Cognitive + Mental Decline
Causes of Pre-Mature Cognitive Decline

1. Age if we are careful it need not cause loss of mental acuity
2. Inactivity, Sleeping longer, couch potato, “Use it or Lose it”
3. Oxidative Stress, SMOKING and emotional stress and immaturity rob oxygen and cause cellular decline.
4. SINthetic doctor prescribed medications, this is a big problem for mental acuity, “A SINthetic Anything is an Insult to the Body.”
5. Antibiotic destruction of Bowel flora + vitamin dys-absorption
6. Bad diet, saturated fat, nutrient depleted, too much processed food with SINthetic food additives.
7. Inflammation from allergy, infection, toxicity, cellular imbalance
8. Infection even just common flu produce inflammation
9. Hormonal Imbalance improperly treated
10. Cerebrovascular health, High Blood Pressure,
11. High Glycemic Sugar and foods, Sugar regulation disease all damage arteries + veins
12. Obesity, burdens blood flow, fat weakens brain cells
13. Cooking of foods, destruction of Fatty Acids, and carcinogenic compounds from browning
14. Dementia Drugs don’t work
15. Hearing Loss, without Brain stimulation function is lost
16. Genetic tendency not corrected with diet
17. Chemical toxicity, we live in a toxic sewer
18. Bad teeth, pockets of bacteria make brain decay
19. Lack of Education of these causes
Mental Training More Effective Than Drugs, Vitamins In Battling Cognitive Decline

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redOrbit Staff & Wire Reports – Your Universe Online

There is no evidence drugs, vitamins or herbal supplements can help prevent cognitive decline in otherwise healthy older adults, claims a new study published Monday in the Canadian Medical Association Journal.

Lead author Dr. Raza Naqvi of the University of Toronto and colleagues conducted a thorough review of 32 previously published randomized trials and reportedly found no proof any of those methods could help keep seniors’ minds sharp, according to the Milwaukee Journal Sentinel.

They did, however, find some evidence that computerized memory training programs and other forms of mental exercise could help those adults from experiencing cognitive decay.

“This review provides some evidence to help clinicians and their patients address what strategies might prevent cognitive decline,” Naqvi said in a statement.

Their work could provide help for the 10 to 25 percent of people over the age of 70 who suffer from mild cognitive impairment — a condition characterized by reduced memory, judgment and decision-making in comparison to someone of a similar age, but not enough to interfere with day-to-day activities.

Naqvi and colleagues discovered no strong proof that popular treatments such as ginkgo, dehydroepiandrosterone (DHEA) or vitamin supplements, like vitamin B6, can help stave off mild cognitive impairment.

The researchers reportedly found no evidence suggesting pharmacologic treatments such as cholinesterase inhibitors developed to improve the effectiveness of acetylcholine (a chemical messenger that assists memory, thought and judgment) could be beneficial in treating these conditions.

They also report evidence regarding the mental benefit of physical exercise is weak. Additionally, estrogen therapy actually showed an increase in dementia and cognitive decline, the Milwaukee Journal Sentinel said. There was stronger evidence that mental exercises and person-to-person training in memory and reasoning could be helpful.

Future research could focus on the impact of such training on the prevention of cognitive decline, Naqvi said.

“We encourage researchers to consider easily accessible tools such as crossword puzzles and Sudoku that have not been rigorously studied,” he said. “The studies in this review that assessed cognitive exercises used exercises that were both labor- and resource-intensive, and thus may not be applicable to most of our patients.”

A 15-minute "selfie" test conducted at home can indicate early signs of mental decline that might be the first glimmer of Alzheimer's.

US researchers who asked more than 1,000 people aged 50 and older to take the self-administered Sage test found that 28% had cognitive impairment, a mild loss of mental functioning.

The results closely matched those from detailed diagnostic tests carried out by experts.

Dr Douglas Scharre, who helped develop the test at Ohio State University, said: "What we found was that this Sage self-administered test correlated very well with detailed cognitive testing.

"If we catch this cognitive change really early, then we can start potential treatments much earlier than without having this test."
The test can be taken at home by patients and the results shared with physicians to help them spot early symptoms of dementia, said Dr Scharre, director of Ohio State University's Division of Cognitive Neurology.

See Also:

Scan That May Spot Signs Of Alzheimer's Disease To Become Available In UK
G8 Dementia Summit: The World Is Watching

While the Sage test cannot diagnose patients' problems, it gives doctors a "baseline" of mental function so that progressive changes can be tracked over time.

"We can give them the test periodically and, the moment we notice any changes in their cognitive abilities, we can intervene much more rapidly," said Dr Scharre.

Earlier research showed that the test can detect four out of five people with mild thinking and memory issues. All but around 5% of those without problems will have normal Sage scores.

Participants in the new study were recruited from a variety of community locations and events including senior citizens' centres, health fairs, educational talks, and free memory screening advertised in newspapers.

Volunteers were tested on mental orientation, language, reasoning, spatial ability, problem solving and memory.

Dr Simon Ridley, from the charity Alzheimer's Research UK, said:
"Further research is needed to confirm whether the Sage test would be suitable to assess and track changes in people's memory and thinking skills.

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"One drawback of this study is that the test was not compared with other existing cognitive tests.

"It's important to note that the test is not designed to diagnose dementia, and people who are worried about their memory should seek advice from a doctor rather than attempting self-diagnosis with a test at home.

"There is currently not enough evidence to suggest that dementia screening for people who do not have memory concerns would be beneficial."


**How Well Are You Thinking?**

Please complete this form in ink **without** the assistance of others.

| Name __________________________________________ | Date of Birth _____/_____/______ |
| How far did you get in school? ___________________ | I am a Man _____ Woman _____ |
| I am Asian _____ Black _____ Hispanic _____ White _____ Other _____ |
| Have you had any problems with memory or thinking? Yes _____ Only Occasionally _____ No _____ |
| Have you had any blood relatives that have had problems with memory or thinking? Yes _____ No _____ |
| Do you have balance problems? Yes ______ No ______ |
| If yes, do you know the cause? Yes (specify reason) ___________________ No ______ |
| Have you ever had a major stroke? Yes _____ No _____ A minor or mini-stroke? Yes _____ No _____ |
| Do you currently feel sad or depressed? Yes ______ Only Occasionally ______ No ______ |
| Have you had any change in your personality? Yes (specify changes) ___________________ No ______ |
| Do you have more difficulties doing everyday activities due to thinking problems? Yes _____ No _____ |

1. **What is today’s date?** (from memory – no cheating!) Month_______ Date_______ Year_______

2. **Name the following pictures** (don’t worry about spelling):

   ![Wreath](image1.png)

   ![Volcano](image2.png)
Answer these questions:

3. How are a watch and a ruler similar? Write down how they are alike. They both are… what?

4. How many nickels are in 60 cents? ____________________

5. You are buying $13.45 of groceries. How much change would you receive back from a $20 bill?

6. Memory Test (memorize these instructions). Do later only after completing this entire test:

   At the bottom of the very last page: Write “I am done” on the blank line provided

7. Copy this picture:

   ![Cube](image)

8. Drawing test
   - Draw a large face of a clock and place in the numbers
   - Position the hands for 5 minutes after 11 o’clock
   - On your clock, label “L” for the long hand and “S” for the short hand
9. Write down the names of 12 different animals (don’t worry about spelling):


Review this example (this first one is done for you) then go to question 10 below: Draw a line from one circle to another starting at 1 and alternating numbers and letters (1 to A to 2 to B to 3 to C).

1 Start

A

2

B

C End

3

10. Do the following: Draw a line from one circle to another starting at 1 and alternating numbers and letters in order before ending at F (1 to A to 2 to B and so on).

1 Start

A

2

B

3

C

4

D

5

6

End

F

E
Review this example (this first one is done for you) then answer question 11 below:
- Beginning with 1 triangle and 1 square
- Move 2 lines (marked with an X)
- To make 2 squares and no triangle
- Each line must be part of a complete square (no extra lines).

1 triangle, 1 square
(Example)

Move these 2 lines
(Example)

Put them here (at arrows)

Make 2 squares (answer)
(Example)

11. Solve the following problem:
- Beginning with 2 squares and 2 triangles
- Move 4 lines (mark with an X)
- To make 4 squares and no triangles
- Each line must be part of a complete square (no extra lines).

2 squares, 2 triangles

Move 4 lines

Draw answer here

Mark with an X

4 squares, no triangles

12. Have you finished? ________________________________
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Some of the Questions and Tasks:

- What are these?
- Write down the names of 12 different fruits or vegetables (don’t worry about spelling)
- How many 20p’s are there in £8.60?
- You are buying £1.20 worth of groceries. How much change would you receive from a £5 note?
- Draw a line from one circle to another starting at 1 and alternating numbers and letters in order (1 to A to 2 to B and so on)
- Draw a large face of a clock and place the numbers
- Position the hands for 10 minutes after 11 o’clock
- On your clock, label ‘L’ for the long hand and ‘S’ for the short one

Adapted from American version.
A simple word test: This is a simple word test that may help in the early diagnosis of Alzheimer's. It deals with the way in which our brain saves and stores memories. Since some words are learned earlier in childhood and used more frequently in adulthood, certain words will be more difficult for the Alzheimer's patient to recall. Word association tests such as this seem to work well in detecting early stage Alzheimer's.

First ask the individual to name all the animals they can think of in one minute. Then ask her/him to name all the types of fruit they can remember in one minute. Researchers have found that people with early Alzheimer's are able to list only 10 to 15 words in contrast to the 20 to 25 words from a healthy individual.

www.alzheimer-herbs.com ALZHEIMER'S ALTERNATIVE NATURAL TREATMENT AND PREVENTION (Please click on the link in description)

CAN YOU ANSWER THESE FIVE QUESTIONS FROM THE STUDY?

1. You are buying £1.95 of groceries. How much change would you receive back from a £5 note?
2. Name the following pictures (don't worry about spelling)
   ![Dice](image1)
   ![Hammer](image2)
3. How are a corkscrew and a hammer similar? Write down how they are alike
4. Place the numbers on this clock face, and position the hands for 10 minutes after 11 o'clock. Label 1 for the long hand and 5 for the short hand
   ![Clock](image3)
5. Name 12 different fruits or vegetables
   ____________________________________________
   ____________________________________________
   ____________________________________________
   ____________________________________________
   ____________________________________________
   ____________________________________________
   ____________________________________________
   ____________________________________________
   ____________________________________________

"Sundowning" is a syndrome in which older adults show high levels of anxiety and agitation.
Dementia

Key Points in the Diagnosis of Dementia in Primary Care

Diagnosis

History
1) Obtain examples of how the problems are actually affecting the individual eg. forgetting appointments, impaired self care, repetitiveness, etc.
2) Clarify the duration of symptoms (minimum of 6 months).
3) Enquire about onset of symptoms – abrupt or gradual.
4) Ask about marked fluctuations, visual hallucinations and personality change.
5) Check for presence of risks (Dementia Risk Assessment Tool).

Mental State Examination
1) Observe for signs of poor self care (dirty clothes, body odour, weight loss, etc).
2) Note presence of dysphasia, perseveration, confabulation, etc.
3) Check cognitive functioning – ideally MMSE, but 6CIT adequate (nursing staff may be agreeable to do this).

Physical Examination & Investigations
1) As determined by previous medical history and any current symptoms.
2) If rapid onset, or younger age, more comprehensive examination required.
3) Minimum bloods – FBC, ESR, LFTs, U&Es, B12 & Folate, TFTs, calcium, glucose, (syphilis and HIV serology only if at high risk).
4) Consider CT scan if sudden onset, younger age or atypical symptoms.
5) Other investigations as appropriate (eg. Chest x-ray, ECG).

Diagnostic Criteria
1) Duration of symptoms of at least 6 months and progressive.
2) Impairment of multiple (at least 2) domains of cognitive function eg. memory, dysphasia, apraxia, dyscalculia, etc.
3) Impairments cause a significant deterioration of function.
4) Symptoms are not better explained by another diagnosis/disability (eg. physical frailty delirium, deafness, learning disabilities or multiple pathology).
Age Related Cognitive + Mental Decline

Age-related cognitive decline / MCI / Alzheimer's / Dementia
First of all - do not panic. A few memory lapses as you get older does not necessarily mean you have got Alzheimer's! However, the earlier you go to see your Doctor the better! Get a proper diagnosis because there is a lot you can do and its best to start early.

