

DIET, AGING, and MIND



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Outline: Diet, Aging, and Mind

- 1. Brain Changes in Aging**
- 2. Dementias**
- 3. Dietary Interventions: DHEA and Soy**
- 4. DHEA**
- 6. Soy**
- 7. Summary and Conclusions**

“I hope I Die Before I Get Old”

Pete Townshend

The WHO

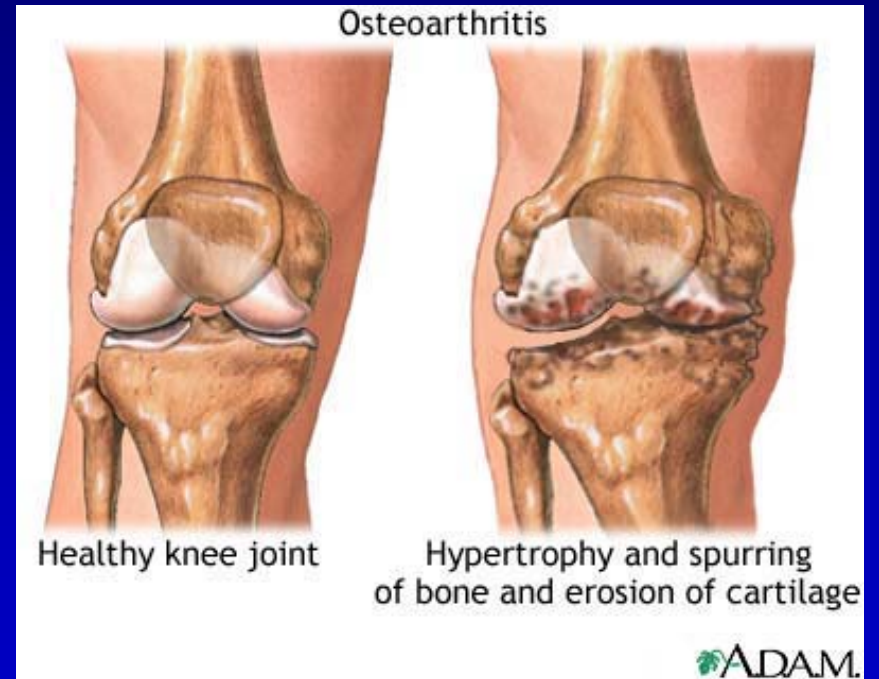
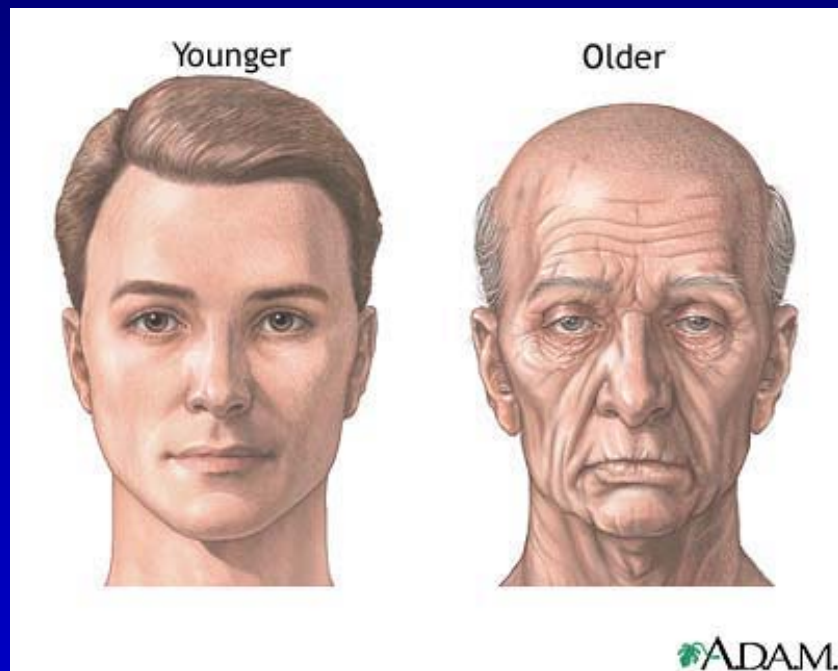
“My Generation”

