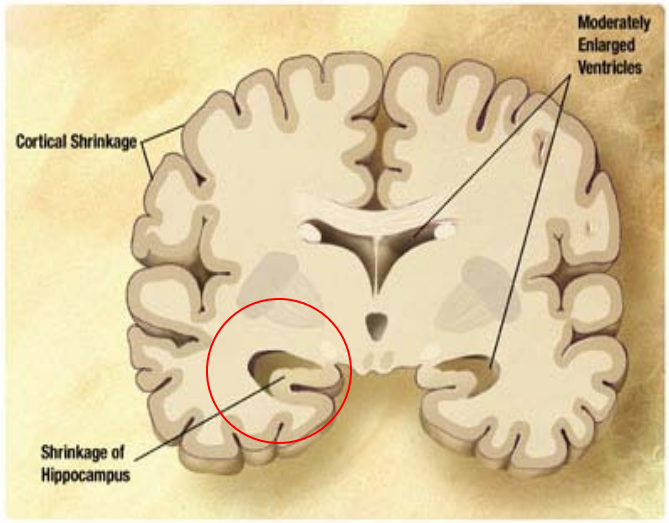
Mild AD



- AD spreads through the brain:
  - The cerebral cortex begins to shrink as more and more neurons stop working and die.
- *Mild AD signs:* can include memory loss, confusion, trouble handling money, poor judgment, mood changes, and increased anxiety.

Alzheimer's Disease and the Brain (Moderate Stage)

Moderate AD



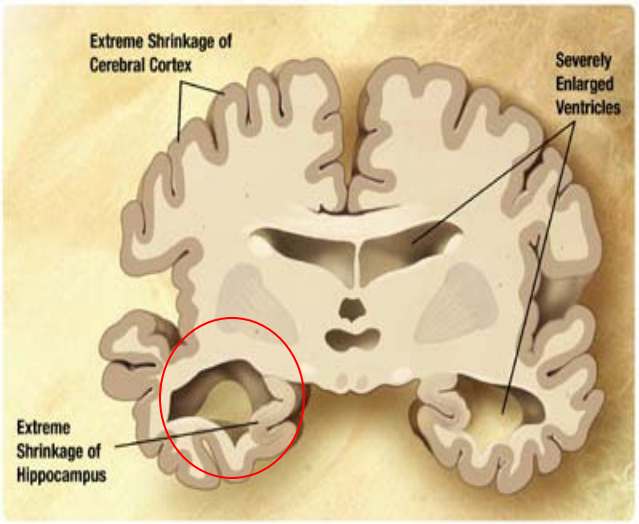
- As the brain shrinks as more and more neurons die

Moderate AD signs:

- ❑ Increased memory loss
- ❑ Confusion and problems recognizing people
- ❑ Language and thinking problems
- ❑ Restlessness and agitation
- ❑ Wandering and repetitive statements.

Alzheimer's Disease and the Brain (Severe Stage)

Severe AD

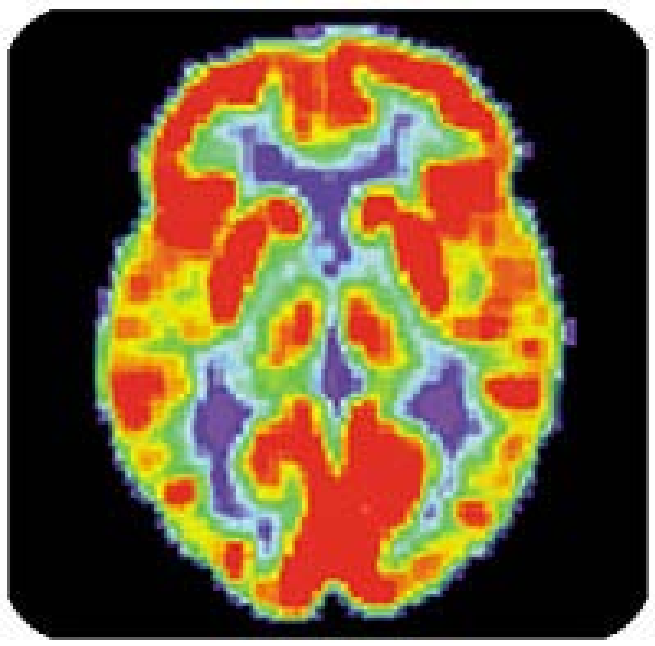


- In severe AD: extreme shrinkage occurs in the brain. Patients are completely dependent on others for care.
- Death usually occurs from aspiration pneumonia or other infections.