Prevention is better than treatment!
Flavonoids - the natural antioxidant and anti-inflammatory compounds in Enzogenol - contribute to keeping your brain healthy. The more flavonoids you get the lesser your brain function declines as you age.

Flavonoid Intake and Cognitive Decline over a 10-Year Period

![Graph showing the change in mean Mini-Mental State Examination (MMSE) score over 10 years in men 65-70 years old by quartiles of flavonoid intake.](Figure 1. Change in mean Mini-Mental State Examination (MMSE) score over 10 years in men 65-70 years old by quartiles of flavonoid intake. Letenneur, L. et al Am J Epidemiol 165: 1364-1371; 2007.)

This epidemiological study shows a clear correlation between Flavonoid intake and cognitive decline with age. One capsule of Enzo Professional per day will immediately put you into the "high intake group".

**Age-related cognitive decline** is a term used to describe normal changes in brain function that occur as people age. When you get older you may experience slower information processing and mild memory impairment. This does not necessarily happen to everyone but it is very common. On average, speed of processing or reaction times do decline with age. Brain volume frequently decreases and some nerve cells, or neurons, are lost. These changes are
normal and are not considered signs of dementia. Basic steps including better nutrition, supplementation, brain exercises (don’t use it - you loose it!), and other strategies can help to minimise age-related changes in brain function. **Mild Cognitive Impairment (MCI)** describes cognitive and memory problems that are not severe enough to be diagnosed as dementia but are more pronounced than the cognitive changes associated with normal aging. MCI can affect many areas of thought and action — such as language, attention, reasoning, judgment, reading and writing. However, most common are memory problems. People with MCI are three times more likely to develop Alzheimer’s or other dementias than are those without MCI. About half the people with MCI will progress to Alzheimer’s disease within five years, although some remain stable and others even return to normal. This is the stage where early interventions including nutritional strategies, brain exercises, and more interaction with others may still have a chance to prevent progression and even reverse symptoms.

**Alzheimer’s disease** is the most common form of dementia (50-70% of cases) named after the German physician Alois Alzheimer, who first described the disease in 1906. Alzheimer’s is a degenerative disease of nerve cells in the brain that leads to atrophy (shrinking) of the brain. The condition worsens over time and is ultimately fatal, however the rate of progression from mild to moderate and severe varies between individuals, and can be very slow as much as 20 years or more. Symptoms start with memory loss and other cognitive deficits, advancing to major personality changes and eventual loss of control over bodily functions.

**Dementia** is a general term describing a combination of symptoms caused by conditions affecting the brain; it is not a term for a specific disease. Memory loss is a common symptom of dementia. However, memory loss by itself does not mean you have dementia. People with dementia have serious problems with two or more brain functions, such as memory and language. Many different diseases can cause dementia, including Alzheimer’s disease, stroke, and other neurological diseases.

All aging humans will develop some degree of decline in cognitive capacity as time progresses. Data indicates that deterioration of the biological framework that underlies the ability to think and reason begins as early as the mid twenties and includes a drop in regional brain volume, loss of myelin integrity, cortical thinning, impaired serotonin, acetylcholine, and dopamine receptor binding and signaling, accumulation of neurofibrillary tangles, and altered concentrations of various brain metabolites. Cumulatively these changes give rise to a variety of symptoms associated with aging, such as forgetfulness, decreased ability to maintain focus, and decreased problem solving capability. If left unchecked, symptoms oftentimes progress into more serious conditions, such as dementia and depression, or even Alzheimer’s disease.

Cognitive decline does not affect all individuals equally; clear associations exist between the rate and severity of cognitive decline and a variety of factors, including oxidative stress and free radical damage, chronic low-level inflammation, declining hormone levels, endothelial dysfunction, excess body weight, suboptimal nutrition, lifestyle, social network, other medical conditions, and various biomarkers. Fortunately, many of these factors are modifiable to a significant extent, and proactive lifestyle changes, cognitive training, and nutritional interventions have been shown to decrease the rate of intellectual decay and potentially reverse age-related cognitive decline.

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8. I am going to give you a series of numbers and I would like you to give them to me backwards. For example, if I say 42, you would say 24.

9. This is a clock face. Please put in the hour markers and the time at ten minutes to eleven o’clock.

10. Which of the above figures is largest?
The Aging Brain

The aging process profoundly impacts the brain in ways that can be observed on multiple levels, ranging from sub-cellularly to macro-structurally. On a diminutive scale, aging causes deterioration of neuronal and mitochondrial membranes, which leads to the loss of cellular integrity and impaired neuronal function.\textsuperscript{28,29,30} Steep age-related declines in neurotransmitter synthesis and signaling,\textsuperscript{31,32,33} coupled with reductions in synaptic density and plasticity (adaptability),\textsuperscript{34,35} and loss of as much as 50% of the length of myelinated axons\textsuperscript{36} (see figure 1) make the brain increasingly less efficient as we age.

In a broader sense, the physical structure of the brain as a whole also deteriorates with age. Shrinkage and death of neurons, and reductions in the number of synaptic spines and functional synapses contribute to annual reductions of as much as 0.5% to 1.0% in cortical thickness (the cortex is the outermost layer of the brain) and sub-cortical volume in some regions of the brain.\textsuperscript{37} Specifically, even in healthy individuals, aging accounts for volume variances of 37% in the thalamus, which is involved in sight, hearing, and the sleep-wake cycle; 36% in the nucleus accumbens, which plays a major role in mood regulation (e.g. pleasure, fear, reward); and 33% in the hippocampus, a critical site for consolidation of short-term to long-term memory.\textsuperscript{38} Taken together, age related neuroanatomical changes account for an estimated 25% to 100% of the variance in cognitive ability between young and aged individuals.\textsuperscript{39} In other words, age related cognitive decline occurs in tandem with the physical degradation of brain structure. Thus, conserving cognitive vigilance into late life requires early and aggressive intervention to preserve the brain in its youthful physical and functional state.

![Figure 1: Anatomy of a neuron]
Biological Risk Factors Contributing to Cognitive Decline

Various biological systems work in conjunction to maintain optimal brain function and cognitive ability. Perturbations in the harmony of these systems, caused by such age-associated insults as chronic inflammation, oxidative stress, insulin resistance, declining hormone levels, and endothelial dysfunction, result in physical deterioration of the brain and subsequent cognitive decline.

Oxidative Stress. The brain is particularly susceptible to oxidative damage since it consumes roughly 20% of the oxygen used by the entire body, and because it contains high concentrations of phospholipids, which are especially prone to oxidative damage in the context of high metabolic rate. As we age, there is a significant and progressive increase in the level of oxidatively damaged DNA and lipids in the brain; this is true even for healthy individuals. Over time, this free radical damage leads to the death of neurons.

Numerous studies have implicated oxidative stress in the pathology of mild cognitive impairment and Alzheimer’s disease alike. In a study of 338 individuals, researchers analyzed blood samples from patients with various neurodegenerative diseases and found that the antioxidant capacity of their blood was reduced by as much as 28%, relative to healthy controls. Subjects with a neurodegenerative condition also exhibited significantly increased levels of thiobarbituric acid reactive substances, a marker of free radical damage.

In a separate study, in which researchers examined the plasma of 34 subjects with mild cognitive impairment, 45 with Alzheimer’s disease, and 28 age-matched healthy controls, revealed that patients with mild cognitive impairment or Alzheimer’s disease displayed markedly increased oxidative damage. Subjects with mild cognitive impairment or Alzheimer’s disease exhibited increased protein oxidation (protein carbonyls) and decreased levels of glutathione, a powerful endogenous antioxidant.

In aged rodents exhibiting signs of cognitive deterioration, increased oxidation of key proteins involved in neuronal metabolism and energy production has been observed. Old animals also display dramatically reduced ability to combat oxidative stress, as assessed by a loss of efficiency of thiol reducing systems.

Inflammation. The inflammatory process in the brain is unique in that the blood-brain barrier (BBB) (tight layer of endothelial cells that separates the brain from regular systemic circulation), during healthy conditions, prevents the infiltration of inflammatory agents and allows only select nutrients and small molecules into the central nervous system (CNS). However, chronic systemic inflammation induced by stimuli such as cigarette smoking, obesity, disrupted sleep patterns and poor dietary habits compromises the integrity of the BBB, allowing irritants to enter the brain and stimulate the production of inflammatory cytokines, such as IL-1β, IL-6 and IL-18. Inside the CNS, these cytokines impair neurogenesis, the process by which new neurons are generated.
from inhibiting neurogenesis, some inflammatory cytokines, such as IL-1β, IL-6 and TNF-α damage and destroy existing neurons.\textsuperscript{60,61}

Several studies have linked biomarkers of inflammation with cognitive impairment.

A prospective study of 779 healthy, high-functioning men and women found that subjects in the highest tertile (one-third) for blood levels of IL-6 were significantly more likely to score below the median when assessed for cognitive function at baseline. During follow-up seven years later those same individuals more frequently exhibited declines in cognition compared to their counterparts with lower baseline IL-6 levels.\textsuperscript{62}

In a study of 97 women between 60 and 70 years of age, elevated baseline high sensitivity C-reactive protein (hs-CRP) levels were correlated with worsening of memory at 12 years follow-up. This data led the authors to conclude that “hs-CRP may be a useful biomarker to identify individuals at an increased risk for cognitive decline.”\textsuperscript{63} Likewise, in a study assessing over 4,000 subjects, higher levels of CRP and IL-6 were found to be associated with decreased cognition and executive function. IL-6 was also associated with steeper declines in memory performance during follow-up at up to five years.\textsuperscript{64}

Another study found that, even in healthy individuals, baseline CRP levels were inversely correlated with the results of a learning and recall test at follow-up six years later. The investigators concluded that “relatively high concentrations of… CRP may be indicative for impaired cognitive performance.”\textsuperscript{65} In a similar study, biological markers were measured in the blood of 93 healthy individuals aged 57 years (mean). At six years follow-up time, those individuals with the highest baseline CRP levels scored lower on a Word Learning test. In this study it was concluded that
“concentrations of serum markers related to inflammation...are not only associated with Alzheimer’s disease, but also with cognitive functioning in the cognitively healthy aging population.”

The deleterious effects of inflammation on cognitive function are observable in real-time as well. Researchers administered a typhoid vaccination, which is known to induce an inflammatory response, or a placebo injection to 16 healthy men aged 18 to 35. Study subjects then completed a series of tests designed to assess cognitive vigilance. Participants who received the typhoid vaccination exhibited significantly slower reaction times than their counterparts who received the placebo, and the degree of delay in reaction time correlated with the intensity of inflammation, as measured by circulating IL-6 levels.

**Hormonal Imbalance.** Distributed throughout the brain are steroid hormone receptors which function to regulate the transcription of a vast array of genes involved in cognition and behavior. Adequate steroid hormone receptor activation in the brain is a fundamental determinant in many aspects of our lives that we take for granted. When hormonal imbalances or deficiencies disrupt receptor activation, cognitive deficits and emotional turmoil are the result.

- **Estrogen**

Animal models indicate that experimentally-induced alterations in the levels of steroid hormones, particularly estradiol, in the brain cause significant behavioral changes observable within minutes, leading some researchers to conclude that steroid hormones actually have the capacity to function directly as neurotransmitters in the central nervous system. In humans, suboptimal (low) levels of estradiol are associated with decreased scores on standardized
assessments of cognition in both men and women. Postmenopausal women with higher levels of endogenous estradiol also have better semantic memory than do those deficient in the estrogen. Accordingly, postmenopausal women treated with estradiol displayed improvements in executive function compared to those taking a placebo.

- **Testosterone**

Maintaining optimal levels of testosterone can help preserve cognitive ability as well. In a study involving over 500 aging men and women, higher levels of testosterone were linked with better performance on the Mini-Mental State Examination at baseline. Men with the lowest levels of testosterone at the beginning of the study period were more likely to exhibit a sharp decline in cognitive ability over the following two-year period as well. Several other studies also conclude that testosterone levels are positively associated with multiple aspects of cognitive function.

Aging men given testosterone replacement therapy display improved cognitive function. In one study healthy men between the ages of 50 and 85 years responded to supplemental testosterone restoration treatment with significantly improved spatial and verbal memory, and spatial ability. Likewise, men with mild cognitive impairment or Alzheimer’s disease responded to testosterone therapy with enhanced spatial and verbal memory, and constructional abilities.