1965

Links

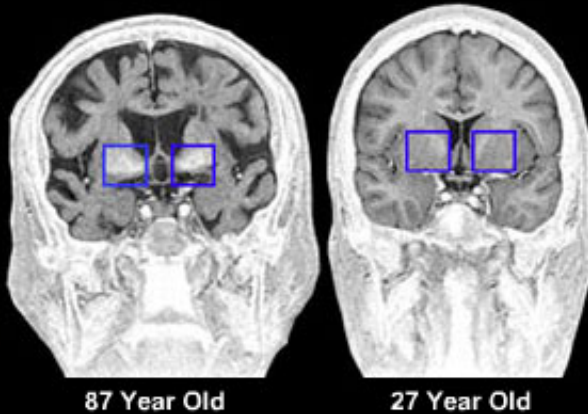
- www.youtube.com/watch?v=zqfFrCUrEbY
My generation The Zimmers 2:18
- <http://www.youtube.com/watch?v=i0XknwXqLDo&mode=related&search=> The Who
37 secs

Changes with Aging

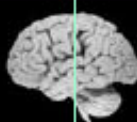


Brain Aging: Normal

Basal Ganglia

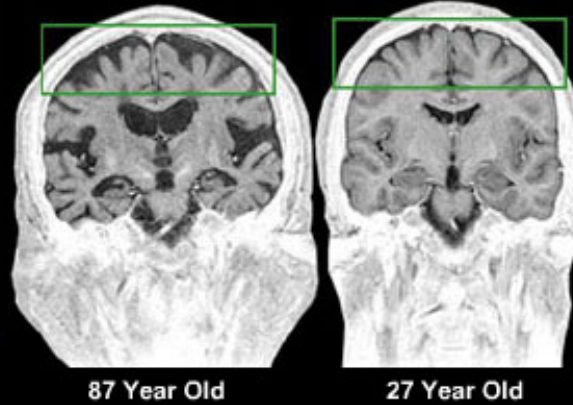


Location of these scans in the brain

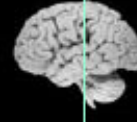


The **basal ganglia** are clusters of nerve cells responsible for initiating and integrating movements. The basal ganglia become bright with age due to iron accumulation.

Subarachnoid Space

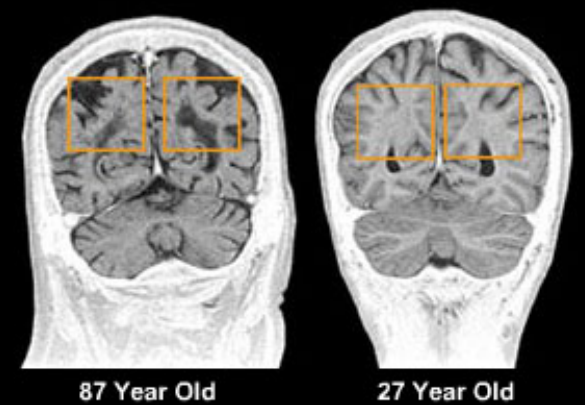


Location of these scans in the brain

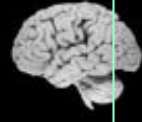


The **subarachnoid space** is the space around the outside of the brain. This area increases in size to fill the space with age-related cell loss