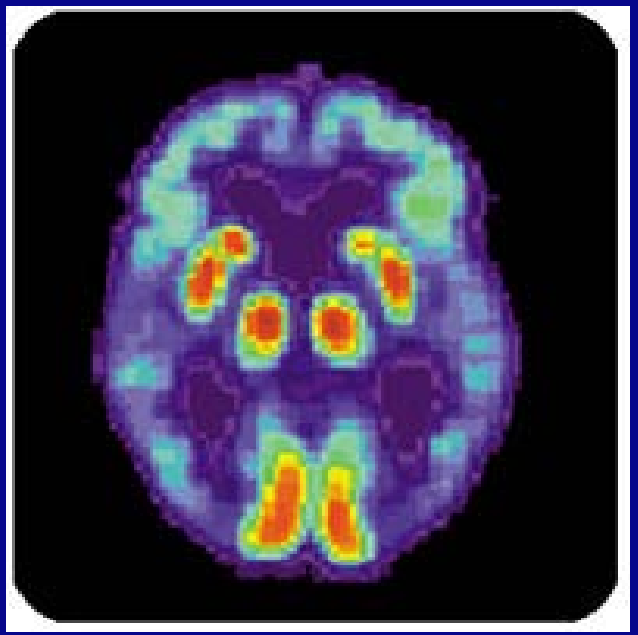
AD and Brain PET Imaging

Brain Glucose Use in Alzheimer's Disease

But, we now know a lot about what happens in the brain after AD begins.