Experimental studies indicate that the connection between testosterone and cognitive function is due in part to the dependence of the hippocampus on androgens to maintain synaptic density. Intriguing data shows that male non-human primates devoid of androgens have a dramatically reduced number of synapses in the hippocampus, which is of paramount importance for consolidation of short-term and long-term memory, as well as learning. Additional experimental data shows that hippocampal synaptic maintenance is androgen dependent.

- **Dehydroepiandrosterone (DHEA)**

Age-associated decline in levels of the adrenal hormone dehydroepiandrosterone (DHEA), which is very active in the central nervous system, are also tied to worsening cognitive performance. In a study involving over 750 aging subjects, Mini-Mental State Examination (MMSE) scores were significantly associated with levels of DHEA-s, the sulfated metabolic derivate of DHEA, which is more highly concentrated in humans. Moreover, those individuals with the lowest levels of DHEA-s at baseline displayed greater cognitive decline over time than those with higher initial levels. In a separate community-based study involving nearly 300 healthy women, levels of DHEA-S correlated positively with superior executive
function, concentration, and working memory. Accordingly, in a double-blind, placebo controlled clinical trial, six-months of supplementation with 25 mg of DHEA daily improved measures of cognitive function, especially verbal fluency, in aging women.

- **Pregnenolone**

Another neurosteroid, pregnenolone, is also involved with a number of cognition-related functions within the brain. For example, experimental studies indicate that pregnenolone modulates neurotransmitter signaling through interaction with select receptor sites, which translates to improvements in long-term memory in rodents. In human clinical trials, supplementation with pregnenolone improved cognition in subjects with neurological disorders. Additionally, levels of pregnenolone metabolites are reduced significantly in the prefrontal cortex, and area involved with higher-order processing, in Alzheimer's disease patients, leading some researchers to speculate that pregnenolone levels may be relevant in the pathology of the disease.

Research indicates that DHEA, pregnenolone, and metabolites thereof exert numerous activities in the central nervous system through activation of the Sigma-1 receptor. This effect may confer benefits including protecting neurons against ischemia (i.e. stroke), and enhancement of long-term potentiation (memory formation).

- **Thyroid hormones**

During the developmental period thyroid hormones play a critical role in ensuring proper growth and maturation of the brain. Thyroid hormone levels may also be related to cognitive function in adults, though the evidence in this area is inconsistent. However, limited associations with both hypo- (low) and hyper- (high) thyroid function and cognitive impairment exist in the peer reviewed literature, thus maintaining levels of TSH, T3, and T4 within normal ranges is suggested.
Cerebrovascular Health. The brain depends on the carotid arteries to obtain the oxygen and nutrient-rich blood that it needs to sustain its high rate of metabolic activity. The carotid arteries emerge from the aorta and carry blood through the neck into the brain where they branch and diverge into many smaller capillaries, which facilitate circulation across the various brain regions. Like other blood vessels, the carotid arteries and their subsidiaries (smaller branches) are susceptible to endothelial dysfunction, dysregulation and damage to the delicate cells that line our blood vessels. Endothelial dysfunction is a critical step in both the initiation, and progression, of atherosclerosis.

If the integrity of the blood vessels that supply the brain is compromised, cognition suffers as a result. Multiple correlates between measures of vascular health and cognitive function are identified in the peer-reviewed literature.

- **HDL levels**

HDL serves to shuttle cholesterol from the blood vessel walls back to the liver for excretion, and thus insufficient levels of HDL are associated with increased endothelial dysfunction and arterial plaque deposition. Studies have linked low HDL levels with declining brain health and function.

Researchers examined the brains of 183 subjects, mean age 58 years, using magnetic resonance imaging (MRI). Tests revealed that HDL levels were positively associated with brain grey matter volume. Not surprisingly, then, subjects with higher HDL levels also scored significantly higher on a visuo-spatial memory test than their counterparts with lower HDL levels. These findings lead the investigators to conclude that “adults with decreased levels of HDL cholesterol may be experiencing cognitive changes and grey matter reductions in regions associated with neurodegenerative disease and therefore, may be at greater risk for future cognitive decline.”

In a study of 139 very elderly subjects, plasma HDL levels were strongly associated with cognitive acuity. Subjects with higher HDL levels performed much better on the Mini-Mental State Examination (MMSE) than those with lower HDL levels. In fact, “each decrease in plasma HDL tertile (74.9 +/- 2.1, 50.6 +/- 0.5, and 36.8 +/- 1.0 mg/dl) was associated with a significant decrease in MMSE [score].”

- **Homocysteine**

Homocysteine is an endogenous amino acid derivative which damages the endothelial cells that line the inside of blood vessels and contributes to the pathogenesis of atherosclerosis and vascular dysfunction. Elevated
homocysteine has been linked with reduced blood flow to the brain, memory impairment, poorer global cognitive function, smaller overall brain volume, and increased silent brain infarcts (subclinical stroke-like blood vessel occlusions in the brain).

In a randomized, placebo-controlled clinical trial, which included over 5,500 subjects with known cardiovascular disease, treatment with the homocysteine-lowering B vitamins folic acid (2.5 mg), B6 (50 mg) and B12 (1,000 mcg) was shown to significantly reduce the risk of stroke versus placebo, highlighting the link between cerebrovascular health and homocysteine levels.

Similarly, lowering homocysteine in individuals over 70 years of age through supplementation with 800 mcg folic acid, 500 mcg B12, and 20 mg B6 daily for a period of 24 months was shown to reduce the rate of brain atrophy by 53% versus placebo control in a randomized, double-blind trial. Subjects receiving the homocysteine lowering B-vitamins also scored much better on their final cognitive tests at the end of the study period.

- **Hypertension**

Small, delicate capillaries, like those that perpetuate the flow of blood throughout the brain, are particularly susceptible to damage caused by elevated blood pressure. Chronic hypertension leads to the breakdown of cerebrocapillaries, a condition associated with the development neurodegenerative diseases and cognitive impairment.

A case-control study of over 700 patients found a statistically significant correlation between blood pressure and rate of cognitive decline over a six-month period for subjects younger than 65 years. Accordingly, an observational study of more than 1,800 people revealed that individuals taking an antihypertensive medication were less likely to have dementia at the study onset, and were also less likely to develop dementia over the following three year period. Significantly, subjects who did have dementia at baseline and were not taking blood pressure medication exhibited a two-fold faster rate of cognitive decline than demented individuals with medication-controlled hypertension.

In a study which followed 717 individuals for 38 years starting from age 45, researchers found that subjects with systolic blood pressure ≥140 mmHg throughout the study period “performed consistently less well than the normal systolic blood pressure subgroups on a composite measure of verbal learning and memory.”
Evidence suggests that blood pressure of 115/75 mmHg significantly reduces the risk for cardiovascular disease, and thus may be an ideal target for those who wish to maintain optimal cognitive performance as well.

**Diabetes and Insulin Resistance.** Due to the high metabolic demand for energy in the brain, even small perturbations in glucose metabolism can noticeably impact cognitive performance. Diabetes (hyperglycemia) has been linked with lower levels of neuronal growth factors, decreased brain volume, and higher incidence of all types of dementia.

Cerebral glucose metabolism was measured by fludeoxyglucose–positron emission tomography (FDG-PET) in 23 adults aged 74 years (mean), who met criteria for diabetes or pre-diabetes. The results were compared to those of six 74 year old (mean) adults without diabetes or pre-diabetes. Subjects were asked to memorize and recall a list of 20 random words they heard through a pair of headphones. FDG-PET scans revealed markedly different patterns of glucose utilization and brain activity between diabetic / pre-diabetic subjects and healthy controls during the memorization task. Subjects with healthy glucose metabolism remembered more words upon recall attempt. Interestingly, FDG-PET scans of those with pre-diabetes / diabetes resembled brain scans of Alzheimer’s patients.

Researchers in another study compared MRI-assessed manifestations of cerebral degeneration in 89 non-demented subjects with type-2 diabetes to 438 age-matched healthy controls over a three-year period. Individuals with diabetes displayed increased progression of brain atrophy, and performed less well on tests of cognitive performance and learning. The investigators concluded that “our data show that elderly patients with [type-2 diabetes] without dementia have accelerated progression of brain atrophy with significant consequences in cognition compared to subjects without [type-2 diabetes]. Our findings add further evidence to the hypothesis that diabetes exerts deleterious effects on neuronal integrity.”

In over 1,300 aging men, researchers observed an inverse correlation between fasting insulin levels and cognitive function in non-diabetics. Baseline insulin levels were assessed and followed by a battery of cognitive testing an average 3.3 years later. Subjects with higher initial insulin levels scored more poorly on all four tests administered. These results indicate that “higher fasting insulin and greater insulin secretion in older men may be related to overall cognitive decline, even in the absence of diabetes.”

**Obesity.** Adipose tissue secretes molecules that directly influence multiple functions within the brain. There is a clearly established reciprocal relationship between adiposity (amount of body fat) and overall brain volume and cognitive function. In other words, as bodyweight increases, brain volume drops and cognitive function worsens.

In a study utilizing MRI brain imaging technology to explore the link between obesity and brain volume, researchers discovered that visceral abdominal obesity in particular was associated with deteriorating brain structure. This was true even in individuals without pre-existing cognitive deficits. The findings were statistically significant and independent of vascular risk factors and overall BMI.
Similar findings were reported by another group, but this time in 700 patients with a prior diagnosis of Alzheimer’s disease or cognitive impairment. Investigators identified a strong correlation between higher BMI and brain volume deficits in the frontal, temporal, parietal, and occipital lobes. It was concluded that “cardiovascular risk factors, especially obesity, should be considered as influencing brain structure in those already afflicted by cognitive impairment and dementia.”

In 90 healthy middle-aged and older adults (ages 54 – 81), who performed tests of manual dexterity, motor speed, and executive function, greater central obesity as manifested by higher waist circumference was associated with poorer performance. Not surprisingly, high blood pressure exacerbated the correlation between increasing waist circumference and declining cognition; “in healthy older adults, there are similar, negative relations of central and total obesity to cognitive function that are potentiated by higher [blood pressure] levels.”

Mid-life obesity was strongly linked to later-life dementia in over 1,000 participants in a longitudinal study carried out over a 36 year period. Subjects with the greatest waist diameters at baseline were nearly three-fold more likely to develop dementia over the following three decades. The investigators in this study concluded that “central obesity in midlife increases risk of dementia independent of diabetes and cardiovascular comorbidities.”

![Projected Global Dementia Rates](image-url)
Training the Older Brain in 3-D: Video Game Enhances Cognitive Control

UCSF Study Finds Brain Training Game Effective in Improving Multitasking Skills
By Laura Kurtzman on September 04, 2013

Scientists at UC San Francisco are reporting that they have found a way to reverse some of the negative effects of aging on the brain, using a video game designed to improve cognitive control.

The findings, published on Sept. 5 in *Nature*, show that a specially designed 3-D video game can improve cognitive performance in healthy older adults, they said. The researchers said the study provides a measure of scientific support to the burgeoning field of brain fitness, which has been criticized for lacking evidence that such training can induce lasting and meaningful changes.

The ability to multitask – or switch rapidly between tasks – declines rapidly over the adult lifespan, something that researchers refer to as “multitasking cost.” But after just one month of training on the NeuroRacer game, researchers found significant improvement in study participants. Click graph to download PDF version.

In the game, which was developed by the UCSF researchers, participants race a car around a winding track while a variety of road signs pop up. Drivers are instructed to keep an eye out for a specific type of sign, while ignoring all the rest, and to press a button whenever that particular sign appears.

The need to switch rapidly from driving to responding to the signs – i.e. multitasking – generates interference in the brain that undermines performance. The researchers found that this interference increases dramatically across the adult lifespan.

But after receiving just 12 hours of training on the game, spread over a month, the 60- to 85-year-old study participants improved their performance until it surpassed that of 20-somethings who played the game for the first time.
The training also improved the participants’ performance in two other important cognitive areas: working memory and sustained attention. And participants maintained their skills at the video game six months after the training had ended.

Adam Gazzaley, MD, PhD

“The finding is a powerful example of how plastic the older brain is,” said Adam Gazzaley, MD, PhD, UCSF associate professor of neurology, physiology and psychiatry and director of the Neuroscience Imaging Center. Gazzaley co-founded the company, Akili Interactive Labs, which is developing the next generation of the video game.

Gazzaley, who has made a career out of studying how distraction affects cognitive performance, said his game, NeuroRacer, does more than any ordinary game – be it bridge, a crossword puzzle, or an off-the-shelf video game – to condition the brain. Like a good teacher, he said, NeuroRacer undermines people’s natural tendency to go on automatic pilot once they’ve mastered a skill, and pushes them further than they think they can go.