White Matter

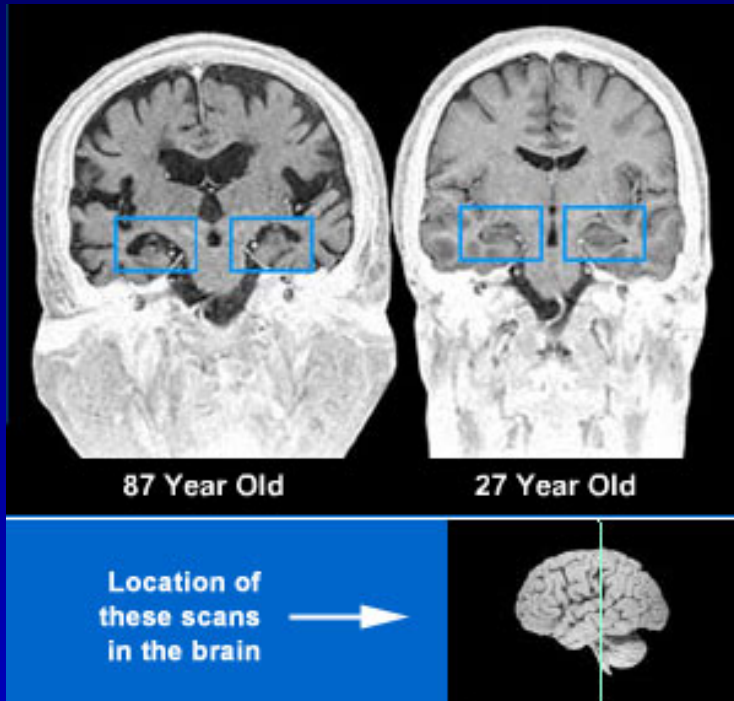


Location of these scans in the brain

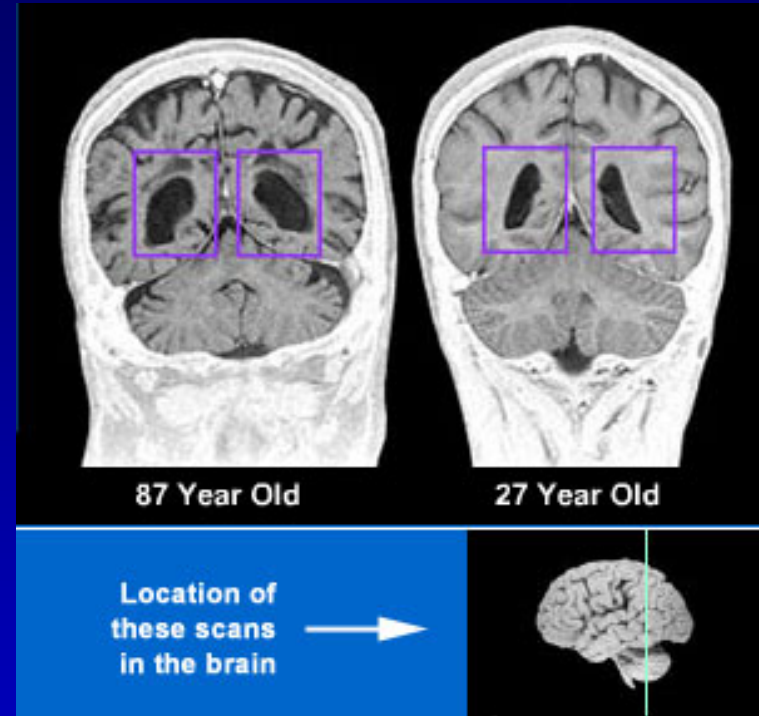


The **white matter** is a communication channel for the brain's information processing gray matter. White matter changes in appearance and may be related to the normal slowing of information processing in the brain with age.

Brain Aging: Normal



The **hippocampus** is the memory center of the brain. There is some cell loss associated with healthy aging, but this by itself does not indicate significant memory loss.



The **ventricles** are hollow spaces filled with cerebrospinal fluid. Like the subarachnoid space, these spaces increase in size as the brain becomes smaller with age.

Social Cost of Dementias: \$150 Billion/Year

Alzheimer's disease, Vascular dementia, Lewy body dementia, Frontotemporal dementia, Huntington's disease, and Creutzfeldt-Jakob disease

