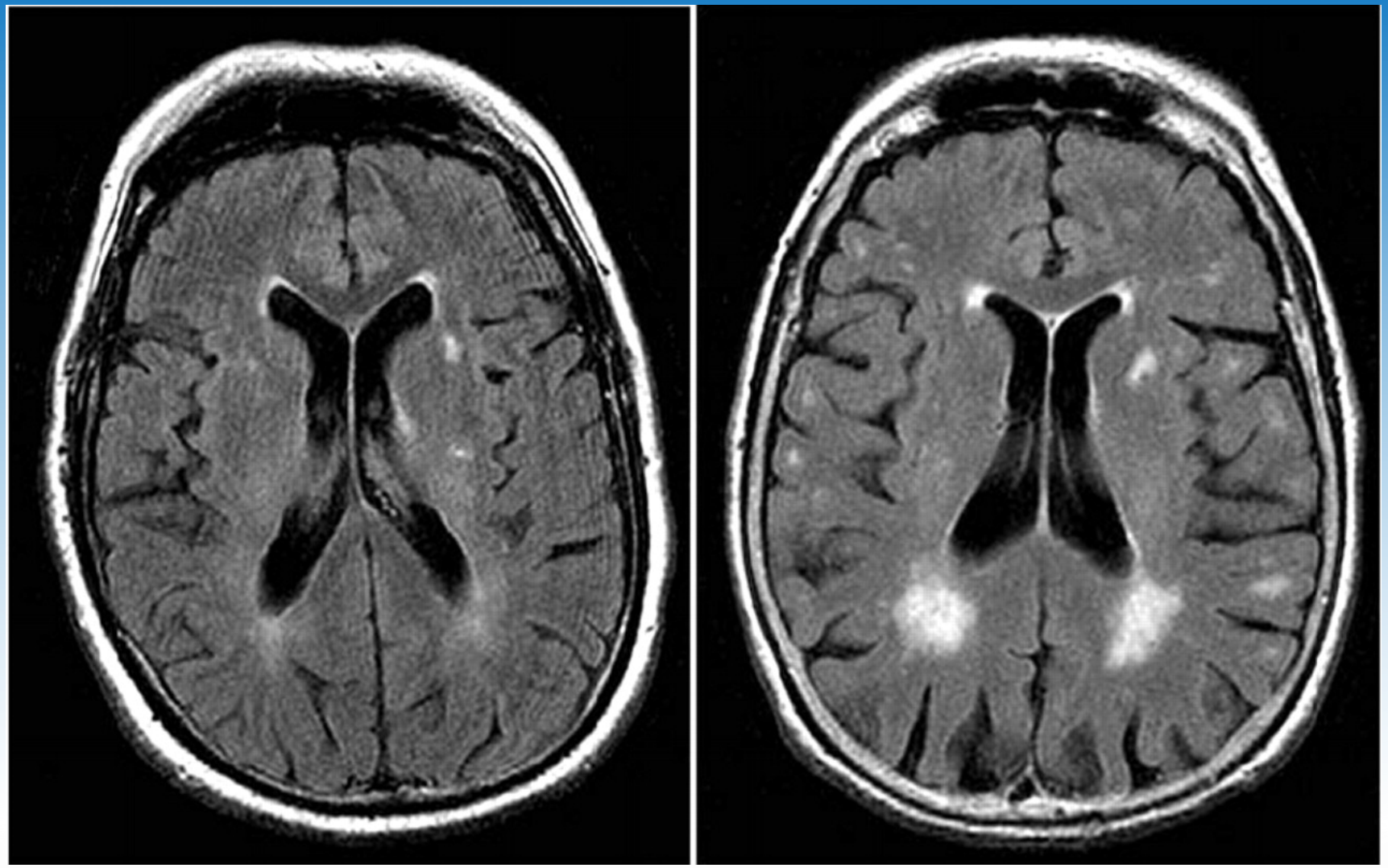