“Normally, when you get better at something, it gets easier,” he said. But with this game, “when you get better, it gets harder.”

Brain Training Reverses Age-Related Decline

Evidence that the adult brain is capable of learning has been accumulating for more than a dozen years. A study of London taxi drivers, for example, found that their brains had changed as they learned to navigate the city’s notoriously complicated streets.

Nevertheless, Gazzaley said the brain’s function often erodes steadily over time in many areas, with some exceptions, like wisdom.
Study participant Ann Linsley plays the NeuroRacer game, designed to train the brain by enhancing cognitive control and reversing the negative effects of aging.

Joaquin Anguera, PhD, assists study participant Ann Linsley as she plays the NeuroRacer game.

Given this, Gazzaley said it’s encouraging that even a small amount of brain training can reverse some of the age-related decline.

Gazzaley’s group found evidence of a possible brain mechanism that may explain the improvements he saw in his older subjects, and why these gains transferred to other cognitive areas. Electroencephalograph (EEG) recordings point to changes in a neural network involved in cognitive control, which is necessary to pursue goals.

The scientists measured midline frontal theta – or low frequency oscillations – in the prefrontal cortex, as well as the coherence in these waves between frontal and posterior regions of the brain. As the older “drivers” became more adept at the multitasking challenges of NeuroRacer, their brains modulated this key neural network and its activity began to resemble that of young adults.

Both of these measures – midline frontal theta and theta coherence – are well established neural markers of cognitive control that have been associated with many of the processes that enable people to pursue their goals.

"We see this as evidence that the training may have improved our study participants’ ability to stay in an engaged, active state for a longer period of time,” said Joaquin A. Anguera, the paper’s first author and a post-doctoral fellow in Gazzaley’s lab.

Indeed, the researchers found that the training-induced changes in this neural network predicted how well participants would do on a different test, called the Test of Variables of Attention (TOVA), which measures sustained attention.

“The amount that midline frontal theta went up was related to something that was untrained, this other measure, the TOVA,” Anguera said. “It implies there’s something that changed that was common to the training and to the task we tested afterwards.”
Wider Applications for Cognitive Control

Gazzaley said these findings point toward a common neural basis of cognitive control that is enhanced by the challenging and high-interference conditions of the video game, and this might explain how racing a car in 3-D could improve something as seemingly unrelated as memory.

This graphic shows increased brain activity for older adults who underwent multi-tasking training (bottom left) versus those who only did single-task training (bottom center) or no training at all (bottom right). Credit: Joaquin A. Anguera/UCSF

If the finding holds, it could have wide application. Other brain disorders like ADHD, depression and dementia are also associated with deficits in cognitive control.

“Follow up studies using functional Magnetic Resonance Imaging and transcranial electrical stimulation are still needed to better understand exactly how this network is involved in the performance changes,” Gazzaley said.

Other authors of the article, “Video game training enhances cognitive control in older adults,” include Jacqueline Boccanfuso, Jean Rintoul, Omar Al-Hashimi, Farshid Faraji, Jacki Janowich, Erwin Kong, Yudy Larraburo, Cammie Rolle and Eric Johnston.

Gazzaley is co-founder and chief science advisor of Akili Interactive Labs, which is developing cognitive video game software as diagnostic and therapeutic tools, and has a patent pending on a game-based cognitive intervention he developed from the research presented in the paper.

The study was funded under Health Games Research, a program of the Robert Wood Johnson Foundation and by the National Institute on Aging. Anguera is also supported by a UCSF Institutional Research and Career Development Award.
Exposure to common infections - even if they do not make you ill - may be linked to decline in brain functions like memory and reasoning, according to new research presented at a conference recently. However, the researchers caution more work needs to be done to confirm their findings.

Lead researcher Dr. Clinton Wright, scientific director of the Evelyn F. McKnight Brain Institute at the University of Miami, presented the study at the American Stroke Association's International Stroke Conference 2014, in San Diego, CA.

He conducted the study with colleagues from Columbia University in New York, NY.

They were interested in further exploring the findings of studies such as that reported in 2013 in the journal *Stroke*, which found **brain function may decline as heart disease risk factors increase**. Other studies have also found links between certain infections and increased risk of **stroke** and **Alzheimer's disease**.

"We were very interested in what were the risk factors for cognitive performance and decline," explains Dr. Wright.

They studied brain function tests and blood sample results from 588 older adults who took part in the Northern Manhattan Study, a research project examining stroke and stroke risk factors in the Northern Manhattan community.

Half of the participants repeated the brain function tests after a 5-year interval.
The results showed links between antibody levels caused by exposure to common infections and worsening cognitive performance in functions like memory, planning and reasoning ability, speed of mental processing and abstract thinking.

The common infections the researchers studied included *Chlamydia pneumoniae* (which can lead to pneumonia and bronchitis), *Helicobacter pylori* (the cause of most stomach and duodenal ulcers), and the herpes viruses *cytomegalovirus* and herpes simplex viruses 1 and 2 (which can cause cold sores and other conditions).

There is evidence that exposure to the infections is linked to increased risk of stroke and atherosclerosis (where arteries become clogged up), and inflammation. Either immune response or infection itself may be the cause.

Although he and his colleagues did not explore how exposure to these infections might relate to cognitive decline, Dr. Wright suggests:

"It could be caused by an immune system response to the infections or the infection itself could result in clinical damage that we're not aware of."

The researchers do not suggest people take action against these infections, as there is no evidence to suggest doing so will do any good. Plus, the infections could have happened decades earlier, and any damage could be the result of a gradual process.

"It would be great if treatment prevented these bad outcomes, but we're very far away from having that type of evidence," notes Dr. Wright, who now wants further studies to confirm these findings in other groups, since 70% of the participants in their sample were of Hispanic origin.
Cooking meat 'may be dementia risk'

- **Slow-cooking could protect diabetics**
  - Browning meat in the oven, grill or frying pan produces chemicals which may increase the risk of developing dementia, US researchers suggest.

Advanced glycation end products (AGES) have been linked to diseases such as type-2 diabetes. Mice fed a high-AGES diet had a build-up of dangerous proteins in the brain and impaired cognitive function. Experts said the results were "compelling" but did not provide "definitive answers".

AGES are formed when proteins or fats react with sugar. This can happen naturally and during the cooking process. Researchers at the Icahn school of medicine at Mount Sinai, in New York, tested the effect of AGES on mice and people.

The animal experiments, published in *Proceedings of the National Academy of Sciences*, showed that a diet rich in AGES affects the chemistry of the brain.
It leads to a build-up of defective beta amyloid protein - a hallmark of Alzheimer's disease. The mice eating a low-AGES diet were able to prevent the production of damaged amyloid.

**This subject has so far not been well studied in people, and we don't yet know whether the amount of AGES in our diet might affect our risk of dementia**

Dr Simon Ridley, Alzheimer's Research UK, said: "Diabetes has previously been linked to an increased risk of dementia, and this small study provides some new insight into some of the possible molecular processes that may link the two conditions.

"It's important to note that the people in this study did not have dementia. This subject has so far not been well studied in people, and we don't yet know whether the amount of AGES in our diet might affect our risk of dementia."

"Because cures for Alzheimer's disease remain a distant hope, efforts to prevent it are extremely important, but this study should be seen as encouraging further work, rather than as providing definitive answers. "But it is grounds for optimism - this paper adds to the body of evidence suggesting that using preventative strategies might reduce the prevalence of Alzheimer's disease and other dementias in society and that could have very positive impact on us all."

Derek Hill, a professor of medical imaging sciences at University College London, commented: "The results are compelling."

The study concluded: "We report that age-related dementia may be causally linked to high levels of food advanced glycation end products. "Importantly, reduction of food-derived AGES is feasible and may provide an effective treatment strategy."
SATURATED FAT TIED TO MENTAL & COGNITIVE DECLINE

High consumption of foods like red meat and butter raises the risk of mental decline.

By PressTV | 22 May 2012

People who frequently eat foods high in saturated fat such as butter and red meat are more likely to develop mental and cognitive decline which are early signs of dementia and Alzheimer’s.

In a 5 year study, published online in the Annals of Neurology, researchers analyzed dietary data from 6,000 women aged over 65 and tested their cognitive function to find any association.

The results demonstrated that women who frequently consumed more saturated fat scored worse on cognitive function tests at the end of the study than their counterparts who ate healthier types of fat.

Many studies have linked foods high in saturated fat such as red meat, fatty dairy foods like ice cream and whole milk to higher risk of developing clogged arteries and related conditions including high blood pressure, heart disease and stroke.

However, the new study by Harvard University researchers has provided more evidence to support the benefits of replacing unhealthy saturated fats with monounsaturated fats such as those found in olive oil, sunflower oil, seeds, avocados, and nuts.

"People will want to think about substituting out saturated fat in favor of monounsaturated foods," said study author Dr. Olivia Okereke. "Making that substitution might be a way to prevent cognitive decline in older people."

"In general, when it comes to dietary fat, the message has been pretty consistent over time that those dietary fats that are beneficial for cardiovascular health might similarly be beneficial for brain health," she recommended.

"Our analysis suggests if you substitute out 5 percent of your saturated fat calories with 5 percent monounsaturated fats, you could have a 50 percent lower risk [of memory and cognitive decay]."
Drug-Induced Cognitive Impairment in the Elderly

- Alan R. Moore
- Dr. Shaun T. O’Keeffe

Abstract

Elderly people are more likely than younger patients to develop cognitive impairment as a result of taking medications. This reflects age- and disease-associated changes in brain neurochemistry and drug handling. Delirium (acute confusional state) is the cognitive disturbance most clearly associated with drug toxicity, but dementia has also been reported. The aetiology of cognitive impairment is commonly multifactorial, and it may be difficult to firmly establish a causal role for an individual medication.

In studies of elderly hospital patients, drugs have been reported as the cause of delirium in 11 to 30% of cases. Medication toxicity occurs in 2 to 12% of patients presenting with suspected dementia. In some cases CNS toxicity occurs in a dose-dependent manner, often as a result of interference with neurotransmitter function. Drug-induced delirium can also occur as an idiosyncratic complication. Finally, delirium may occur secondary to iatrogenic complications of drug use.

Almost any drug can cause delirium, especially in a vulnerable patient. Impaired cholinergic neurotransmission has been implicated in the pathogenesis of delirium and of Alzheimer’s disease. Anticholinergic medications are important causes of acute and chronic confusional states. Nevertheless, polypharmacy with anticholinergic compounds is common, especially in nursing home residents. Recent studies have suggested that the total burden of anticholinergic drugs may determine development of delirium rather than any single agent. Also, anticholinergic effects have been identified in many drugs other than those classically thought of as having major anticholinergic effects.

Psychoactive drugs are important causes of delirium. Narcotic agents are among the most important causes of delirium in postoperative patients. Long-acting benzodiazepines are the commonest drugs to cause or exacerbate dementia. Delirium was a major complication of treatment with tricyclic antidepressants but seems less common with newer agents. Anticonvulsants can cause delirium and dementia.

Drug-induced confusion with nonpsychoactive drugs is often idiosyncratic in nature, and the diagnosis is easily missed unless clinicians maintain a high index of suspicion. Histamine H3-receptor antagonists, cardiac medications such as digoxin and β-blockers, corticosteroids, non-steroidal anti-inflammatory agents and antibiotics can all cause acute, and, less commonly, chronic confusion.

Drug-induced confusion can be prevented by avoiding polypharmacy and adhering to the saying ‘start low and go slow’. Special care is needed when prescribing for people with cognitive impairment. Early diagnosis of drug-induced confusion, and withdrawal of the offending agent or agents is essential.
Adverse Drug Reactions Associated with Global Cognitive Impairment in Elderly Persons

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Adverse drug reactions causing cognitive impairment are an important problem in the elderly. Thirty-five patients with adverse drug reaction were identified among more than 300 patients evaluated for cognitive impairment and compared with patients without adverse drug reaction. Sedative hypnotic agents, especially long-acting benzodiazepines, were the commonest drugs associated with cognitive impairment in this population. The number of drugs used, use of sedative hypnotics and antihypertensives, and falling were strongly associated with adverse reactions in logistic regression analyses. The relative odds of an adverse reaction associated with cognitive impairment increased as the number of prescription drugs increased, exceeding 9.0 for patients taking four or more prescription drugs. Adverse drug reactions are an important source of excess morbidity in patients with dementia or suspected dementia. Strategies that could minimize this problem include a high index of suspicion, drug-free trials in suspected cases, and careful monitoring of drug therapy.
Drug-Induced Cognitive Impairment: Delirium and Dementia

As people age, they become more susceptible to delirium and dementia caused by drugs. This is known as drug-induced cognitive impairment, and it is an important syndrome to recognize, because in almost all cases it can be reversed or returned to the pre-drug state (in the case of people whose cognitive impairment was worsened by drugs) by stopping the offending drug.