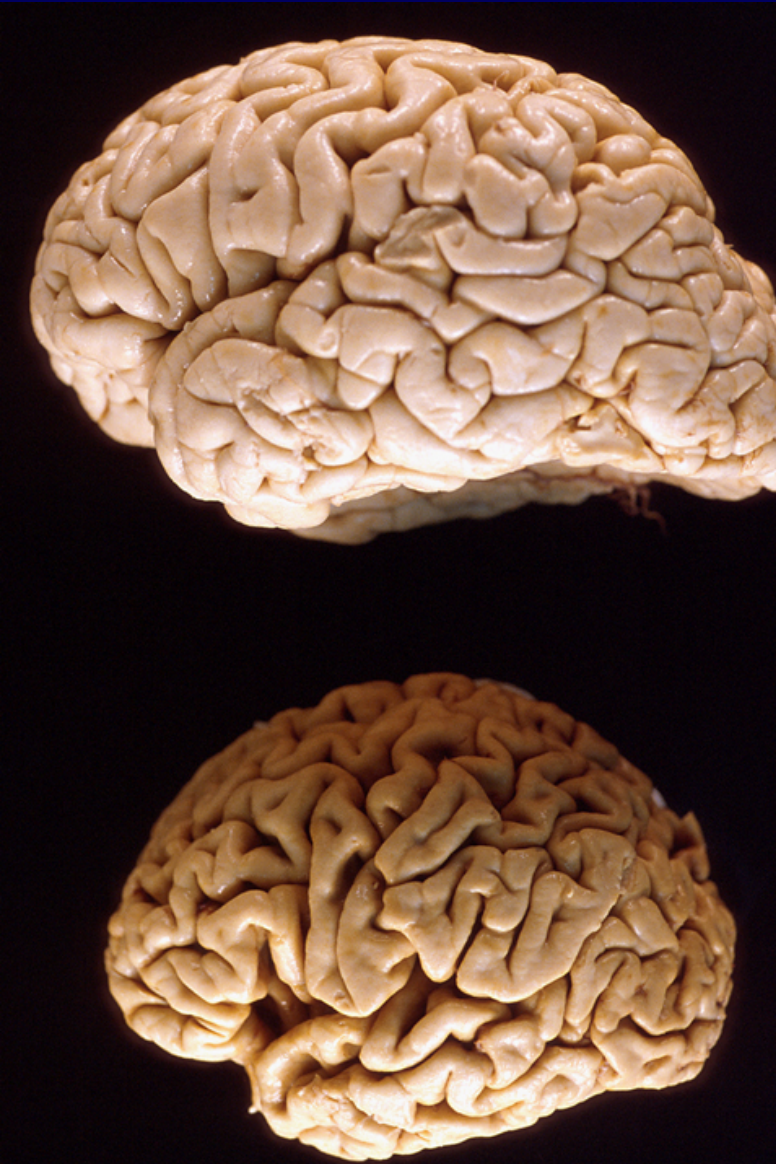
- 30 million cases worldwide and growing**
- New case of AD every 72 seconds in the US**
- significantly impaired intellectual functioning that interferes with normal activities and relationships.**
- Inability to solve problems and maintain emotional control**
- Experience personality changes and behavioral problems, such as agitation, delusions, and hallucinations.**
- Memory loss is a common symptom of dementia**
- Doctors diagnose dementia only if two or more brain functions - such as memory and language skills -- are significantly impaired without loss of consciousness.**

Alzheimer's Disease

- **Memory loss**
- **Language deterioration**
- **Impaired ability to mentally manipulate visual information**
- **Poor judgment**
- **Confusion**
- **Restlessness**
- **Mood swings**

