

Animal Models of Menopause: Cognitive Function

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Issues for Cognitive Function

- Age
- Timing
 - Rats
 - Monkeys
- Route
 - Parenteral
 - Oral
- Regimen
 - Continuous vs cyclical
 - E alone vs E + P
 - Types of E and P
- Dose
 - Rats tested only

Issues for Cognitive Function

- Cognitive Domains
- Brain Systems
- Brain Regions

Issues for Cognitive Function

- Cognitive Domains
 - Memory
 - Attention
- Brain Systems
- Brain Regions

Behavioral Tasks & Cognitive Functions

Rats

- Morris Water Maze
spatial reference memory
- Radial Arm Maze
spatial working and reference memory
- Delayed Matching to Position in a T-maze
spatial working memory

Monkeys

- Delayed Response
spatial working memory
- Delayed Nonmatching to Sample
visual working memory
- Delayed Recognition Span
visual or spatial working memory
- Discriminations & Reversals
associative learning & cognitive flexibility
- Visuospatial Cued Reaction Time
visuospatial attention

Issues for Cognitive Function

- Cognitive Domains
- **Brain Systems**
- Brain Regions

Ovarian Hormones Affect Brain Neurobiology

- Neurochemical systems
 - Cholinergic
 - Dopaminergic
 - Serotonergic
 - Noradrenergic
 - Gabaergic
 - Glutamatergic
 - Neurotrophic
- Neuronal excitability
- Synaptogenesis/spines
- Glial cells
- Cerebral blood flow
- Glucose uptake
- Neurotoxicity
- Oxidative Stress

Issues for Cognitive Function

- Cognitive Domains
- Brain Systems
- **Brain Regions**
 - Hippocampus
 - Cortex

Sites of Ovarian Hormone Actions in the Brain Relevant to Cognition

- Hippocampus
- Cerebral Cortex:
 - Frontal Lobe
 - Parietal Lobe
 - Entorhinal Cortex

Natural vs Surgical Menopause

Natural

- Gradual drop in hormones
- Androgen production by ovaries
- Mean age of 51 years

Surgical

- Abrupt drop in hormones
- Ovarian androgens absent
- Mean age of 45 years

Next Steps

Need better integrated communication between basic science and clinical factions working on the issues of ovarian hormone therapy and its affects on cognition and the brain:

Clinical → Basic: what are the studies we need to perform in our animal models to best inform you about critical issues related to treating women for their cognitive and brain health

Basic → Clinical: information coming from the basic science studies in animals and cell culture can assist clinicians in deciding when and how to treat women