Both in the hospital and office settings, drug-induced cognitive impairment is often overlooked and attributed to an underlying medical illness or merely to "old age," when it is actually a side-effect of a drug. In many cases, the reason for prescribing the culprit drug is questionable, or the cognitive impairment is related to taking multiple drugs at once.

As discussed in Part I of this series, there are many drugs that cause delirium and dementia (see Box 2 for definitions of delirium and dementia) through their anticholinergic effects. Most of these drugs have important functions other than blocking the neurotransmitter acetylcholine. In addition, there are several other classes of drugs that can cause cognitive impairment in susceptible individuals.

Drugs that can cause cognitive impairment

Drug-induced cognitive impairment is most commonly linked to benzodiazepines, opiates, tricyclic antidepressants and anticonvulsants (drugs used to treat and prevent seizures).

View our list of 136 drugs that cause cognitive impairment in the full version of this article. This is not an exhaustive list, but includes many of the most commonly...
Drugs that can cause cognitive impairment

Benzodiazepines

Benzodiazepines — which include tranquillizers and sleeping pills — have a wide range of effects on the central nervous system. They are commonly used to treat anxiety in the short-term, and also to sedate critically ill patients or those undergoing surgery.

People who take benzodiazepines chronically for anxiety, which is not recommended, can also develop more chronic cognitive impairment. Furthermore, because addiction to benzodiazepines is common, stopping them abruptly can result in a withdrawal syndrome similar to what is seen with alcohol withdrawal, including sweating, agitation, confusion, hallucinations and even seizures.

Patients on benzodiazepines are at greater risk for developing delirium while hospitalized, and when benzodiazepines are used to treat agitation associated with delirium from other causes, they often make it worse.

Sedatives that have similar central nervous system effects as benzodiazepines, such as the commonly used sleep agents zolpidem (AMBIEN), zaleplon (SONATA) and eszopiclone (LUNESTA) can also induce delirium. As with benzodiazepines, stopping these agents abruptly after chronic use can result in a withdrawal syndrome.

Box 1. Three Reasons Older People Are More Susceptible to Drug-Induced Delirium and Dementia

1. The body’s ability to clear drugs decreases with age, often because of a normal age-related decrease in kidney and liver function. This results in a greater accumulation of drugs in the body.
2. Older patients are often prescribed multiple drugs at the same time. Due to complicated interactions between different drugs, side effects can become more prominent.

3. Some research suggests that neurotransmitters become naturally imbalanced as people age, increasing the brain’s sensitivity to drugs that have activity in the central nervous system.

**Opiates**

Opiates, also called narcotics, are a class of highly effective pain medication that act on the opioid receptor in the brain. Opiates can cause delirium and the more chronic cognitive changes seen in dementia.

Like benzodiazepines, chronic use of opiates has been linked to increased tolerance (in which case the patient requires increasing amounts of the medication to achieve the same therapeutic result), and abrupt cessation causes a withdrawal syndrome that includes agitation, sweating, chills, diarrhea, and severe discomfort.

*View* our list of 15 opiates that cause cognitive impairment in the full version of this article.

**Tricyclic antidepressants**

Tricyclic antidepressants (TCAs) are an older class of antidepressants that are known to cause cognitive impairment. Although TCAs are still used to treat severe depression in some patients, they are also used to treat pain syndromes, especially pain caused by a neuropathy (damaged or diseased nerves). The TCAs with the greatest anticholinergic properties are the ones most strongly linked to cognitive impairment, but even TCAs with weak anticholinergic effects can cause problems with thinking, possibly via other mechanisms.
Selective-serotonin release inhibitors (SSRIs), a newer and more commonly prescribed generation of antidepressants, have not been linked with cognitive impairment. Severe depression itself can be associated with difficulty thinking and concentrating, as well as with more serious consequences. Thus, if you think that your antidepressant may be causing problems with your thinking, it is very important that you consult with your physician to determine if you should stop taking the drug.

View our list of tricyclic antidepressants that cause cognitive impairment in the full version of this article.

Others

A few other notable classes of drugs to mention include corticosteroids, fluoroquinolone antibiotics, H2-receptor antagonists, anticonvulsants and drugs used to treat Parkinson’s disease.

Corticosteroids are a type of hormone commonly used to treat severe asthma attacks and to suppress the immune system including the treatment of so-called auto-inmmune diseases such as rheumatoid arthritis, but an excess can cause agitation and even actual psychoses.

Fluoroquinolone antibiotics are increasingly used to treat a variety of infections and have been linked with delirium in elderly patients.

H2-receptor antagonists are an older class of drug used to decrease stomach acid production. They, too, can cause delirium in elderly patients.

There are many different classes of anticonvulsants, which act on brain through different mechanisms. Nearly all of them have been associated with drowsiness and difficulty thinking, some more commonly than others.

View our list of 9 corticosteroids, 12 fluoroquinolone antibiotics,
What You Can Do

Because cognitive impairment caused by drugs is so frequently overlooked, it is important that when symptoms of confusion, altered concentration or difficulty thinking occur that you and your physician review any medications you are taking to determine if any of them might be the cause.

Fortunately, if the cause is a medication, your symptoms should go away or become less severe after stopping the drug, even if it takes weeks or months.

Box 2. The Difference Between Delirium and Dementia

Delirium is a syndrome of changes in attention perception (i.e., vision and hearing), and thinking that is commonly seen in the hospital setting or during an acute illness. Delirium usually starts abruptly, over the course of hours or a few days, and has a fluctuating course. There are many causes of delirium, but the most common are acute medical illnesses (such as a serious infection) and medications.

Older individuals are the most susceptible to delirium, which can result from problems as simple as constipation or urinary blockage in these patients. Almost all cases of delirium improve when the cause is treated or removed.

Dementia, on the other hand, is a chronic alteration in thinking that beings more insidiously, sometimes progressing over a course of months or years. It is more common the older you get. However, this does not mean that dementia is simply due to "old
Alzheimer’s disease is the most common cause of dementia, but other neurologic conditions, including strokes, can cause it. So can drugs which can cause or worsen dementia. Unlike most of the medical causes for dementia, which are irreversible, stopping a drug that has caused dementia can lead to improvement.
How a Root Canal Can Affect Your Health and make mental decline

October 02, 2012 | 330,815 views
Spread the Word to By Hal A. Huggins, DDS, MS
"You need a root canal!" "Why?"

Do you really "need" a root canal? What are the conventional reasons for performing root canals over the past century?

- Pain
- Deep decay that has invaded the nerve chamber
- Trauma (as in getting hit in the mouth with a baseball bat), and
- Discomfort of unknown reason

What, exactly, are you getting for your money?

As recently as 1906, Mayo Clinic in conjunction with Weston Price DDS, MS as head of research for the dental association of that time, announced that root canals were a haven for disease-producing bacteria. Six PhDs working with Dr. Price for decades, and a team of microbiologists from Mayo Clinic identified these bacteria.

Dr. Price implanted root canal fragments under the skin of the belly of 60,000 rabbits. Results unequivocally proved that diseases of the humans, traveling in the root canaled teeth, could produce the same disease in the rabbit in a matter of weeks. Heart attacks could be transferred 100 percent percent of the time – implicating root canals as one of the primary causes of heart disease.

**Root Canals are Breeding Grounds for Bacterial Toxins**

Does it surprise you that dentistry has been able to keep this secret for over a century?

Consider the liability. Ask your dentist about this, and watch him/her run, hide, and "fire you as a patient." Fear of license revocation prevents dentists from disclosing what they have been told does not exist. Dr. Price and Mayo identified dozens of diseases related to bacterial toxins created by bacteria in root canals. If one percent of the people with root canals and subsequent diseases sued their dentist, all the money in the world would be in the hands of lawyers.

Dentists are kept in the dark by conflicting reports by their own associations. Most dental associations say root canals are 97 percent successful, while not defining the term 'successful.' The American Association of Endodontists (AAE) says only 90
percent are successful. Back in 1925, Coolidge said 95 percent were successful. The Department of Health and Human Services said in 1984 that there is no way to evaluate the success of a root canal. Burket published that only 42 percent of root canaled teeth were "mechanically" correct in filling the canals. That was in the US. European journals on the topic reported about 30 percent.

Haden published that 87 percent of 1,500 teeth he studied microscopically were contaminated with bacteria. And Okabe published that 72.1 percent of the patients with root canals had bacteremia (i.e. bacteria in the blood that were identical to those found in the root canal tooth).

Most dentists will tell you that a front tooth has a single canal. Dr. Price showed that that same front tooth can have as many as 75 auxiliary canals running from the pulp chamber to the outside of the tooth. Clean and fill 75 canals? Yeah, sure. Especially if you're not even aware they exist.

**How Dental Practices Can Alter Your DNA and Promote Disease**

So, how can anyone be sure who's telling the truth?

DNA testing is currently recognized as being one of the most dependable methods of identifying anything that is living. Or dead, for that matter. Dinosaurs have had their DNA tested. That template is there, dead or alive.

Which brings up my primary concern. Toxins from these bacteria together with mercury from dental amalgam have the ability to alter your DNA. Deletions, substitutions, additions – lots of things can happen to your DNA molecules, or your RNA, which is the "carbon copy" of the original DNA. It's the RNA that actually does the work of creating proteins that make up your body. Mess up the RNA, and you're setting yourself up for disease. But, if you alter the DNA of a "germ cell," that is sperm or egg, and your children – and grandchildren, as long as your family line continues to reproduce – will be forever altered. Alterations of this DNA are permanent. They cannot be reversed.

With DNA alterations readily available due to mercury and bacterial toxins, we now have the opportunity to create many new diseases, and/or birth defects. There are many popular diseases today that were not known a thousand years ago – or even 200 years ago. Sickle cell anemia, for example, was not around until 1910. Multiple sclerosis wasn't known until (circa) 1832. Leukemia came close on its heels. Diabetes got a strong foot hold just after 1900. Heart disease was then becoming more prevalent – up to nearly 10 percent of the deaths in 1900. Today, it is given credit for being the number one killer! Multiple sclerosis went from an average 8,800 cases per year from 1970 through 1975, then suddenly skyrocketed to 123,000 in 1976.

Are there reasons for these dramatic increases?
Yes. Unfortunately, dental procedures can be implicated in all of these increases.

Are all root canals infected with bacteria? Today, non-invasive testing of the fluid around a root canal tooth by DNA can tell if pathological bacteria are growing along its root. After extraction of the tooth, pathological bacteria can be identified 100 percent of the time.

But, wait! There’s more... It was recently discovered that the bacteria are not confined to the tooth. We tested root fragments and found many bacteria, which is not too surprising. Then we tested the periodontal ligament – the attachment between tooth and bone – and found even more bacteria. There is no way to get to this area to sterilize it. An even more surprising discovery was that the blood surrounding the tooth also contained bacteria – as much as half an inch around the tooth is highly contaminated.

Unfortunately, surgical removal of the offending root canal tooth is not just a matter of yanking it out. There is a protocol that a few brave dentists – who defy the dictates of the dental associations – can perform to protect their patients and rid them of potential disease-producing condominiums called root canals.

What Kind of Diseases are Associated with Root Canals?

We have identified 28 bacteria that the literature reports are related to heart diseases, including heart attack, endocarditis, and heart valve infection. Neurological diseases are in second place with 23 bacteria reported to be causative or contributing factors. Liver function, kidney, breast cancer – the list becomes alarming, so it is time to inform the public what dentists cannot tell you out of fear of retribution from injured patients and their own association. The Dental Association would move from being one of the most respected professions to the least respected...

How many people are affected, and how?

While I cannot list every potential in this article, our figures indicate that over 90 percent of the patients seeking help for dental related problems suffer from chronic fatigue, and that’s just one example. How tiring can bacteria be? One group certainly can contribute. They are called "porins." Few doctors and even fewer humans have ever heard of porins. The word comes from "pores." These bacteria drill holes in red blood cells – pores – that allow hemoglobin to escape into the surrounding blood where the bacteria are lurking to suck up the iron. These bacteria, the porin producers, have a very high appetite for iron, and hemoglobin furnishes a never ending supply.