AD eventually destroys cognition, personality, and the ability to function

Alzheimer's Disease: Gross Pathology

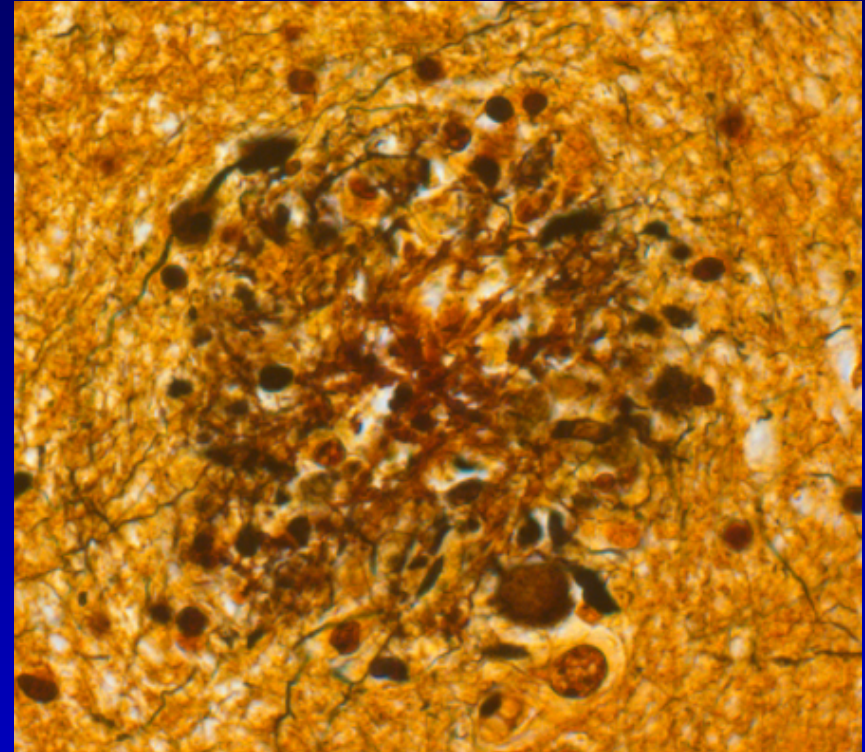
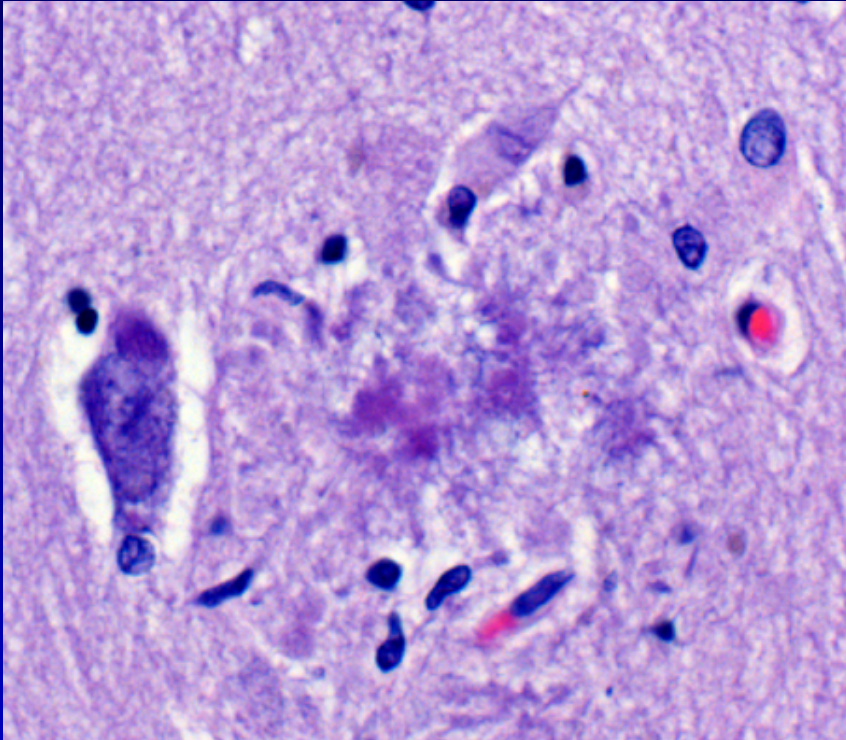


Alzheimer's disease demonstrating significant cortical atrophy. Note the widening of the sulci and the narrowing of the gyri.