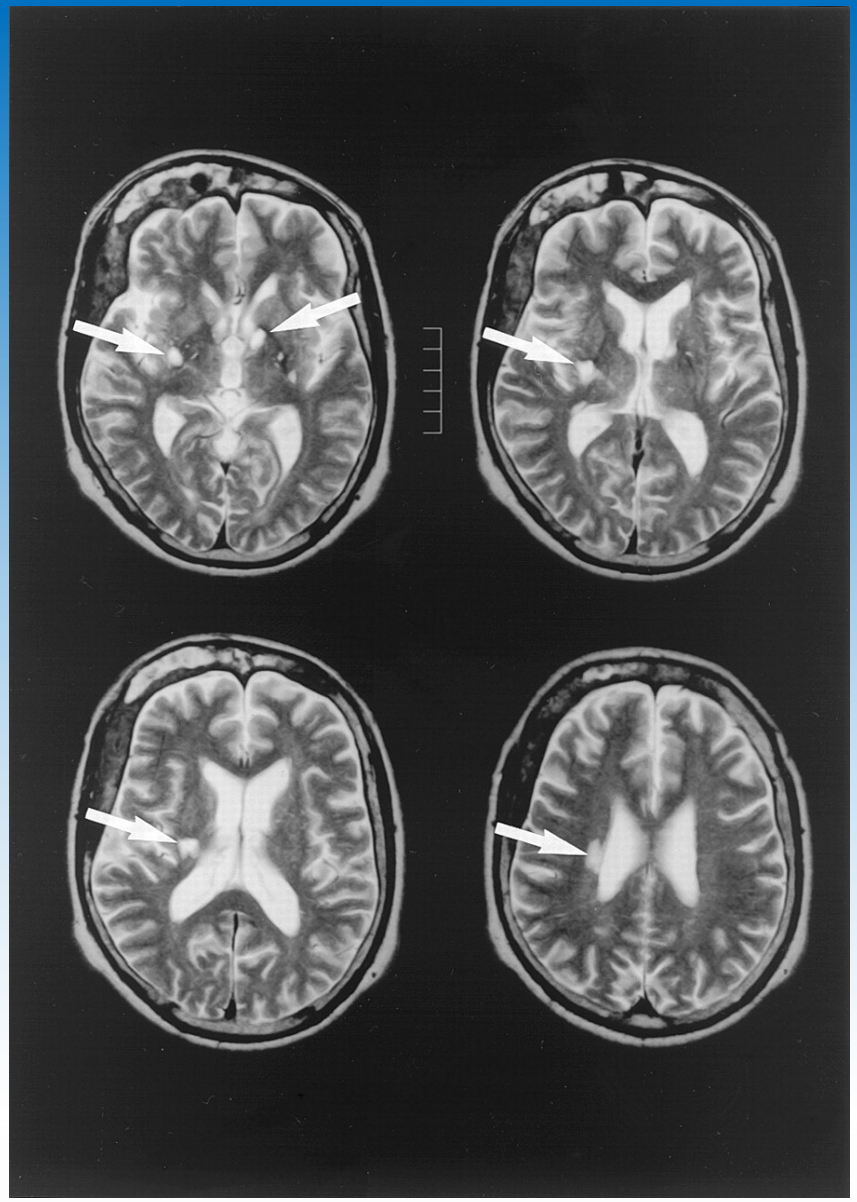