Once a red blood cell has a few pores punched in it – a sleeve is inserted as well, such that the red blood cell cannot heal – the red cell bleeds to death. Now the liver has to process all that hemoglobin scrap relieved of its iron, and calm the body from irritations due to the red cell contents being where they do not belong.
Another new kid on the block that may be dentally related is meningitis, which is a growing epidemic. When reading an article about the need for another meningitis vaccine, I recalled seeing meningitis listed as an effect of a few different bacteria that thrive in root canals and cavitations. Capnocytophaga ochracea; Gemella morbillorum; Klebsiella oxytoca; Neisseria meningitidis; Pseudomonas aeruginosa, and a few more.

For explanation, cavitations and root canal bacteria are grouped together in our testing of over 400 samples, as both are eliminated simultaneously. Cavitations are bony holes almost always (4,999 out of a measured 5,000) left after extraction of wisdom teeth. The sockets rarely heal and become lined with pathogenic anaerobic bacteria. This newspaper said that we need to vaccinate teenagers because meningitis is a potentially fatal disease that comes on fast. With these bacteria occurring in the sockets of wisdom teeth, and wisdom tooth extractions being popular with teens, is there a connection?

Here, you have a choice: to vaccinate or prevent.

Cleaning out a cavitation is a tricky procedure, and in many states an oral surgeon who cleans one out will lose his license, for cavitations "do not exist." Yeah. Try dropping into one that is two centimeters big and tell me it doesn't exist! General dentists can do it without as much threat.

Another new one is the human papilloma virus (HPV). We just identified two bacteria associated with HPV in dental implants.

**Beware: Antibiotics are NOT the Answer**

Why not just give everyone lots of antibiotics? Because most antibiotics are what are called "bactericidal," meaning they explode the bacteria, causing even more grief for your immune system. Instead of having one bacterium to destroy, now your system has a hundred little pieces called "endotoxins" to dispose of. Besides, there are other side effects to the use of massive antibiotics, such as the destruction of beneficial gut bacteria, which also dampens your immune system.

It has been over 100 years since Mayo and Dr. Price announced their findings, but you do not have to wait another 100 years to protect yourself, your RNA, or the future DNA of the human race. This is a serious accusation. One that is very logical and provable by today's DNA science. Scientists know it is possible. Now you do too.

*Over the Counter Brain Damage: Common ‘OTC Medicines’ that Cause Long Term Cognitive Impairment*
Drugs commonly taken for a variety of common medical conditions negatively affect your brain, causing long term cognitive impairment. These drugs, called anticholinergics, block acetylcholine, a nervous system neurotransmitter.

They include such common over-the-counter brands as Benadryl, Dramamine, Excedrin PM, Nytol, Sominex, Tylenol PM, and Unisom.

Other anticholinergic drugs, such as Paxil, Detrol, Demerol and Elavil are available only by prescription.

Physorg reports:

"Researchers ... conducted a six-year observational study, evaluating 1,652 Indianapolis area African-Americans over the age of 70 who had normal cognitive function when the study began ... ‘[T]aking one anticholinergic significantly increased an individual’s risk of developing mild cognitive impairment and taking two of these drugs doubled this risk.’"

From Dr. Mercola:

Many view over-the-counter (OTC) drugs as safe because they don’t require a prescription. Well nothing could be further from the truth.

In fact, many OTC drugs were previously carefully monitored prescription drugs. Many people are not aware that while I was in college in the 1970s, I worked as a full time pharmacy apprentice and helped sell drugs to patients all day long.
Motrin was the first non-salicylate prescription NSAID. Now it is a popular OTC ibuprofen option. Similarly, anti-ulcer drugs like Tagamet, Zantec, and Prilosec used to be carefully controlled. Now they can all be easily purchased in a smaller “OTC strength” that nearly doubles the number of pills required to equal the prescription dose.

Just because a drug is available without a prescription does not make it any less dangerous. It is still a chemical, which in no way, shape, or form treats the cause of the problem and can lead to complications that can seriously injure, if not kill, you or someone you love.

So this is clearly important information that can help you or someone you love reduce your risk of dementia as you get older. Based on the findings of this study, I would strongly recommend that seniors in particular avoid all anticholinergic drugs, like Benadryl (generic is diphenhydramine) which is a pervasive and commonly used in virtually all of the OTC sleeping pills.

Researchers will continue studying the matter to see whether anticholinergic-induced cognitive impairment can be reversed, but don’t hold your breath. Avoidance is really the best solution.

What are Anticholinergic Drugs?

Anticholinergic drugs block a nervous system neurotransmitter called acetylcholine. Those suffering from Alzheimer’s disease typically have a marked shortage of acetylcholine.

Anticholinergic drugs are available both over-the-counter and by prescription, as medications used for a variety of symptoms can have this effect. Examples include night-time pain relievers, antihistamines, and other sleep aids, such as:

- Excedrin PM
- Tylenol PM
- Nytol
- Sominex
- Unisom
- Benadryl
- Dramamine

Prescription drugs with anticholinergic effects include certain antidepressants, medications to control
incontinence, and certain narcotic pain relievers.
Examples of prescription meds in these categories include:
Paxil
Detrol
Demerol
Elavil

A Special Note for Aspartame ‘Reactors’

Many of the drugs listed here, as well as a long list of additional ones, contain diphenhydramine. As an important side note, you need to beware that chewable tablets and rapidly disintegrating tablets that contain diphenhydramine may be sweetened with aspartame.
If you have the genetic disease phenylketonuria (PKU), you must be particularly careful to avoid these types of drugs and all other types of aspartame-sweetened foods and beverages in order to prevent mental retardation.
But many other people also suffer detrimental health effects from aspartame, so you should know that this is yet another potential source of this toxic sweetener.

Anticholinergic Drugs Increases Dementia in the Elderly

I’ve previously written about the health dangers of many of these individual drugs. Paxil, for example, is an addictive antidepressant that is well known to increase the risk of suicide in children and teens. It is also known to increase violent behavior.
Benadryl and Sominex have previously been found to cause hallucinations in the elderly, and a number of the drugs on the list also promote dental decay.
The results of this study indicate that drugs with anticholinergic effects may be yet another piece of the puzzle that might explain the sharp rise in dementia and cognitive decline.
According to the University of Michigan, dementia strikes about 50 percent of people who reach the age of 85. Of those, about 60 percent go on to develop Alzheimer’s disease.
In this study, the researchers tracked the intake of anticholinergic drugs and monitored the cognitive abilities of 1,652 African-American seniors, aged 70 and older, for six years. All of the
participants had normal cognitive function at the outset of the study.
Fifty-three percent of the participants used a ‘possible anticholinergic,’ and 11 percent used a ‘definitive anticholinergic’ drug.
They found that those who took drugs classified as ‘definite anticholinergics’ had a four times higher incidence of cognitive impairment.
In those who were not carriers of the specific gene, APOE ε4 allele, the risk was over seven times higher. (The APOE ε4 gene is known to influence many neurological diseases, and is considered a high risk factor for Alzheimer’s.)
Taking two of these drugs further increased the risk of cognitive impairment.
PhysOrg reports:
“Simply put, we have confirmed that anticholinergics, something as seemingly benign as a medication for inability to get a good night’s sleep or for motion sickness, can cause or worsen cognitive impairment, specifically long-term mild cognitive impairment which involves gradual memory loss.
As a geriatrician I tell my Wishard Healthy Aging Brain Center patients not to take these drugs and I encourage all older adults to talk with their physicians about each and every one of the medications they take,” said Malaz Boustani, M.D., IU School of Medicine associate professor of medicine, Regenstrief Institute investigator and IU Center for Aging Research center scientist.”
Even More Reasons to Ditch the Sleep Meds
In 2008, Americans filled more than 56 million prescriptions for sleeping pills and spent more than $600 million on over-the-counter sleep aids. But anticholinergic sleep medications in particular may be causing far more harm than good, especially long term, without providing any benefit at all.
In a recent article, CBC News reported that the U.S. Food and Drug Administration has had data for 15 years which shows that over-the-counter sleep aids like Tylenol PM and Excedrin PM do not offer any significant benefit to patients.
There’s no explanation for why the FDA took 15 years to evaluate the industry’s research, but upon final analysis “the data suggests the combination products are statistically better than a placebo but
not by much,” CBC News reported.

I guess it can be chalked up as yet another vibrant example of how industry research frequently amounts to little more than corporate wishes and good PR fodder.

Another analysis of sleeping pill studies from 2007 (financed by the National Institutes of Health) found that sleeping pills like Ambien, Lunesta, and Sonata reduced the average time to go to sleep by just under 13 minutes compared with fake pills — hardly a major improvement.

Yet, the participants believed they had slept longer, by up to one hour, when taking the pills.

This may actually be a sign of a condition called anterograde amnesia, which causes trouble with forming memories. When people wake up after taking sleeping pills, they may, in fact, simply forget that they had been unable to sleep!

You would be far better off putting your money toward authentic solutions to help you sleep than on sleeping pills, as it’s now clear that they do next to nothing to help you sleep — in fact, they may actually make it more difficult for you to get a good night’s rest naturally — and may significantly increase your risk of dementia.

**Sleeping Pills are NOT a Safe Solution for Sleepless Nights**

Please understand that resorting to sleep medications is risky business, and that these pills do not address the underlying reasons why you’re having trouble sleeping in the first place.

In addition to the long-term problems already discussed, there are other serious, not to mention bizarre, risks involved.

For starters, these pills are notorious for being addictive, which means that once you want to stop taking them, you’ll likely suffer withdrawal symptoms that could be worse than your initial insomnia.

Some, such as Ambien, may also become less effective when taken for longer than two weeks, which means you may find yourself needing ever higher dosages.

Ambien may also make you want to eat while you’re asleep — and I don’t mean sneaking down to grab a piece of fruit. The sleep eating can include bizarre foods such as buttered cigarettes, salt sandwiches, and raw bacon.

Sleeping pills, and again Ambien in particular, are also known to increase your risk of getting into a
traffic accident. Ambien actually ranks among the top 10 drugs found in the bloodstreams of impaired drivers, according to some state toxicology labs.

Among the elderly, using sleeping pills may increase the risk of nighttime falls and injuries, and anyone who takes them may find they wake up feeling drowsy if the effects of the drug have not worn off yet.

You’re far better of finding safe and natural solutions that will actually address the underlying causes of your sleepless nights instead of just cover up the resulting symptoms.

How to Get a Good Night’s Sleep Without Dangerous Drugs

If you are having trouble sleeping, please do not ignore the problem or simply wait for it to go away. Quality sleep just as important as your need for food, water, and pure air — and there are very simple methods to help you get yours.

Please read my comprehensive sleep guide 33 Secret’s to a Good Night’s Sleep for my full set of recommendations, but to start, make certain you are exercising regularly.

A Stanford University Medical School study found that after 16 weeks in a moderate-intensity exercise program, subjects were able to fall asleep about 15 minutes earlier and sleep about 45 minutes longer at night. However, don’t exercise too close to bedtime or it may keep you awake. Stress is another major reason why people have trouble sleeping, which is why I suggest you start to wind down from your day at least an hour before your bedtime (but preferably two or more).
136 Drugs That Can Cause Cognitive Impairment

http://www.worstpills.org/includes/page.cfm?op_id=458

/Home/Alzheimer's Treatments/Medicines to Avoid for Alzheimer's Patients

Drug-induced dementia and delirium are commonly misattributed to underlying medical illness or merely to "old age." But patients (and even their doctors!) might not know that by stopping or modifying the dosage of numerous, frequently prescribed drugs, most patients can be restored to a pre-drug state of mental function.

Fortunately, the drug safety experts at WorstPills.org have identified 136 drugs from published studies that can cause memory loss, confusion and other forms of cognitive impairment in older adults.

PART 1

DRUG-INDUCED COGNITIVE IMPAIRMENT: ANTICHOLINERGIC EFFECTS

As you age, some degree of difficulty recalling memories is considered normal. However, more pronounced memory loss could indicate a serious problem, such as dementia (which includes Alzheimer’s disease). That’s why the occurrence of memory loss or other forms of cognitive impairment — such as difficulty with attention, language or other brain function — can be so alarming. Although most types of dementia cannot be reversed, there are several form that can be undone.