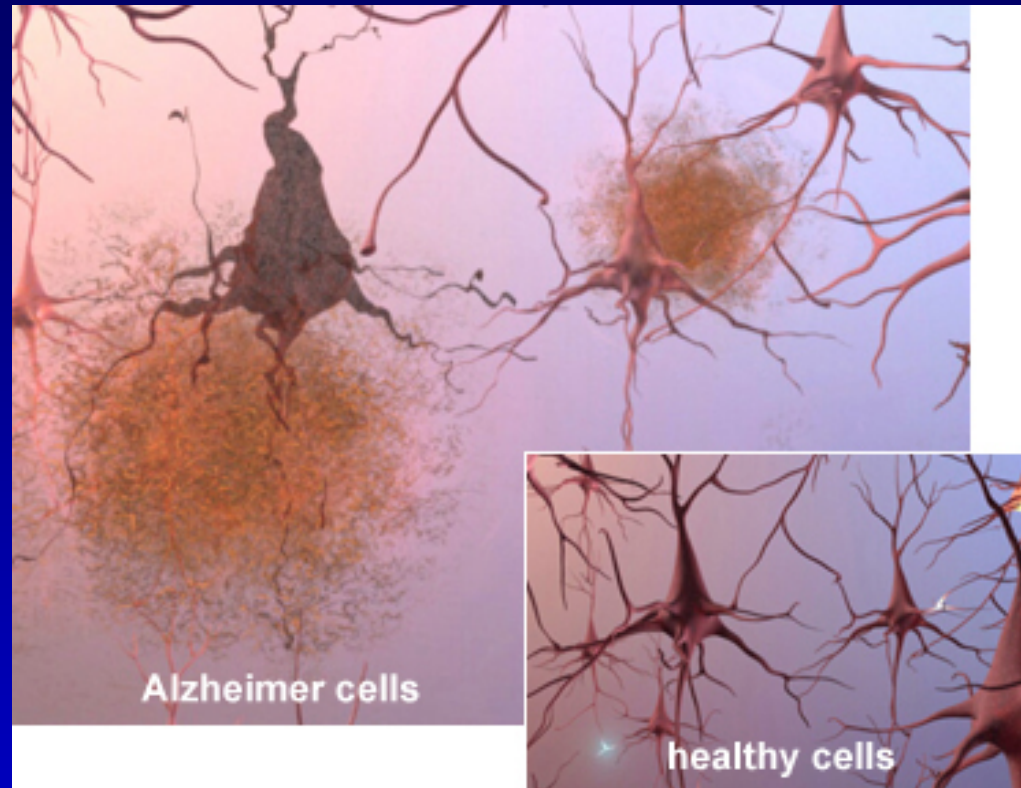
Normal brain half on the left and an abnormal half on the right. Note how much smaller the brain on the right and the effect on the hippocampus (arrow)

Alzheimer's Disease: Micropathology



High-power views of neuritic plaques. The dense center of the plaque is the amyloid core, which is a magenta color on H&E (left) and brown on Bielschowsky (right). This amyloid is called beta-amyloid. Around the core are dystrophic neurites; these are the black strands you can see on the Bielschowsky stain (right). The dystrophic neurites contain neurofibrillary tangles made of tau protein.

Alzheimer's Disease: Micropathology



- Fewer Nerve Cells
- Plaques: abnormal protein clusters between nerve cells
- Neurofibrillary Tangles: dying cells show Tau protein

Dietary Interventions

Supplements:

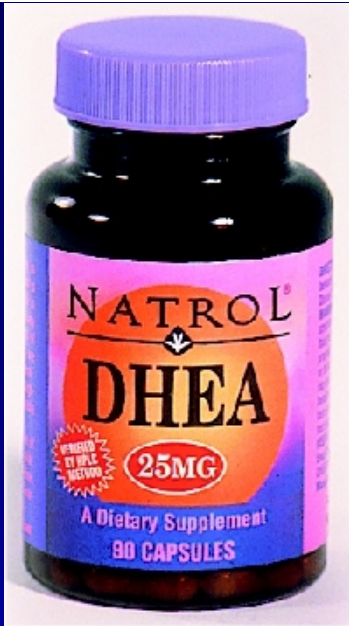
\$7 billion

DHEA

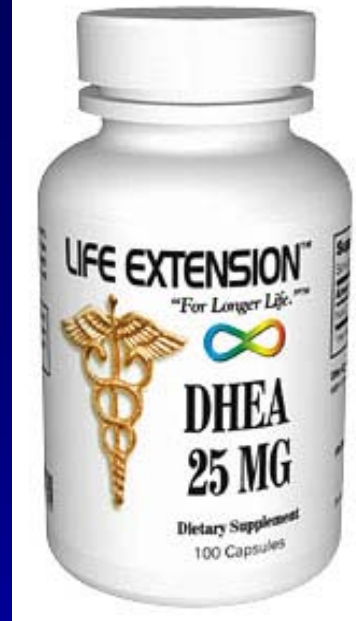
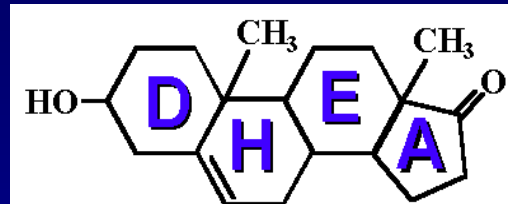
\$43 million