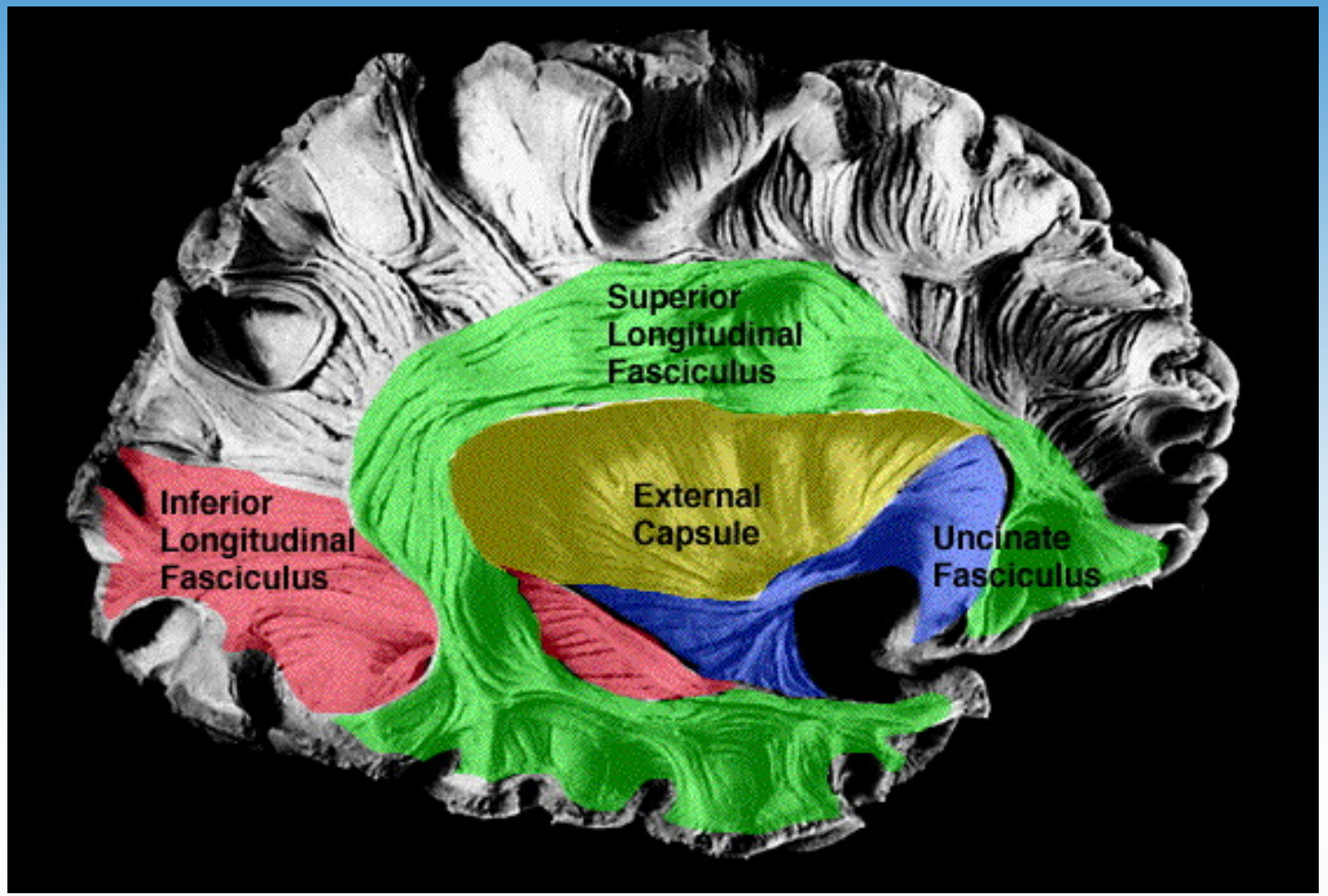