Importantly, a wide array of commonly prescribed medications, especially certain antidepressants and pain medications, can cause cognitive impairment which may be reversed by stopping the drug. Unfortunately, this reversible cause is often over-looked. But new evidence is emerging that shines additional light onto this important drug-induced adverse event.
While medications are known to cause many unwanted side, many doctors fail to identify the drug as the culprit. In the elderly, adverse effects of medications are generally more pronounced. This is due to a host of factors, including increased sensitivity to a drug’s effects, slower rates of elimination from the body and consumption of multiple drugs at a time. A well-known side effect of many drugs involves their effects (specifically interference) with one of the chemicals responsible for transmitting signals between nerve cells in our bodies, called "acetylcholine."

This "neurotransmitter" is vital for diverse array of nervous system functions from muscle movement to sweating to memory, so it is no surprise that interfere with it, or drugs with "anticholinergic" properties, can cause a host of symptoms (see Box).

**Anticholinergic effects confused with early signs of dementia**

Drugs with anticholinergic properties can cause delirium, but longer term effects, which may be mistaken as the early signs of dementia, have not been studied as well for this class of drugs. However, a recently published study specifically looked at this problem. The authors created a tool in which they rated many medications according to their anticholinergic properties on a scale of zero (no anticholinergic properties) to three (extremely anticholinergic; see Table). After adjusting for other factors that may account for cognitive decline, the authors noted a decrease on two measures of cognitive performance in men aged 65 and older. For each point on their scale, patients had a decrease of 0.8-percent on a cognitive test and 1.1-percent on a measure of routine activities one can perform for themselves (another measure of intact cognition).

Unfortunately, cognitive decline that is due to anticholinergic medications is often overlooked because most medications listed in the accompanying Table would not necessarily, alone, account for a striking decline in memory or other cognitive function. But, the cumulative impact of consuming multiple medications with anticholinergic effects may be significant, resulting in unnecessary distress among patients, families and physicians alike.

While these findings are only preliminary, they permit physicians and patients to semi-quantitatively account for the anticholinergic effects of a patient’s medications when the patient complains of memory and other cognitive problems.

If you are suffering from a troubling decline in one of your cognitive functions, the first
thing you and your physician should do is take a look at your medication list. The answer

### Table. Anticholinergic properties

Drugs with a score of 0 are not shown; a score of 3 indicates the strongest side effects.

<table>
<thead>
<tr>
<th>Drug (BRAND NAME)</th>
<th>Anticholinergic Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alprazolam (XANAX)*</td>
<td>1</td>
</tr>
<tr>
<td>Amitriptyline (ELAVIL)*</td>
<td>3</td>
</tr>
<tr>
<td>Atenolol (TENORMIN)</td>
<td>1</td>
</tr>
<tr>
<td>Atropine*</td>
<td>3</td>
</tr>
<tr>
<td>Baclofen (LIORESAL)</td>
<td>2</td>
</tr>
<tr>
<td>Belladonna</td>
<td>3</td>
</tr>
<tr>
<td>Benazepril (ETHEX, LOTENSIN)**</td>
<td>1</td>
</tr>
<tr>
<td>Betaxolol (KERLONE)</td>
<td>1</td>
</tr>
<tr>
<td>Bupropion (WELLBUTRIN)**</td>
<td>1</td>
</tr>
<tr>
<td>Carbamazepine (CARBATROL, TEGRETOL)</td>
<td>1</td>
</tr>
<tr>
<td>Carbidopa (SINEMET)</td>
<td>1</td>
</tr>
<tr>
<td>Cetirizine (ZYRTEC)**</td>
<td>2</td>
</tr>
<tr>
<td>Chlordiazepoxide (LIBRIUM)*</td>
<td>1</td>
</tr>
</tbody>
</table>
Chlorpheniramine (ALERGINE, CHLOR-TRIMETON): 3
Chlorpromazine (THORAZINE)**: 3
Codeine: 1
Cyclobenzaprine (FLEXERIL)*: 1
Desipramine (NORPRAMIN): 2
Dextromethorphan (BENYLIN, DELSYM)*: 1
Diazepam (VALIUM)*: 1
Diphenhydramine (BENADRYL, DYTAN SUSPENSION, DYTAN-D SUSPENSION, SOMINEX FORMULA): 3
Doxepin (SINEQUAN)** : 3
Fexofenadine (ALLEGRA)** : 2
Fluoxetine (PROZAC)**: 1
Guaifenesin (MUCINEX, ROBITUSSIN)*: 1
Homatropine (ISOPTO HOMATROPINE) : 3
Hydrocodone: 2
Imipramine (TOFRANIL, TOFRANIL PM)** : 3
Ketorolac (TORADOL)*: 1
Loperamide (IMODIUM)** : 1
Loratadine (CLARITIN)**: 1
Metoclopramide (REGLAN)** : 3
Methadone (DOLOPHINE, METHADOSE)**: 2
Methocarbamol (ROBAXIN)*: 1
Metoprolol (LOPRESSOR, TOPROL XL) : 1
Morphine (AVINZA, KADIAN, MS CONTIN): 1
Nefazodone (SERZONE)*: 1
Nortriptyline (AVENTYL, PAMELOR) : 3
Olanzapine (ZYPREXA)**: 1
Oxycodone (OXYCONTIN)**: 1
Paroxetine (PAXIL, PEXEVA)** : 2
Perphenazine (TRILAFON): 2
Phenobarbital (LUMINAL, SOLFOTON)**: 1
Prochlorperazine (COMPAZINE)**: 2
Propantheline (PRO-BANTHINE) : 2
Propoxyphene (DARVON)*: 2
Quetiapine (SEROQUEL)** : 2
Ranitidine (ZANTAC): 2
Risperidone (RISPERDAL)** : 1
Scopolamine (TRANSDERM-SCOP) : 3
Sertraline (ZOLOFT)** : 1
Thioridazine (MELLARIL)* : 3
Tolterodine (DETROL, DETROL LA)**: 3
Tramadol (ULTRAM)*: 2
Trandolapril (MAVIK)** : 1
Trazodone (DESYREL)** : 1
Triazolam (HALCION)* : 1
Trihexyphenidyl (ARTANE)* : 3
Venlafaxine (EFFEXOR, EFFEXOR XR)**: 1

* Do Not Use

** Limited Use

PART 2

DRUG-INDUCED COGNITIVE IMPAIRMENT: DELIRIUM AND DEMENTIA

As people age, they become more susceptible to delirium and dementia caused by drugs. This is known as drug-induced cognitive impairment, and it is an important syndrome to recognize, because in almost all cases it can be reversed or returned to the pre-drug state (in the case of people whose cognitive impairment was worsened by drugs) by stopping the offending drug.

Both in the hospital and office settings, drug-induced cognitive impairment is often overlooked and attributed to an underlying medical illness or merely to "old age," when it is actually a side-effect of a drug. In many cases, the reason for prescribing the culprit drug is questionable, or the cognitive impairment is related to taking multiple drugs at once.

As discussed in Part I of this series, there are many drugs that cause delirium and dementia (see Box 2 for definitions of delirium and dementia) through their anticholinergic effects. Most of these drugs have important functions other than blocking
the neurotransmitter acetylcholine. In addition, there are several other classes of drugs can cause cognitive impairment in susceptible individuals.

**Drugs that can cause cognitive impairment**

Drug-induced cognitive impairment is most commonly linked to benzodiazepines, opiates, tricyclic antidepressants and anticonvulsants (drugs used to treat and prevent seizures). These, and a few other drugs, are listed in the Table and described below. This is not an exhaustive list, but includes many of the most commonly implicated drugs and ones for which we have the most evidence. Some of the drugs discussed and listed below were also mentioned in Part 1 because they had anticholinergic effects.

**Benzodiazepines**

Benzodiazepines — which include tranquillizers and sleeping pills — have a wide range of effects on the central nervous system. They are commonly used to treat anxiety in the short-term, and also to sedate critically ill patients or those undergoing surgery.

People who take benzodiazepines chronically for anxiety, which is not recommended, can also develop more chronic cognitive impairment. Furthermore, because addiction to benzodiazepines is common, stopping them abruptly can result in a withdrawal syndrome similar to what is seen with alcohol withdrawal, including sweating, agitation, confusion, hallucinations and even seizures.

Patients on benzodiazepines are at greater risk for developing delirium while hospitalized, and when benzodiazepines are used to treat agitation associated with delirium from other causes, they often make it worse.

Sedatives that have similar central nervous system effects as benzodiazepines, such as the commonly used sleep agents zolpidem (AMBIEN), zaleplon (SONATA) and eszopiclone (LUNESTA) can also induce delirium. As with benzodiazepines, stopping these agents abruptly after chronic use can result in a withdrawal syndrome.

**Box 1. Three Reasons Older People Are More Susceptible to Drug-Induced Delirium and Dementia**

1. The body’s ability to clear drugs decreases with age, often because of a normal age-
related decrease in kidney and liver function. This results in a greater accumulation of drugs in the body.

2. Older patients are often prescribed multiple drugs at the same time. Due to complicated interactions between different drugs, side effects can become more prominent.

3. Some research suggests that neurotransmitters become naturally imbalanced as people age, increasing the brain’s sensitivity to drugs that have activity in the central nervous system.

Opiates

Opiates, also called narcotics, are a class of highly effective pain medication that act on the opioid receptor in the brain. Opiates can cause delirium and the more chronic cognitive changes seen in dementia.

Like benzodiazepines, chronic use of opiates has been linked to increased tolerance (in which case the patient requires increasing amounts of the medication to achieve the same therapeutic result), and abrupt cessation causes a withdrawal syndrome that includes agitation, sweating, chills, diarrhea, and severe discomfort.

Tricyclic antidepressants

Tricyclic antidepressants (TCAs) are an older class of antidepressants that are known to cause cognitive impairment. Although TCAs are still used to treat severe depression in some patients, they are also used to treat pain syndromes, especially pain caused by a neuropathy (damaged or diseased nerves). The TCAs with the greatest anticholinergic properties are the ones most strongly linked to cognitive impairment, but even TCAs with weak anticholinergic effects can cause problems with thinking, possibly via other mechanisms.

Selective-serotonin release inhibitors (SSRIs), a newer and more commonly prescribed generation of antidepressants, have not been linked with cognitive impairment. Severe depression itself can be associated with difficulty thinking and concentrating, as well as
with more serious consequences. Thus, if you think that your antidepressant may be causing problems with your thinking, it is very important that you consult with your physician to determine if you should stop taking the drug.

**Others**

A few other notable classes of drugs to mention include corticosteroids, fluoroquinolone antibiotics, H2-receptor antagonists, anticonvulsants and drugs used to treat Parkinson's disease. Corticosteroids are a type of hormone commonly used to treat severe asthma attacks and to suppress the immune system including the treatment of so-called autoimmune diseases such as rheumatoid arthritis, but an excess can cause agitation and even actual psychoses. Fluoroquinolone antibiotics are increasingly used to treat a variety of infections and have been linked with delirium in elderly patients.

H2-receptor antagonists are an older class of drug used to decrease stomach acid production. They, too, can cause delirium in elderly patients. There are many different classes of anticonvulsants, which act on brain through different mechanisms. Nearly all of them have been associated with drowsiness and difficulty thinking, some more commonly than others.

**What You Can Do**

Because cognitive impairment caused by drugs is so frequently overlooked, it is important that when symptoms of confusion, altered concentration or difficulty thinking occur that you and your physician review any medications you are taking to determine if any of them might be the cause.

This is in accordance with our Rule # 7 for safer drug use: "Assume that any new symptom you develop after starting a new drug may be caused by the drug."

Fortunately, if the cause is a medication, your symptoms should go away or become less severe after stopping the drug, even if it takes weeks or months.

______

**Box 2. The Difference Between Delirium and Dementia**
Delirium is a syndrome of changes in attention perception (i.e., vision and hearing), and thinking that is commonly seen in the hospital setting or during an acute illness. Delirium usually starts abruptly, over the course of hours or a few days, and has a fluctuating course. There are many causes of delirium, but the most common are acute medical illnesses (such as a serious infection) and medications.

Older individuals are the most susceptible to delirium, which can result from problems as simple as constipation or urinary blockage in these patients. Almost all cases of delirium improve when the cause is treated or removed.

Dementia, on the other hand, is a chronic alteration in thinking that begins more insidiously, sometimes progressing over a course of months or years. It is more common the older you get. However, this does not mean that dementia is simply due to "old age."

