Triad 5: Stacking with Triad 2
The Role of Sex Hormones and Brain Health
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Reference

Pregnenolone and Memory
Pregnenolone

• Precursor to DHEA, estrogen, progesterone, testosterone, and cortisol.
• Is made from cholesterol.
  — If the total cholesterol goes below 140 then pregnenolone is not as effectively made.

Pregnenolone (Cont.)

• Decreases with age
  — At age 75, most people have a 65% decline compared to age 35.

Pregnenolone and Memory

• Regulates the balance between excitation and inhibition in the nervous system
• Increases resistance to stress
• Improves energy both physically and mentally
• Enhances nerve transmission and memory
• Modulates NMDA receptors

Pregnenolone and Memory (Cont.)

• Directly influences acetylcholine release
• Reduces pain and inflammation
• Blocks the production of acid-forming compounds
• Promotes new nerve growth factor
• Modulates GABA
• Helps to repair nerve damage
• Improves sleep

References


Causes of Low Pregnenolone

• Aging process
• Eating too much saturated fat and trans-fats
• Low cholesterol levels
• Hypothyroidism
• Pituitary tumor
• Having a severe illness
  — Pregnenolone will make more cortisol and less of the other hormones to help with stress.
Symptoms of Pregnenolone Deficiency

- Arthritis
- Depression
- Fatigue
- Inability to deal with stress
- Insomnia
- Lack of focus
- Memory decline

Pregnenolone and Memory

- Like all hormones, pregnenolone levels must be measured before giving the hormone.
- Start with pregnenolone 10 mg SR.
- Repeat levels in 90 days.

Possible Side Effects of Pregnenolone Use

- Acne
- Drowsiness
- Muscle aches
- Fluid retention
- Headache
- Heart racing
- Insomnia due to overstimulation
- Irritability, anger, anxiety

Sex Hormones and Memory

- Sex hormones and their metabolites have many actions on the brain.
- Sex hormones have direct and indirect effects on neurons, glia, and vessels.
- The effects require steroid receptor-mediated gene expression, transcription, and translation which may take days to result in changes.

Reference

Sex Hormones and Memory (Cont.)

- Other effects of sex hormones act directly on ion channels and take seconds to minutes to activate a change when they are coupled to second messengers and to the early-intermediate genes.
  - CFOs
  - Jun
    - Ibid., Polcz.

Effects of Sex Hormones on Neurons

- Delayed action: genomic response mediated by steroid receptor.
  - Estrogen and progesterone
    - Nerve growth and differentiation
    - Modulation of intramembranous protein particles
    - Cytoarchitectural changes
    - Synaptologic changes in hypothalamus
      - Ibid., Polcz.

Effects of Sex Hormones on Neurons (Cont.)

- Delayed action: genomic response mediated by steroid receptor
  - Estrogen
    - Increased choline acetyl transferase synthesis
    - Stimulates neuronal NO synthase
    - Increased degradation of monoamine oxidase
    - Increased number of NMDA sensitive receptors in hippocampus
      - Ibid., Polcz.

Effects of Sex Hormones on Neurons (Cont.)

- Intermediate action: involves second messenger systems or early intermediate genes (e.g., c-Fos, Jun)
  - Estrogen
    - Increased G-protein coupled cAMP dependent kainate-induced ion current in CA1 neurons
      - Ibid., Polcz.

Effects of Sex Hormones on Neurons (Cont.)

- Rapid action: direct action on cell membrane (e.g., Ion channel, synaptic transmitters)
  - Estrogen
    - Modulation of dopamine receptor binding in striatum
    - Increased K+ permeability of postsynaptic membrane in amigdala neurones
    - Postsynaptic potentiation of non-NMDA receptors in CA1 neurones
    - Calcium transport mechanism in nerve endings
      - Ibid., Polcz.

Effects of Sex Hormones on Neurons (Cont.)

