Hormones and the Brain
“Mind Body Interactions”

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“I only do what the voices in my wife’s head tell her to tell me to do”

What about Estrogen and the Brain?
Perimenopausal Women Notice Cognitive Changes With Aging

- 230 women enrolled in the Seattle Midlife Women’s Health Study were interviewed (mean age = 46.7 yrs)
- 62% reported an undesirable change in memory
- Changes included:
  - Difficulty recalling words or numbers
  - Forgetting events and actions
  - Difficulty concentrating
- Women attributed these changes to stress, health, and age rather than hormonal changes


ET/HT is Associated With Better Performance on a Test of Verbal Memory in Postmenopausal Women

*P<.05; †P<.01 compared with never-users.

Cache

Short term HRT in younger women decreases incidence of dementia

Effect of HT Use in Reducing Cognitive Decline in Older Women: Cache County Study
Mean Age ≥ 72 Years at Baseline, 3-Year Follow-Up


Olmsted County

Removed ovaries prior to 65 yo – no HRT
Shows increased risk of cognitive impairment
Effect of Surgical Menopause on Short-term Verbal Memory

Nappi, Gynecol Obstet Invest 47:29, 1999

KEEPS
The Kronos Early Estrogen Prevention Study

Summary of Study
Double-blinded, placebo-controlled of low dose oral or transdermal (patch) estrogen and cyclic monthly progesterone. Age 42-58 (mean 52) 3 yrs post menopause. 727 women, randomized to 3 arms for 4 yrs
Control
- Premarin 0.45 mg qd
- Climara patch 50 μg/day

Findings
- No ↑ in BP
- Oral CEE ↑ HDL and ↓ LDL, ↑ triglyc.
- Transdermal ↓ insulin resistance
- No effect on CV disease
- ↓ CNS symptoms
- ↑ mood, sexual function and bone density
- No effect on breast or endometrial cancer, MI, TIA, stroke, VTE

662 patients enrolled in the NIH Cognitive and Effective Ancillary Study
- ↓ depression
- Better recall
- Improved memory
Dementia – Short and Sweet…

Effect of Age on Sway

Mechanism for Maintenance of Balance
Effect of Estrogen Deprivation on Postural Balance (Sway Velocity)

*P = .007


Effect of Estrogen on Postural Balance (Sway Velocity)

Interactions: Proximity to menopause p<0.018

Mean age = 52
N=44

Adjusted for menopausal symptoms and proximity to LMP

Naessen T et al. Menopause. 2006

Age-Associated Effects on Falls

Young Faller

Old Faller

Naessen T et al. Menopausal. 2006
What about hormones and neurocardiac effects

The Patient

45 yo white female P2002 complains of ↑ wt, ↓ libido, insomnia, fatigue, headache, depression

Failed “hormone therapy”
Further Questions Reveal
- Dizziness on change of position
- Chronic fatigue
- Anxiety
- Tightness of chest and neck
- GI disturbance
- Cycles Q 22 days
- Poor memory
- Palpitations
- + FH of such problems

Dx – Perimenopause
- Unmasked neurocardiac issues
History

- Nerves were thought to be hollow tubes carrying animal spirits to the body - sympathy
- 1552 Eustachius depicted sympathetic nerves and the adrenals
- 1732 Winslow described a chain of ganglia connected to the thoracic and lumbar spinal chord
- Bernard described results of sympathetic nerve stimulation

History

- 1895 Oliver and Schafer described CV stimulation of adrenal extracts
- Abel and Takamine ID epinephrine

History

- Langley coined the term autonomic nervous system. An involuntary, unconscious function of internal organs
- Langley also introduced the term parasympathetic nervous system
- 1920’s Walter Cannon defined sympathetico-adrenal system. The two systems would antagonize each other = homeostasis
- 1920 Bradbury and Eggleston demonstrated neurogenic postural hypertension
**Concepts**

- Orthostatic intolerance constitutes a cardinal clinical manifestation of sympathetic neurocirculatory failure
- Dysautonomia refers to a condition which alters autonomic function adversely and affects health

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**Concepts**

- This ranges from transient episodes in healthy people to progressive neurodegenerative disease

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*Ann Intern Med, 2002*
The Players

- Norepinephrine - sympathetic
- Acetylcholine - parasympathetic
- Plasma contains - NE, Epi, DA, L-Dopa, DHPG (dihydroxyphenylglycol)

Presentations

- Dizziness
- Visual change
- Head and neck discomfort
- L concentration
- Fatigue
- Palpitations
- Tremor
- Anxiety
- Presyncope
- Syncope
Orthostatic Intolerance
- Occurs in young patients 15-45 yo
- Common
- 500,000 in USA
- Females > males
- Delayed orthostatic hypotension

Orthostatic Hypotension
- Rapid ↓Bp >20/10 mmHg
- Can't stand for more than 1-2 min

Autonomic Failure
- ↓Bp 20mmHg systolic or ↓Bp 10mmHg within 3 min of standing or head-up tilt
Work Up

- Hx (good family Hx)
- PE (HT/WT relationship)
- Echocardiogram (30%)
- Tilt test
- Hormone evaluation
**Treatment**

- Lifestyle – hydrate, exercise, no caffeine
- Beta blockers
- Drugs that alter DA and serotonin
- Hormone therapy

**Remember**

- Puberty (8-14 yo)
- Youth (14-21)
- Perimenopause (2-14 yrs duration)
- Menopause 51.4 (35-57)

**Hormone Work Up**

- LH, FSH
- PrL
- T4, TSH
- E2
- Total testosterone
- Free testosterone
- SHBG

Look for Pattern!
Causes

- Example – deficiency of plasma
- Deficiency of plasma membrane NE transporter
- Proline for alanine substitution
- May be polymorphisms of other monoamine transporters

Where to Get Help

MVP Center at Trinity
- Phil Watkins
- Paula Moore
- Susan Philips

“Bad things happen to people who don’t buy my cookies, Sir.”