Top: lacunar infarcts in basal ganglia; Bottom: infarcts in deep white matter

Intrahemispheric White Matter Tracts



Aging and Brain Structure

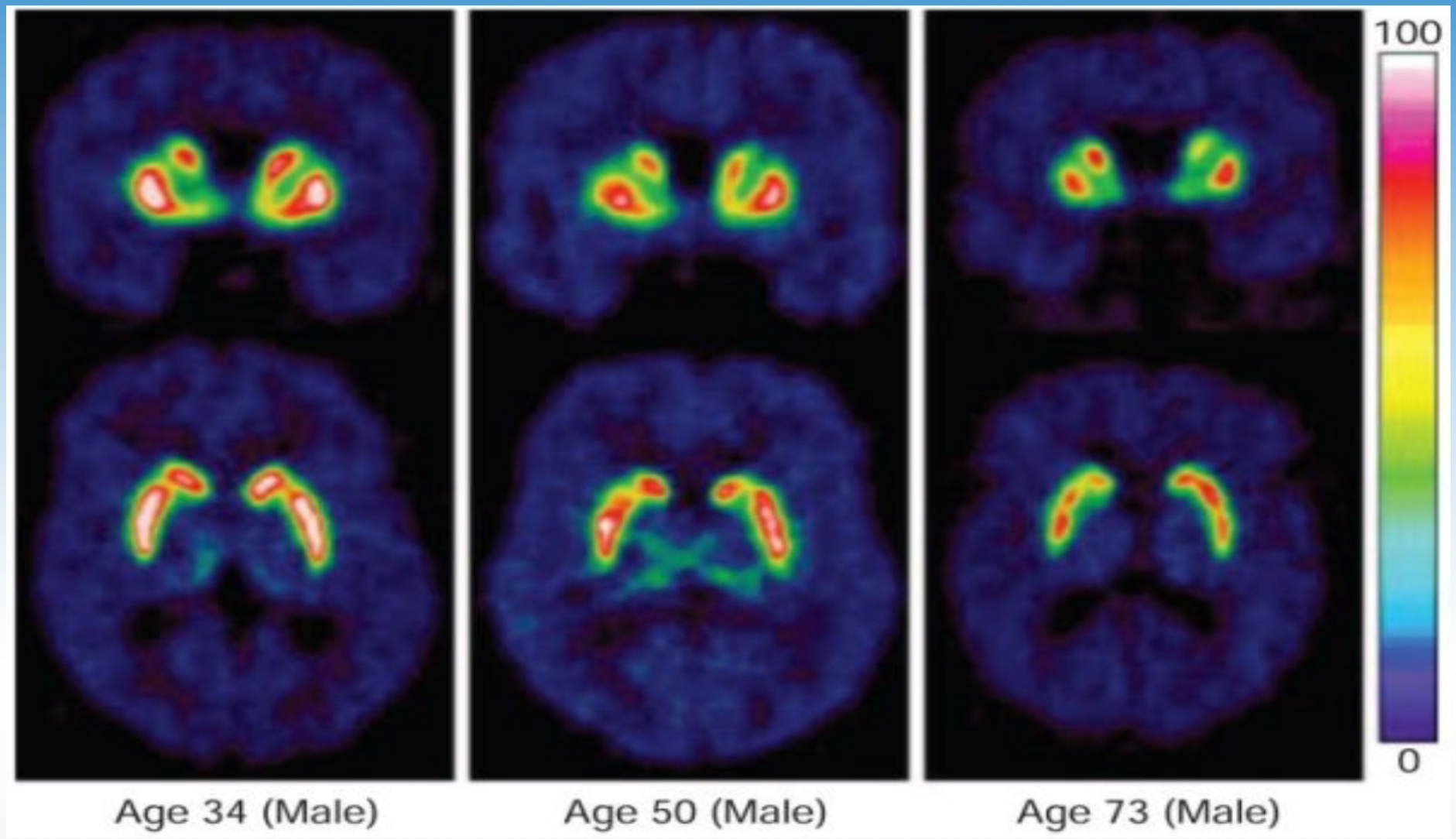
- Gray volume
- Number of neurons
- Neuronal density
- Neuronal features (e.g., size, pigment acquisition, dendrites)
- Synaptic density
- White matter volume and integrity
- Ventricular size

Aging and Neurochemistry

- ↓ Dopamine
- ↓ Acetylcholine
- ↓ Norepinephrine
- ↓ Serotonin
- ↓ NMDA receptors (but not AMPA or kainate)
- ↓ Cholinergic receptors

PET: Age related decline in dopamine transporter availability

Erixon-Lindroth N. et al. The role of the striatal dopamine transporter in cognitive aging. Psychiatry Res. 2005; 138



Communication in the aging brain

- ↓ number of synapses
- ↓ density/functionality of receptors
- ↓ availability of key neurotransmitters
- White matter pathways develop lesions
- “Silent” focal cortical lesions

Normal

The American Heritage® Dictionary of the English Language, Fourth Edition

1. Conforming with, adhering to, or constituting a norm, standard, pattern, level, or type; typical
2. Functioning or occurring in a natural way; lacking observable abnormalities or deficiencies.

How about some good news?

Plasticity

- Changes that occur due to learning and experience
- Normal development
- Shift of functional organization after injury
- Synaptic pruning in aging – elimination of weak synapses
- Apoptosis (programmed cell death) – relinquishing cell after purpose is served
- Neuronal change (structure, synapses)
- Neurogenesis

Neurogenesis and Plasticity

- THEN: The brain is equipped with a finite complement of neurons. Once a neuron dies, it is never replaced. Therefore aging entails a relentless, subtractive process.

- NOW: The change in the absolute number of neurons is not significant. New neurons sprout in the hippocampus throughout the lifespan.

Peter Eriksson & Fred Gage, Neurogenesis in the adult human hippocampus. Nature Medicine 1998

Roberto Cabeza Ph.D.