- Rapid action: direct action on cell membrane (e.g., Ion channel, synaptic transmitters)
  - Progesterone
    - Stimulates release of dopamine in striatal tissue
    - Stimulates release of GnRH from hypothalamic neurones
    - Modulation of oxytocin receptor binding in the hypothalamus
      - Ibid., Polcz.
### Effects of Sex Hormones on Neurons (Cont.)
- Rapid action: direct action on cell membrane (e.g., ion channel, synaptic transmitters) (cont.)
  - Progesterone (cont.)
    - Inhibition of opioid receptor binding
    - Potentiation of GABA
    - Direct incorporation of steroids in cell membrane?
      - Ibid., Polcz.

### Sex Hormones and Memory
- Pregnenolone, pregnenolone sulfate, progesterone, allopregnanolone, dehydroepiandrosterone, dehydroepiandrosterone sulfate, testosterone, and estradiol all have modulatory effects on the release of neurotransmitters.

### Reference

### Sex Hormones and Memory (Cont.)
- Many of the effects of these neurotransmitters occur in areas of the brain involved in learning and memory, emotion, motivation, motor, and cognition.
  - Ibid., Zheng.

### Sex Hormones and Memory (Cont.)
- The mechanisms of affect of the neurotransmitters are complicated.
  - Numerous involve rapid non-genomic effects on presynaptic receptors and ion channels.
Sex Hormones and Memory (Cont.)

- Presynaptic receptors and ion channels that may be affected
  - Sigma-1 receptor
  - Alpha(1) receptor
  - Nicotine receptor
  - D1 receptor
  - NMDA receptor
  - GABA(A) receptor
  - L-type Ca(2+) channels

Consequently, sex hormones with their neuroactivity are important regulators of synaptic transmission in the CNS including brain function.

Estrogen and Memory

- Estrogen’s affects within the CNS and more specifically the hippocampus are governed by estrogen receptors alpha and beta.

Reference

Estrogen and Memory (Cont.)

- Protects neurons
- Decreases neuronal generation of Alzheimer’s beta amyloid peptides
- Is a natural antioxidant
- Increase manual speed and dexterity
- Increases availability of acetylcholine

Estrogen and Memory (Cont.)

- Boosts by 30% NMDA receptors to maintain strength and durability of synaptic connections involved in creating long-term memories
- Decreases distractibility
- Turns on progesterone receptors

Estrogen and Memory

- Women who have had unilateral or bilateral oophorectomies before menopause have an increased risk of memory loss.

Cognitive Symptoms Due To Menopause

- “I’m losing it.”
- “I’m going crazy.”
- “I’m flipping out.”
- “I do the weirdest things.”
- “I’m having a nervous breakdown.”
- “I think I am getting early Alzheimer’s.”
- “I cannot spell anymore.”

Symptoms

- Can be four to fifteen years before menopause.

Great Book For Your Patients

Warga’s Hormonal Misconnection Syndrome

- The following is a list of symptoms that is referred to as Warga’s Hormonal Misconnection Syndrome. These are the symptoms that you will commonly see in your patients with memory “changes.”

Thinking Changes

- Losing your train of thought more often
- Forgetting what you came into a room to get
- Not being able to concentrate as well upon demand
- Feeling foggy, hazy, and cotton-headed and not being able to clear it up at will
- Experiencing a though blockade: an inability to pull ideas out at will
- Fluctuating agility in prioritizing

Speech Changes

- Naming difficulties for long-known names: children, best friends, things, places
- Finding yourself at a loss for words in how to express something while speaking
- Experiencing “It’s on the tip of my tongue but I can’t get it out” sensation
- Making malapropisms: saying wrong words that are related somehow to the intended one

Speech Changes (Cont.)

- Reversing whole words while speaking
- Reversing the first letters of words while speaking
- Experiencing “echo” words as unintentional intrusions into present speech
- Relying on “filler” words more often” “whatchamacallit,” “that thing,” “you know what I mean”
- Organizing sentences and ideas less efficiently while speaking

Changes In The “Beam” Of Attention

- Blinking social attention when interested and interacting: listening but not always attending
- Blanking-out amnesia for what you just did
- Experiencing increased distractability

Memory Changes: Short And Long Term

- Forgetting what you just did, or past occurrences, with no threads of association to getting back to what’s missing; missing links
- Changing certainty in how words should be spelled in once good or great spellers
- Fluctuating agility in calculating and in “counting with a quick scanning look”
Memory Changes: Short And Long Term (Cont.)