Soy

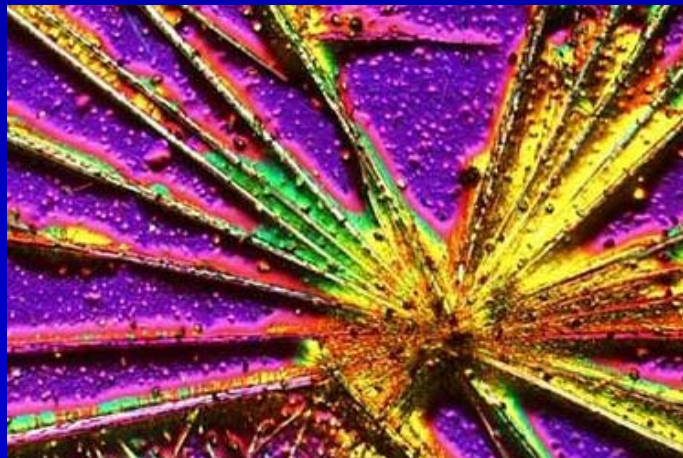
\$4 billion



Dehydroepiandrosterone



Over the Counter Replacement Therapies



Soy Phytoestrogens



Economic Burden of Major CNS Disorders

- **Dementias/Other Psychiatric Conditions: \$150 billion**
- **Stress-Related Affective Illness: \$135 billion**



DHEA and Soy: Marketed Benefits

CNS: Cognition/Memory, Libido, Well Being, Antidepressant, Neuroprotection, Decreased Impulsivity/Agitation

Peripheral: Cardiovascular Tone, Immune System, Bone Density, Muscle Deposition, Skin Hydration



Bert Morrow



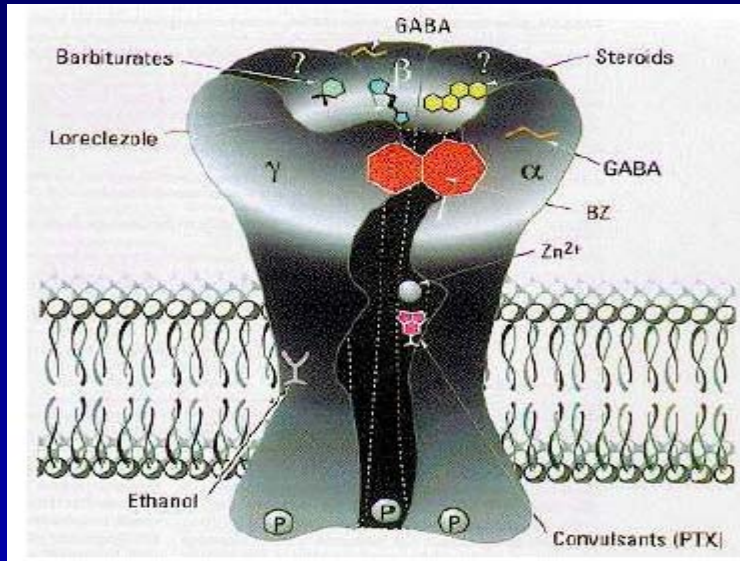
Lenore McDaniels



Everett Hosack

DHEA: Mechanism of Action

➤ Non-Genomic: Cell Surface



GABA-A Receptor

- Cl^- Channel
- Pentameric Structure: α , β , γ , δ , ϵ , ρ
- Regional heterogeneity in Structure
- Multiple Binding Sites
- Direct and Indirect Effects