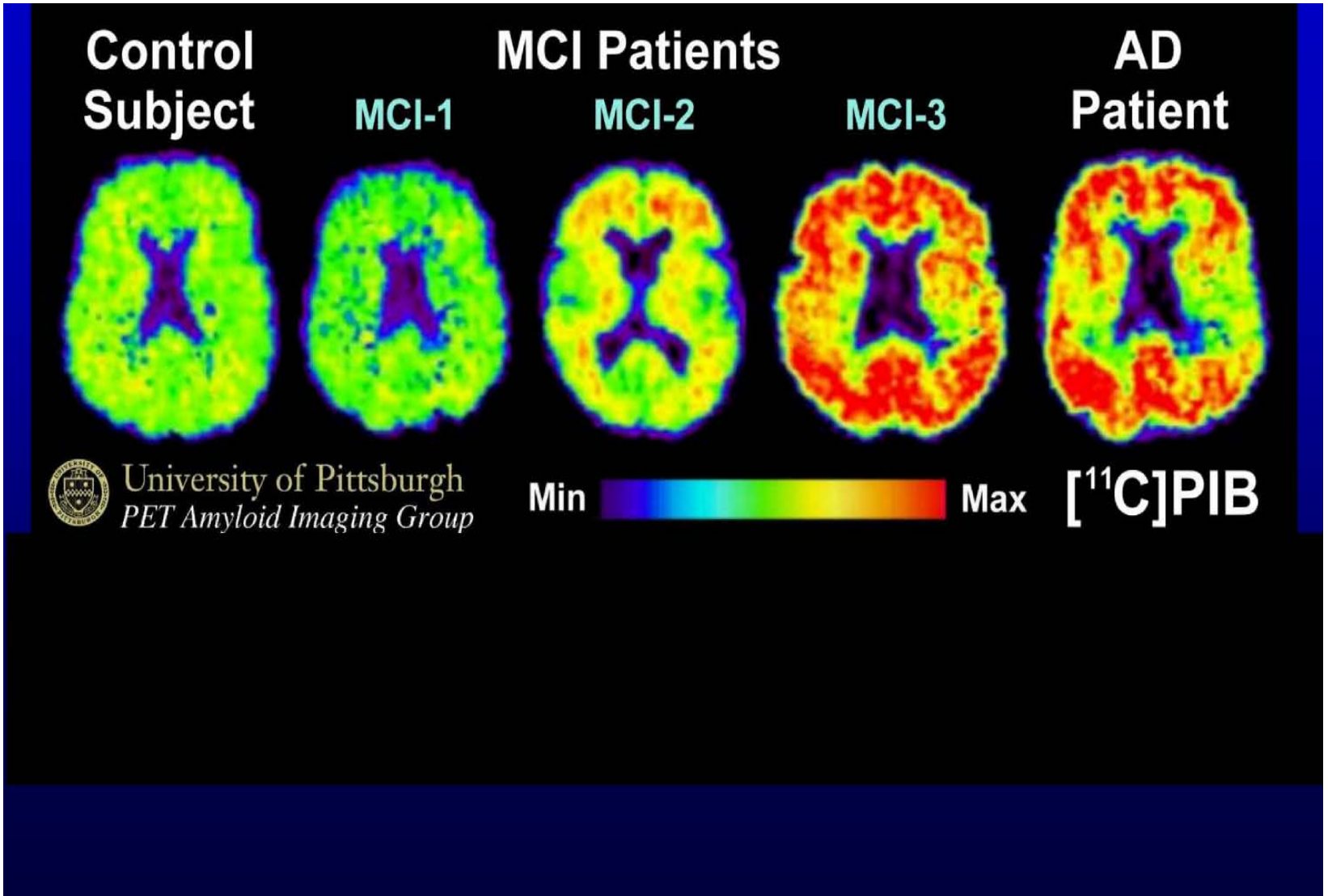


Pet Scan of
Normal Brain

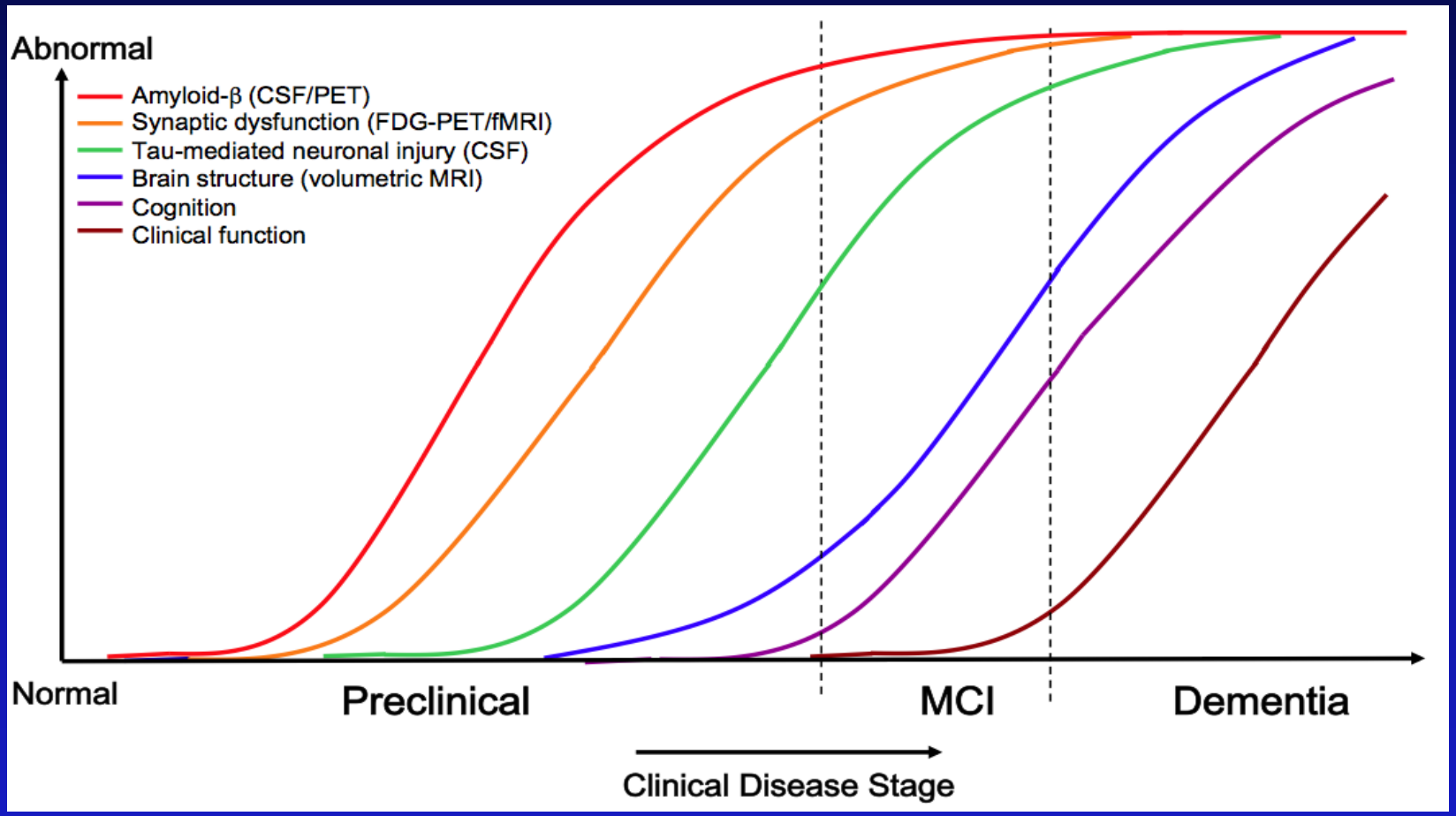


Pet Scan of Alzheimer's
Disease Brain

Amyloid Imaging



Hypothetical model of dynamic biomarkers of the Alzheimer's pathological cascade, expanded in the preclinical phase