Duke U. Center for Cognitive Neuroscience

PET Brain Activity during Source Memory Task

Young | Old-Low | Old-High

Cabeza et al. (2002, *Neuroimage*)

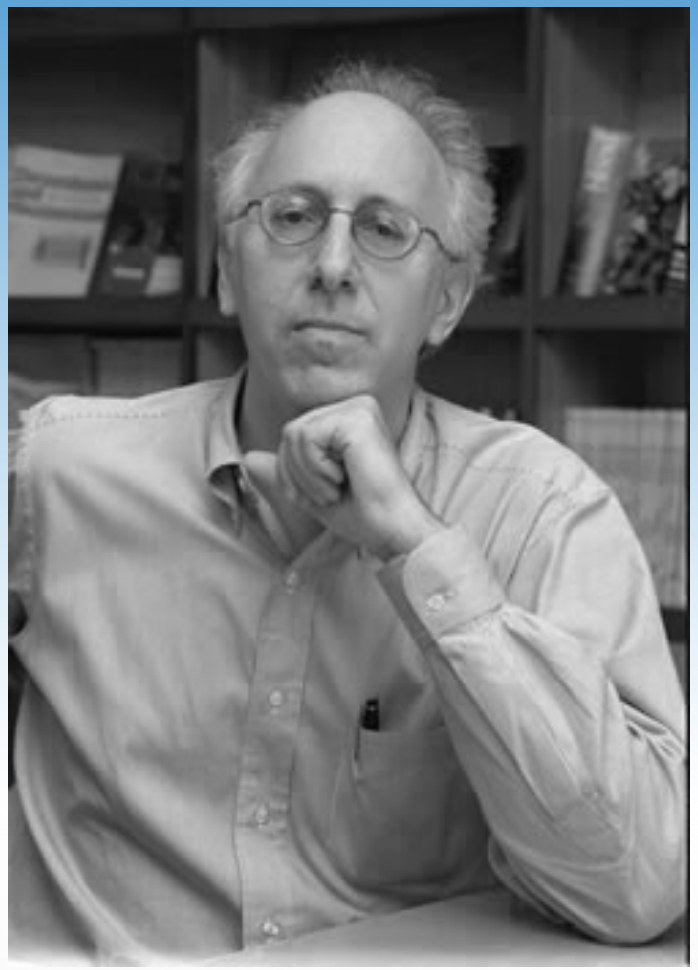
- Old-Low performing subjects recruited similar PFC regions as young adults but used them inefficiently
- Old-High performing subjects compensated for age-related memory decline by reorganizing the episodic retrieval network

→ SUPPORTS COMPENSATION VIEW OF HAROLD

Hemispheric Asymmetry Reduction in Old Adults

Cognitive Reserve

Yaakov Stern



- Relationship between brain pathology and cognitive effect is moderated by CR.
- CR composed of genetic and acquired (environmental) factors
- CR markers: education, occupation, leisure interests
- Greater CR → less impact on function with similar level of pathology
- Greater CR → Steeper decline once pathology overwhelms
- Neurophysiologic substrate?

Aging Scorecard

Bad News

- Degradation of cortical/subcortical networks
- ↓ Redundancy
- ↓ Connectivity

Good News

- Plasticity
- Compensation
- Reserve

Optimizing memory in aging

What factors are within our control?

National Institute on Aging

Cognitive Health in Older Adults

- Take care of your health
- Eat healthy foods
- Be physically active
- Keep your mind active
- Stay connected

The Nun Study

- NIA Longitudinal study of aging and Alzheimer's disease
- David Snowden Ph.D. (began at U. Minn., then to U Kentucky)
- Begun in 1986; ongoing
- Participants: 678 members of the School Sisters of Notre Dame, aged 75-102 at start of study, located in 7 centers throughout the US
- All participants agreed to brain donation

Potentially Controllable CVD Risk Factors

- BEHAVIORS
  - Cigarette smoking
  - Poor nutrition
  - Physical inactivity
  - Excessive alcohol use
- DISEASES
  - HTN
  - Hypercholesterolemia
  - Diabetes
  - Syndrome X (aka Metabolic s.; Insulin resistance s.)
- BRAIN EFFECTS
  - Atherosclerosis→
  - Impaired cerebral blood flow →
  - Brain infarction

Nutritional Risk Factors

- Saturated fats and trans fats
  - Saturated Fat: Meat, dairy
  - Trans fat: Processed foods, fast foods, snack foods baked goods
  - ↑ serum cholesterol
  - ↑ atherosclerosis and CVD
  - Unsaturated fats (e.g., veg oils, nuts, olives) protective
- Homocysteine
  - High level associated with ↑risk of CV events
  - ↑ Risk of AD via potentiation of copper and Aβ peptide neurotoxicity
  - Can be caused by deficiency in folic acid, B6, B12
  - Although evidence for the benefit of lowering Hcy is lacking, patients at ↑ risk should be advised to get enough folic acid and B vitamins in their diet