• Experiencing changes in the speed and accuracy of memory retrieval
• Forgetting the content of a movie right after seeing it but remembering your emotional reaction to it

Behavioral Changes

• Making behavioral “malapropisms”: unintended slips in behavior that are related to the intended behavior somehow, such as putting shampoo in the refrigerator
• Forgetting briefly how to do things long known, such as where to turn on the computer

Behavioral Changes (Cont.)

• Feeling that automatic skills such as driving for a few moments are not “automatic” in the same way as usual
• Dropping things more often that require fine finger/hand coordination

Behavioral Changes (Cont.)

• Absentmindedly, leaving out or reversing letters in words while writing
• Forgetting how to write an word in the middle of writing and having to leave blanks
• Experiencing “translating” hesitations in converting what’s heard into writing
• Not handling the same amount of stress in the same way

Spatial Skills Changes

• Changing skill in remembering and/or recognizing faces (not well-known faces)
• “Looking at but not seeing” what you are looking for when it’s right there ultimately, more than in the past
• Changing reading skill in visually “seeing” and comprehending reading material

Spatial Skills Changes (Cont.)

• Spending less time reading, without difficulties above (for formerly heavy-duty readers)
• Forgetting briefly how to get to long-known landmarks in your life
• Experiencing familiar locales in one’s experience as momentarily unfamiliar
Altered Sense Of Time

- Forgetting appointments more or not anticipating events of personal importance with the same accuracy
- Forgetting important events in your personal history timeline, i.e., which breast you had biopsied
- “Living more in the moment” out of necessity: a “spliced-film-frames” sense of personal time

Hormonal Misconnection Syndrome

- Cognitive/behavioral/speech episodes that are mis-hits
- The mind’s intentions are not producing the right physiological connections that they used to in the preexisting circuitry and/or chemical flow patterns of the brain.

Reason For Misconnections?

- A body/brain retooling or “retuning” brought on by the effects of declining ovarian function and declining estrogen hormone supplies on a thinking, remembering, attention-creating brain that depends heavily on estrogen as a brain “transmission fluid”, as a fortifying performance-enhancing steroid or multivitamin.

THE WHM Syndrome Parallels Hypothyroidism

- Estrogen, progesterone, testosterone, DHEA, and cortisol changes may all trigger changes in thyroid function.

Women And Cognitive Symptoms

- Women may be embarrassed to discuss these symptoms with their doctors.
- If you do not take a good history, you will not uncover the symptoms.
- Women may feel they will be “written off” by their doctors as incompetent or crazy.
- Symptoms may be treated with anti-depressant, as ADD, anti-anxiety medications, or told it is probably nothing. None of these treat the cause of the problem.

Are These Symptoms A Normal Part Of Aging?

- Women often assume that cognitive changes are a normal part of aging and that they have to live with them, and that they are not reversible.
Studies In Our Practice

• Show that cognitive changes at peri-menopause and menopause are the most common symptoms of all menopause symptoms: 99.7% of women.

Estrogen And The Brain

• “There is not a cell in the brain that is not directly or indirectly sensitive to estrogen.”
  – Frederick Naftolin, M.D., Professor and Chairman of Yale Medical School’s Department of Obstetrics and Gynecology
  – Is also a neuroscientist

Estrogen And The Brain

• “Menopause is a state of estrogen deficiency. It is an endocrinopathy in the same way that diabetes and hypothyroidism are hormone deficiency states. People worry about bone density and coronary artery disease in the postmenopausal state, but they should also be worrying about what’s happening to the brain’s neurons.”
  – Dr. Dominique Toran-Allerand. She is a neurobiologist who has been studying the role of estrogen on fetal and postnatal rat-brain tissue for over 30 years at Columbia University’s College of Physicians and Surgeons.