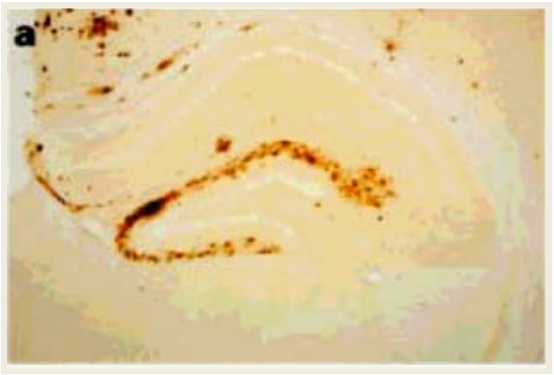
Curtsey: Cliff Jack, Mayo Clinic

Progress in Treatment

Are current treatments are effective?

Immunization Reduces Amyloid Deposition in Mice Brain and Prevents Memory Deficit

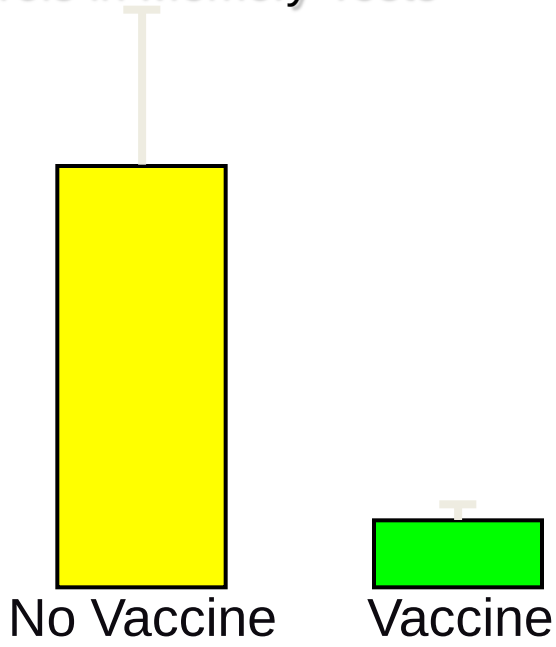
Amyloid Burden



Schenk et.al, Nature, 400:173-177, 1999

Amyloid Burden and Memory Performance

Immunized Mice Perform Better than Controls in Memory Tests

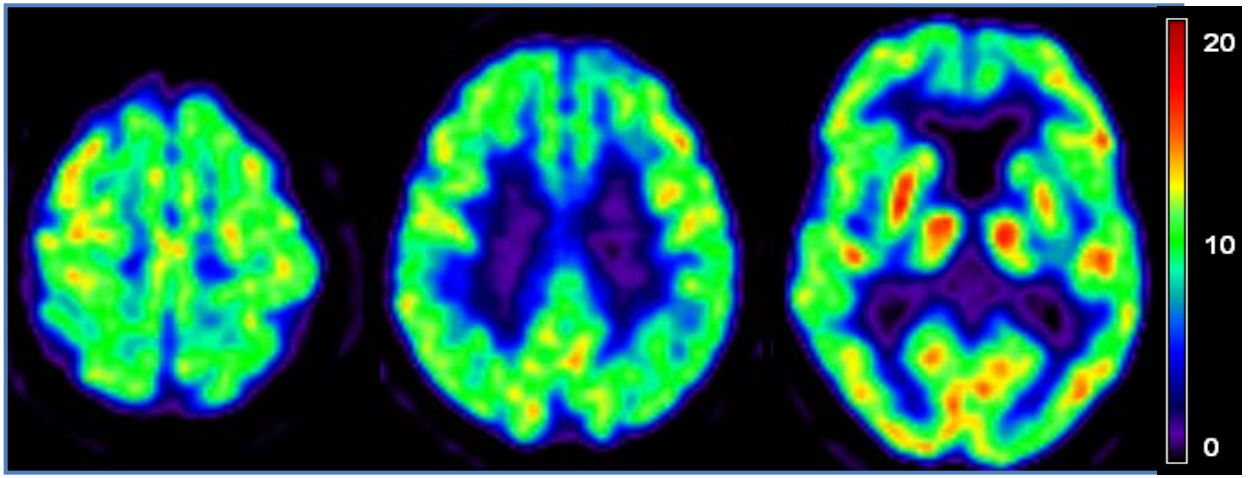


Morgan et.al, Nature, 408:932-935, 2000

The Effects of IgIV (Immunoglobulin) on Alzheimer's Brain Metabolism

Before IgIV treatment

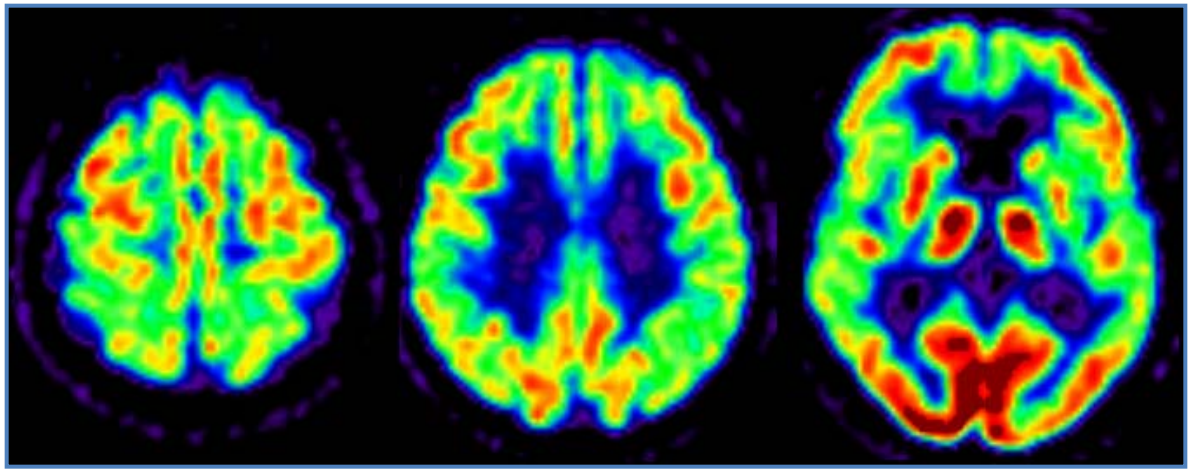
ADAScog = 21



umol/100g/min

After 6 months IgIV treatment

ADAScog = 19, CGIC change = +1



Source: N Relkin 2008

Emerging Risk Factors

Implications for Prevention?