➤ Genomic: Transcription

Androgen Receptor

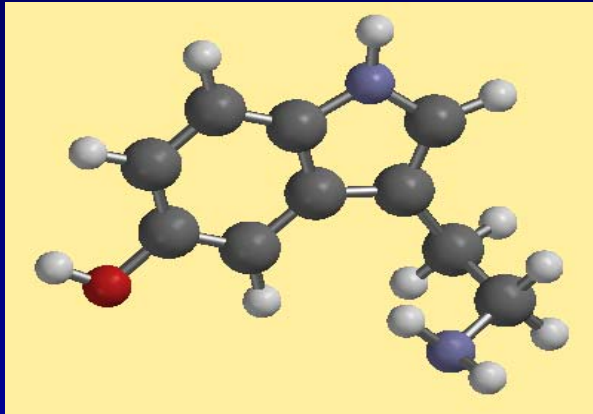
- Intracellular Trafficking
- Transcriptional Activity
- Ligand Dependent



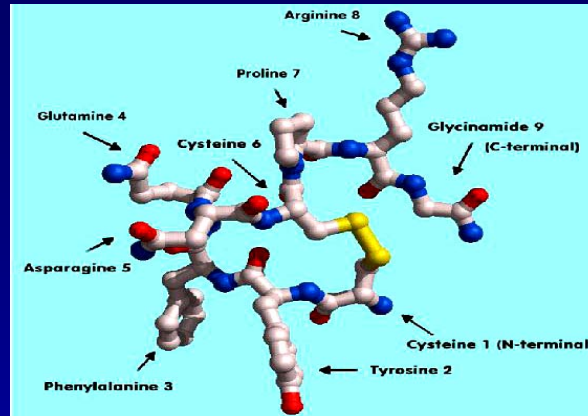
Functional Assays

- **Inter-female Aggression**
- **Androgen Receptor: Immunocytochemistry and Western Blot**
- **Gene Expression: CAT Reporter**
- **AR Intracellular Trafficking: Confocal Microscopy**
- **DNA Microarray: Gene Regulation**
- **PCR: Microarray Validation**

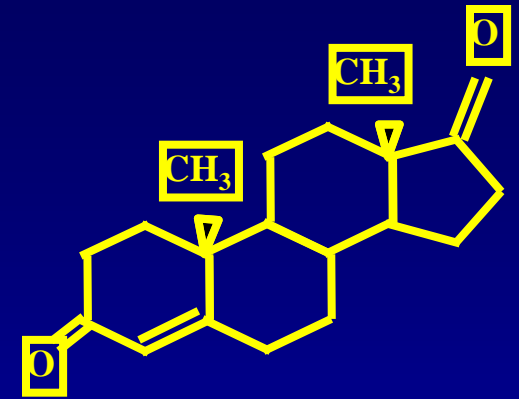
Target Systems



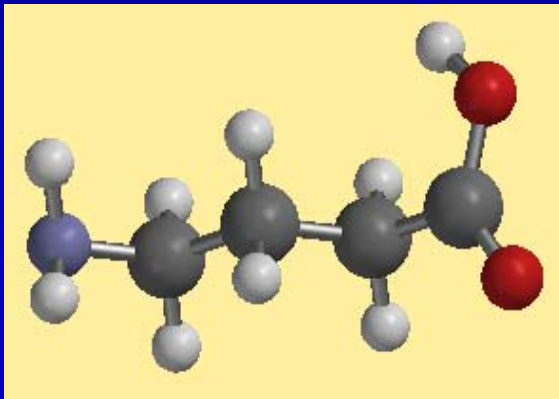
5-HT



AVP



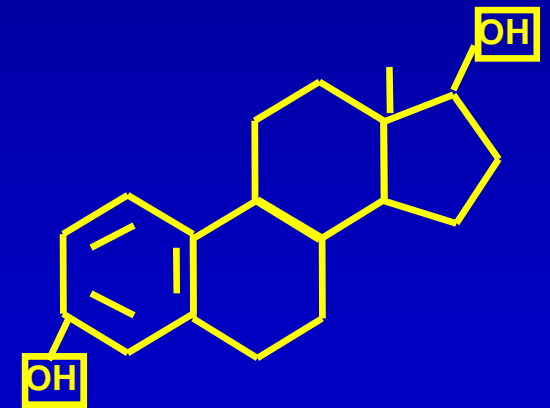
TESTOSTERONE



GABA



DHEA



ESTRADIOL