Estrogen And The Brain

• Article proposed that the loss of estrogen’s important functions might “lead to age-related impairment of memory and cognition.” He goes on to say, “such multiple roles for estrogen would suggest that reproductive senescence (i.e., perimenopause and menopause) may have a multifaceted impact on memory loss and cognitive decline through decreased regulation of intact (memory) circuits as well as decreased protection of such circuits from degeneration.”

Estrogen And The Brain

• Estrogen has effects on the nerve communication systems that project messages throughout the cortex and other major areas of the brain, especially the hippocampus.
Estrogen has many affects on the brain. 

**Estrogen Alters The Neurochemistry of the Brain**

- By affecting the supplies of multiple neurotransmitters: serotonin, dopamine, acetylcholine, glutamate, GABA, noradrenaline
- By affecting critical enzymes (choline acetyltransferase)
- By stimulating nerve growth factors
- By affecting neuropeptides
- By reducing the formation of toxic brain-destroying proteins implicated in Alzheimer's

Estrogen increases choline acetyltransferase activity in specific basal forebrain nuclei and projection areas of female rats. 

Estrogen stimulates neuronal nitric oxide (NO) synthase which produces the neuromodulator/neurotransmitter NO. 

Estrogen stimulates the changes in the catabolism of serotonin by increasing the degradation of monoamine oxidase. 

All of the above functions are related to memory, learning, and mood.
Estrogen Alters The Architecture And Structure Of The Brain

- By increasing the surface area of potential “docking sites” for connections to incoming messages on nerve cells arms via monthly sprouting of new spines and potential synapses
- By stimulating the growth of more dense branches on nerve cells (arborization) that potentially increase connectivity and complexity

Estrogen Maintains The Interconnections Of The Brain And Supports Nerve Growth

- By maintaining a denser mesh of nerve fiber outgrowths for potential connections than when it is not there
- By increasing synapse formation after neuronal damage
- By inducing nerve growth via induced release of different nerve growth factors in a complex feedback loop

Estrogen Affects The Work Tone Of The Brain

- By stimulating and promoting the function of the brain’s cholinergic projecting system
- The serotonergic projecting system
- The dopaminergic projecting system
- The adrenergic projecting system
- The neurotransmitter projecting system that depends on the neurotransmitter GABA

Estrogen Increases The Neuronal Plasticity Of The Brain

- By regulating the formation and breakdown of synapses and branches
- By facilitating response to injury after strokes
- By having the ability to orchestrate the turning on of different genes

Estrogen and Memory

- Estrogen has been shown to increase the number and length of dendritic spines and the density of NMDA receptors in the hippocampus.
  – Ibid., Polcz.

Estrogen and Memory (Cont.)

- During the menstrual cycle the changing levels of estrogen drive synaptic remodeling in the arcuate nucleus of the hypothalamus.
- The glia responds to estrogen by increasing its processes and increasing neuronal ensheathment.
Estrogen Is Neuroprotector

- By acting as a natural antioxidant
- By boosting the body’s own natural antioxidant system
- By protecting brain cells from beta-amyloid plaque deposits
- By helping brain cells survive deprivation of vital classes of substances longer
- By increasing the expression of more nerve growth factor receptors

References

Ibid., Polcz.


Estrogen Is A Neuroprotector (Cont.)

- By recruiting the aid of nerve growth factors
- By decreasing the toxicity excitotoxins such as glutamate
- By acting as an anti-inflammatory

References


Estrogen Boosts The Metabolic Function Of The Brain

- By increasing availability of glucose to the brain
- By increasing cerebral blood flow and preventing ischemia
- By maintaining the elasticity of blood vessels
- By increasing the resting rate of metabolism of the body

References

Ibid., Polcz.


Estrogen Acts As An Activator And Performance Enhancer

- By increasing speed of rapid limb-coordinated movements in animals
- By increasing finger-tapping skills and manual speed and dexterity in women
- By increasing verbal fluency, speech articulation agility, syllable repetition, speeded counting, word reading
- By increasing sensory perception: hearing, smell, visual signal detection, fine touch
- By maintaining central processing motor integration in such tasks as driving

References

Ibid., Polcz.