Emerging Risk Factors for Alzheimer's Disease

Obisesan TO

Immutable Risk

Unchangeable risk factors

- Age
- Family History
- Genetic: APOE Gene
- Female Gender
- Ethnicity

Mutable Risk

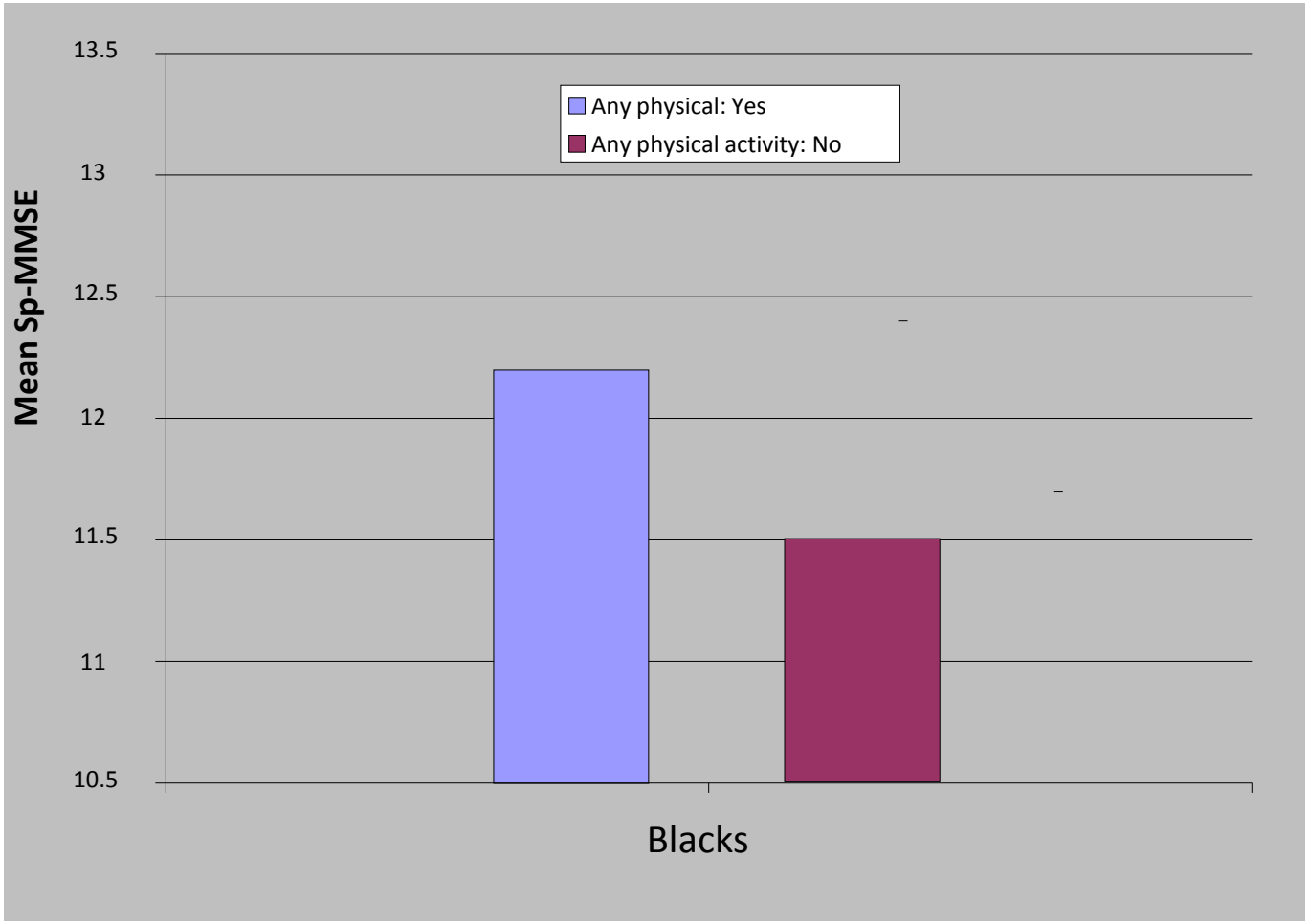
Scientists also believe that the following preventable risk factors contribute to Alzheimer's disease risk

- Low levels of education
- Elevated blood pressure
- High cholesterol
- Overweight and Obesity
- Cigarette smoking
- Diabetes
- Lack of exercise (Sedentary Lifestyle)

CVD

Deposition of Abnormal Protein (Amyloid)
Result in Alzheimer's Disease

Relationship of Physical Activity to Performance on Test of Memory (NHANES III)



Disability

"YOU"

Made all These Progress Possible

An Important Way Forward is:

Clinical Trials

Importance of Research on Alzheimer's Research

- Research is our only hope for defeating Alzheimer's
- Clinical studies are the way that promising new treatments are tested for safety and effectiveness
- By volunteering for clinical studies, you can make an important contribution to the fight against Alzheimer's

Imagine

- For a moment: let's put on our thinking caps and imagine
- Imagine a world without treatment for **HYPERTENSION AND STROKE**
- Imagine a world without treatment for **DIABETES**
- Imagine a world without treatment for **HEART DISEASES**
- Imagine a world without treatment for **CANCER**
- Imagine a world without treatment for **VISION LOSS AND EYE GLASSES**
- Imagine a world without antibiotics and treatment for **INFECTIONS**
- Imagine a world without treatment for **ARTHRITIS**
- Imagine a world without **PAIN MEDICATIONS**
- A world without treatment for ALZHEIMER'S DISEASE is unimaginable

Thomas O. Obisesan December 15, 2011

Memory!

”Memory….without it … all life and thought were an unrelated succession. As gravity holds matter from flying off into space, so memory gives stability to knowledge; it is the cohesion which keeps things from falling into a lump or flowing in wave… Memory performs the impossible for man by the strength of his divine arms; holds together past and present, beholding both, existing in both, abides in the flowing, and gives continuity and dignity to human life. It holds us to our family, to our friends. Hereby a home is possible….”

Ralph Waldo Emerson(1803-1882)
11.12. 1879, age 76

Thank You

Thank You!!!

Ongoing Research Studies at HUH

1) Exercise and Memory
2) REVEAL
3) ADNI
4) ASPREE
5) Resveratrol (soon)
6) Intranasal Insulin (coming)

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