Estrogen As An Activator And Performance Enhancer (Cont.)

- By boosting metabolic activity of many areas of the brain and spinal cord within hours of administration
- By acting as an “upper” to increase feelings of energy and well-being, mood, feelings of elation, and euphoria in human studies
- Boosts attention to tasks in monkeys
- By decreasing distractability

Estrogen Acts As A Neuromodulator

- By turning on many but not all progesterone receptors
- By boosting neurotransmitter response
- By amplifying the sensitivity of a nerve cell
- By strengthening the electrical pathways for memory retention for at least six to eight hours
- By making neurons more sensitive to a helpful protein substance believed to play a role in growth of dendrites and axons

Estrogen Affects Learning, Memory And Old Knowledge

- Boosts by 30 percent NMDA receptors in the hippocampus believed to be important in maintaining the strength or durability of synapse connections involved in creating longer-term memories or learning
- By producing effects on the hippocampus (animal studies)
- By building and maintaining synapses
- By maintaining verbal memory, verbal learning, and spatial memory

Estrogen Has Cardiovascular-Protecting Effects

- Reduced LDL and raises HDL
- May slow the progression of cerebral atherosclerosis and prevent vascular dementia
References


References (Cont.)


References (Cont.)


References (Cont.)


References (Cont.)


References (Cont.)

References (Cont.)

• Williams, G.V., et al., “Modulation of memory fields by dopamine D1 receptors in prefrontal cortex,” nature, 1995; 376(6541):572-75.

References (Cont.)


References (Cont.)


References (Cont.)


References (Cont.)

• Ibid., Polcz.
Estrogenic Effects on Neurons

• Synaptic transmission is also modulated by estrogen effects on the Ca2+ transport mechanisms in nerve endings.
  – Ibid., Polcz.

Estrogen and Memory

• Estrogen has been shown to increase the cerebral circulation in women after menopause which has been associated with an improvement in memory.

Reference


Major Studies On Estrogen And Memory

• Researchers in this 1996 study found a 54 percent reduction in the risk of developing Alzheimer’ s disease in those who had taken estrogen. These women had been tracked for up to sixteen years.

Major Studies (Cont.)

• In another 1996 study scientists found that estrogen reduced by 50%, not only the risk of developing Alzheimer’ s disease, but delayed the onset of the disease, even in those at increased hereditary risk of developing Alzheimer’ s disease.

Major Studies (Cont.)

• A recent study conducted on 1,889 older women in Utah revealed that women who had taken ERT were 40% less likely to develop Alzheimer’ s disease. Furthermore, the longer they were on hormone replacement therapy the lower was their risk.
Major Studies (Cont.)

• In a prospective study the rate of developing Alzheimer’s disease among patients using estrogen was less than among patients who had never used estrogen.

Major Studies (Cont.)

• Estradiol hormone replacement has an affect on cholinergic function which may benefit memory.
• Estrogen replacement therapy has been shown to positively influence
  — Attention span
  — Concentration

Major Studies (Cont.)

• Estrogen replacement therapy has been shown to improve cognition and regional cerebral blood flow in women with Alzheimer’s disease.

Major Studies (Cont.)

• Estrogen supplementation has been shown to prevent and/or delay the onset of Alzheimer’s disease.
  — Ibid., Polcz.

References

Major Studies (Cont.)

• Estrogen replacement has been shown to improve memory in postmenopausal women without dementia.
  — Ibid., Polcz.

• Estrogen replacement therapy has been shown to be most effective to maintain cognition if taken during the onset of menopause and the first few years afterward.

References


Estrogen: Men and Memory

• Estradiol has a protective effect on the brain structures in older males.

Estrogen: Men and Memory (Cont.)

• Serum estradiol and testosterone levels have been shown to be lower in men with Alzheimer’s disease compared with age-matched controls.

Reference

Progesterone and Memory

Progesterone Effects on Neurons
• Progesterone stimulates the release of dopamine in striatal tissue.
  — Ibid., Polcz.

Progesterone Effects on Neurons (Cont.)
• Stimulates the release of GnRh from hypothalamic neurons after binding to specific sites on the cell membrane to affect movement and autonomic functions.
  — Ibid., Polcz.

Progesterone Effects on Neurons (Cont.)
• Progesterone modulates oxytocin receptor binding in the hypothalamus.
  — Ibid., Polcz.

Progesterone Effects on Neurons (Cont.)
• Progesterone inhibits opioid receptor binding.
  — Ibid., Polcz.

Progesterone Effects on Neurons (Cont.)
• Progesterone effects the potentiation of GABA.
  — Ibid., Polcz.
Progesterone Effects on Neurons (Cont.)

- Progesterone directs the incorporation of steroids into the cell membrane.
  – Ibid., Polcz.

Progesterone and Memory

- Progesterone is made in the brain, spinal cord, and peripheral nerves from pregnenolone.
- Progesterone may promote the formation of myelin sheaths.
- Scientists are now looking at progesterone replacement to aid in the prevention of memory loss.

Reference


Neuroprotective Effects of Progesterone

- Study looked at progesterone and allopregnanolone treatment in patients after global cerebral ischemia.
- Progesterone and allopregnanolone reduced the impairment in spatial learning and memory, as well as in reference and working memory, and prevented the narrowing of the hippocampus which is otherwise induced by ischemia.

Reference


Testosterone and Memory


Testosterone and Memory

- Testosterone helps to both men and women with cognitive function.

Women: Testosterone and Memory

- A small pilot study that was just completed suggests that testosterone replacement might protect the memory of healthy aging women.
- Transdermal testosterone spray was used in this trial.
  — Davison, S., Endocrine Society 93rd annual meeting 2011, Abstract P1-314.

Women: Testosterone and Memory (Cont.)

- The hormonal symphony is very important with relationship to hormonal function and cognition.
- Without enough estrogen, testosterone cannot attach to the brain receptors.

Men: Testosterone and Memory

- In men, testosterone levels decline at a rate of approximately 1% per year starting at the age of 30.

Men: Testosterone and Memory (Cont.)

- Testosterone levels that are bioavailable decline at twice the rate of total testosterone levels.

Men: Testosterone and Memory (Cont.)

- 30% to 60% of men in their 70s are hypogonadal.
Men: Testosterone and Memory (Cont.)

- Men develop Alzheimer's disease at a rate that is slower than women.
- Men with dementia have a higher mortality rate.

Men: Testosterone and Memory (Cont.)

- The development of memory loss in males is related to the loss of testosterone that occurs with age in a male.

Reference


Men: Testosterone and Memory (Cont.)

- In men, testosterone plays a major role in brain functioning.
- Subclinical androgen deficiency has been suggested to increase the expression of amyloid-B-related peptides in vivo.

Men: Testosterone and Memory (Cont.)

- In this study, age-related decline in free testosterone predicted age-related decline in visual and verbal memory.

Men: Testosterone and Memory (Cont.)

- Low levels of bioavailable testosterone are a positive predictor of memory loss in men as they age.
Men: Testosterone and Memory (Cont.)

- In a medical trial done in Hong Kong, in men with low bioavailable testosterone levels there was a strong correlation with memory loss/Alzheimer’s disease.

Men: Testosterone and Memory (Cont.)

- Males that have a higher ratio of total testosterone to SHBG have a lower rate of development of Alzheimer’s disease.

Men: Testosterone and Memory (Cont.)

- Patients with Alzheimer’s disease have been shown to have a lower ratio of total testosterone to SHBG when compared with age-matched controls.

Men: Testosterone and Memory (Cont.)

- In another medical trial, which was a prospective longitudinal study, revealed that the risk of Alzheimer’s disease was decreased by 26% for each 10-unit (nmoL/nmol) increase in free testosterone at 2, 5, and 10 years before the diagnosis of Alzheimer’s disease was made.

Reference


Men: Testosterone and Memory

- Low levels of testosterone may occur prior to the diagnosis of Alzheimer’s disease.
  - Ibid., Moffat.
Men: Testosterone and Memory (Cont.)

• Low testosterone levels have also been associated with mild memory loss.

Men: Testosterone and Memory (Cont.)

• Studies have also shown a correlation between testosterone levels and cognitive abilities such as spatial performance and mathematical reasoning.

Men: Testosterone and Memory (Cont.)

• Studies done in animals have shown that depletion of androgens results in increased pathologic conditions that are associated with Alzheimer’s disease.
  – Increased antibody levels
  – Increased neuronal death
  – Hyperphosphorylation

Reference


Reference

Men: Testosterone and Memory

• Higher levels of free concentrations have been associated with better performance in specific aspects of memory and cognitive function.
• Optimal processing capacity was found in men between the ages of 35 and 90 even after adjustment for age, education, and CV morbidity.

Men: Testosterone and Memory (Cont.)

• The same was not true of total testosterone levels.

Men: Testosterone and Memory

• In men that have undergone hormonal treatments for prostate cancer with suppression of endogenous testosterone synthesis and blockade of the androgen receptor, studies have shown that there is a beneficial effect on verbal memory but an adverse effect on spatial performance.

Reference


Men: Testosterone and Memory

• These same patients also had visuomotor slowing and slowed reaction times in several attentional domains.

References

• In the same patients plasma amyloid levels elevated as testosterone levels declined.
  — Ibid., Salminen.

• When treatment was discontinued, memory improved but visuospatial abilities did not.

• Study showed that testosterone therapy in elderly men showed some reversal of cognitive dysfunction.

• Testosterone therapy has been shown to help with mild cognitive impairment.

• Testosterone replacement helps to prevent the production of beta amyloid precursor protein in men.

• Animal studies have shown that testosterone replacement can improve memory possibly by reducing amyloid-B peptide production.
Men: Testosterone and Memory (Cont.)

- Testosterone therapy in older hypogonadal men improved spatial cognition and verbal fluency.

Reference


Men: Testosterone and Memory

- In older men without dementia testosterone replacement reduced working memory errors.

Men: Testosterone and Memory (Cont.)

- Testosterone replacement in men in this study improved verbal and spatial memory.

Men and Dementia

- One form of dementia that men may have is Fragile X-associated Tremor/Ataxia Syndrome (FXTAS).

- Average age of onset is 60.
- Verbal understanding is preserved.
Men and Dementia

• Symptoms of FXTAS
  – Impaired balance and tremor
  – Parkinsonism symptoms
  – Decline in executive function
  – Decline in processing speed
  – May have irritability, hostility, and agitation

Men and Dementia (Cont.)

• MRI done on patients with FXTAS shows increased T2 signaling in the middle cerebellar pedunes.
• Dx: confirming the existence of high level of CGG repeats in the fragile X mental retardation1 gene.
  – Ibid., Little.

DHEA and Memory

• Low DHEA levels due to stress and aging lead to cognitive decline.
• Patients with Alzheimer’s disease have levels of DHEA that are 48% lower than their normal counterparts.

DHEA and Memory (Cont.)

• Studies are mixed as to whether DHEA replacement has a strong effect on memory.

References

DHEA and Memory

- In studies on DHEA in the military, warfighters who exhibited higher levels of DHEA during extreme stress were those who also had better hippocampal and prefrontal dependent cognitive abilities during stress.

References


DHEA and Memory

- Recent double-blind, placebo-controlled, crossover study in which DHEA was given to postmenopausal women.
- Study showed a large benefit of DHEA replacement therapy on mental rotation, subject-ordered pointing, fragmented picture identification, perceptual identification, and same-different judgment.

Reference


Treatment

- Optimization of hormonal function in both men and women.
- Case histories
Summary

- Stacking triad 5 with triad 2
- The sex hormones affect cognitive function and memory.
- All of them have to be working in concert in order for the patient to have optimal health.