Alzheimer’s disease is the most common cause of dementia, but other neurologic conditions, including strokes, can cause it. So can drugs which can cause or worsen dementia. Unlike most of the medical causes for dementia, which are irreversible, stopping a drug that has caused dementia can lead to improvement.

Partial List of Drugs Associated with Drug-Induced Cognitive Impairment

Anticonvulsants

- Carbamezepine (CARBATROL, TEGRETOL)
- Clonazepam (KLONOPIN)
- Ethosuximide (ZARONTIN)
- Felbamate (FELBATOL)
- Fosphenytoin (CEREBYX)
- Gabapentin (NEURONTIN)**
- Lamotrigine (LAMICTAL)
- Levetiracetam (KEPPRA)
- Lorazepam (ATIVAN)*
- Oxcarbazepine (TRILEPTAL)
- Phenytoin (DILANTIN)
- Pregabalin (LYRICA)*
- Primidone (MYSOLINE)
- Tiagabine (GABITRIL)
- Topirimate (TOPAMAX)
- Valproic acid (DEPAKENE)
- Zonisamide (ZONEGRAN)

Antihistamines (these are OTC meds, and too numerous to list)

- Azelastine (ASTELIN)*
- Chlorpheniramine injection
- Cyproheptadine (PERIACTIN)
- Desloratadine (CLARINEX)*
- Diphenhydramine injection
- Hydroxyzine (ATARAX, HY-PAM, VISTARIL)
- Olopatadine (PATANOL)

Benzodiazepines

- Amitriptyline and chlordiazepoxide (LIMBITROL)*
- Chlordiazepoxide and clidinium (LIBRAX)**
- Clonazepam (KLONOPIN)
- Clorazepate (TRANXENE)*
- Estazolam (PROSOM)*
- Flurazepam (DALMANE)*
- Halazepam (PAXIPAM)*
- Lorazepam (ATIVAN)*
- Oxazepam (SERAX)**
- Prazepam (CENTRAX)*
- Quazepam (DORAL)*
- Temazepam (RESTORIL)*

Benzodiazepine-like Sedatives

- Eszopiclone (LUNESTA)
- Zaleplon (SONATA)
- Zolpidem (AMBIEN)

Corticosteroids

- Betamethasone (ALPHATREX, DIPROLENE, DIPROSTONE)
- Cortisone (CORTONE)
- Dexamethasone (DECADRON, HEXADROL, MYMETHASONE)
- Fludrocortisone (FLORINEF)
- Hydrocortisone (ALA-CORT, HI-COR, HYTONE, NEACLEAR LIQUID OXYGEN SCAR ADVANTAGE, PENECORT, SYNACORT, CORTEF, HYDROCORTONE)
- Methylprednisolone (MEDROL)
- Prednisolone (PRELONE)
- Prednisone (DELTASONE)
- Triamcinolone (ARISTOCORT, KENALOG, TRIACET, TRIDERM)

Drugs with Anticholinergic Properties
- See Part 1

Drugs Used to Treat Parkinson’s Disease
- Benztropine (COGENTIN)*
- Bromocriptine (PARLODEL)**
- Entacapone (COMTAN)**
- Entacapone with levodopa and carbidopa (STALEVO)**
- Selegiline/deprenyl [oral] (ELDEPRYL)**
- Tolcapone (TASMAR)*

Fluoroquinolone Antibiotics
- Ciprofloxacin (CILOXAN, CIPRO)**
- Gatifloxacin (TEQUIN)*
- Gemifloxacin (FACTIVE)*
- Levofloxacin (LEVAQUIN)**
- Lomefloxacin (MAXAQUIN)**
- Moxifloxacin (AVELOX)*
- Moxifloxacin [eye drops] (VIGAMOX)
- Norfloxacin (CHIBROXIN, NOROXIN)**
- Ofloxacin (FLOXIN)**
- Ofloxacin [eye] (OCUFLOX)
- Sparfloxacin (ZAGAM)*
- Trovafloxacin (TROVAN)*

H2-antagonists (Typically associated with delirium only)
- Cimetidine (TAGAMET)
- Famotidine (PEPCID)
- Nizatidine (AXID)

Opiates (Typically associated with delirium only)
- Acetaminophen and codeine (APAP, TYLENOL WITH CODEINE)
- Acetaminophen and hydrocodone (BANCAP-HC, LORTAB, VICODIN)
- Acetaminophen and oxycodone (PERCOCET, ROXICET, TYLOX)**
- Aspirin and oxycodone (PERCODAN)**
- Butalbital, acetaminophen and caffeine (ESGIC PLUS, FIORICET)*
- Butalbital, caffeine and aspirin (FIORINAL)*
- Butalbital, caffeine, aspirin and codeine (FIORINAL WITH CODEINE)*
- Butorphanol (STADOL)*
- Fentanyl [patch] (DURAGESIC)**
- Hydrocodone and ibuprofen (VICOPROFEN)
- Hydromorphone (DILAUDID)
- Meperidine (DEMEROL)
- Pentazocine (TALWIN)*
- Pentazocine and naloxone (TALWIN-NX)*
- Tramadol and acetaminophen (ULTRACET)*

Tricyclic Antidepressants
- Amitriptyline and chlordiazepoxide (LIMBITROL)*
- Amitriptyline and perphenazine (TRIAVIL)*
- Amoxapine (ASENDIN)**

Other
- Digoxin (DIGITEK, LANOXICAPS, LANOXIN)
- Lithium (ESKALITH, LITHOBID, LITHONATE)**
<table>
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<th>Type of drug</th>
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<td>Antihistamine</td>
<td>Hydroxyzine, diphenhydramine, OTC cold/allergy remedies</td>
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<td>Antispasmodic</td>
<td>Alverine, hyoscyamine</td>
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<tr>
<td>Antidepressants</td>
<td>Fluoxetine, paroxetine, amitriptyline</td>
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<td>Codeine, morphine, meperidine</td>
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<td>Diuretic</td>
<td>Furosemide, hydrochlorothiazide</td>
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<td>Antiparkinsonian</td>
<td>Carbidopa-Levodopa (Sinemet®), benztrapine</td>
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<td>Ciprofloxacin, metronidazole, cephalaxin</td>
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<td>Bladder stabilizer</td>
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<td>H2 receptor Antagonists</td>
<td>Cimetidine, ranitidine</td>
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<td>Anti-inflammatories</td>
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<td>Brochodilator</td>
<td>Theophylline</td>
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Source: Geriatrics.Aging © 2008 1453987 Ontario, Ltd
Thyroid medication use and subsequent development of dementia of the Alzheimer type

Patrick C. Harper\textsuperscript{a} and Catherine M. Rice, PhD\textsuperscript{b}

Abstract

Associations between medication use and the development of Alzheimer’s disease have been investigated since the late 1990s. Thyroid hormone supplementation is rarely a studied medication class in this area of research. We examined data from participants enrolled in longitudinal studies at the Washington University Alzheimer’s Disease Research Center for associations between thyroid disease, thyroid hormone supplementation therapy, and subsequent development of dementia of the Alzheimer type (DAT). Data collected between April 1992 and June 2008 from 499 participants, 184 men and 315 women, were analyzed. Mean age was 76.9 years (S.D. = 9.2). At baseline, 61 participants reported thyroid medication use and 87 were identified as having a history of thyroid dysfunction. These participants progressed to a DAT diagnosis more rapidly than individuals not taking thyroid medication (HR: 1.67, 95% CI: 0.99–2.78, p = 0.054). While an interesting trend was seen, baseline thyroid disease was not significantly (p = .093) associated with time to DAT diagnosis. Our findings suggest that utilization of thyroid medication may be associated with the development of DAT.

Keywords: thyroid, dysfunction, hormone replacement, Alzheimer's, dementia
Dementia Drugs Ineffective at Slowing Mental Decline

Written by Brian Krans | Published on September 17, 2013

New research shows that Alzheimer’s drugs don’t help people with mild cognitive impairment.

Cognitive enhancement drugs only have short-term benefits and can cause significant side-effects for people with mild memory problems, according to researchers.

In a new review of existing data, researchers at St. Michael’s Hospital in Toronto, Canada studied eight randomized clinical trials and three companion reports on the efficacy of four drugs in people with mild cognitive impairment. The drugs were donepezil (Aricept), rivastigmine (Exelon), galantamine (Razadyne), and memantine (Namenda). They found that while the drugs do have short-term benefits, they are lost after a year and a half of treatment.

“As far as what’s out there in randomized clinical trials, these drugs don’t help people with mild cognitive impairment,” Andrea C. Tricco, a researcher with St. Michael’s Li Ka Shing Knowledge Institute, told Healthline. “We found for people who have been given this diagnosis, cognitive enhancers don’t work.”

More importantly, researchers found that those who used these drugs for mild cognitive impairment had a greater risk of headaches, nausea, diarrhea, and vomiting.

Dr. Dean Hartley, director of science initiatives for the Alzheimer’s Association, said the study is a confirmation of earlier work, except that this time the researchers focused on earlier stages of cognitive decline.

“This study is important. This is why we need more research,” he said. “Research is the answer to changing the trajectory of the disease.”
Alzheimer’s Drugs and Mild Cognitive Impairment
Aricept, Exelon, Razadyne, and Namenda are approved in the U.S. and Canada to treat Alzheimer’s-related dementia, but researchers examined existing data on their effectiveness for those with mild cognitive decline not related to Alzheimer’s.

While the drugs are only approved to treat Alzheimer’s, in Canada the drugs can be accessed by people with mild cognitive impairment when they have special written authorization.

Mild cognitive impairment is the mental state between age-related mental decline and dementia. Memory problems are typically noticeable by the person and their loved ones, but are not severe enough to interfere with day-to-day living.

About 4.6 million people worldwide have mild cognitive impairment, and between three and 17 percent of them progress to dementia. There are currently no drugs approved by the U.S. Food and Drug Administration (FDA) to treat the condition.

‘Indication Creep’
Researchers fear an “indication creep,” where medications for one condition are prescribed to people with similar symptoms. In this case, doctors may be using Alzheimer’s drugs to treat mild cognitive impairment.

Some in the mental health field have hypothesized that cognitive enhancement drugs may delay the onset of dementia, but researchers say there isn’t enough evidence to back up that claim.

“Cognitive enhancers did not improve cognition or function among patients with mild cognitive impairment and were associated with a greater risk of gastrointestinal harms. Our findings do not support the use of cognitive enhancers for mild cognitive impairment,” the researchers concluded in the Canadian Medical Association Journal.

What Can Help Prevent Cognitive Decline?
While the new St. Michael’s study shows that people with mild cognitive impairment aren’t helped by drugs, experts say certain lifestyle choices may be able to slow cognitive decline.
A study from earlier this year in the *Journal of Aging Research* found that physical exercise is a promising non-pharmaceutical way to prevent age-related cognitive decline and neurodegenerative diseases. Hartley, as well as others, says that challenging brain exercises, such as crossword puzzles and Sudoku, are good ways to stay mentally and emotionally engaged to prevent decline.

Eating a low-cholesterol, low-calorie diet is another excellent step toward reducing your risk of dementia and other brain woes.

“No data suggest [that] we can change the progression of the disease,” Hartley said. “Those all seem to be things that can slow the progression, but we need more data to ensure that.”
An extract of *Salvia* (sage) with anticholinesterase properties improves memory and attention in healthy older volunteers

Andrew B. Scholey • Nicola T. J. Tildesley • Clive G. Ballard • Keith A. Wesnes • Andrea Tasker • Elaine K. Perry • David O. Kennedy

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Abstract

*Salvia* (sage) has a long-standing reputation in European medical herbalism, including for memory enhancement. In recent controlled trials, administration of sage extracts with established cholinergic properties improved cognitive function in young adults.

**Objective**

This randomised, placebo-controlled, double-blind, balanced, five-period crossover study investigated the acute effects on cognitive performance of a standardised extract of *Salvia officinalis* in older adults.

**Materials and Methods**

Twenty volunteers (≥65 years of age; mean 72.95) received four active doses of extract (167, 332, 666 and 1332 mg) and a placebo with a 7-day wash-out period between visits. Assessment involved completion of the Cognitive Drug Research computerised assessment battery. On study days, treatments were administered immediately following a baseline assessment with further assessment at 1, 2.5, 4 and 6 h post-treatment.

**Results**

Compared with the placebo condition (which exhibited the characteristic performance decline over the day), the 333-mg dose was associated with significant enhancement of secondary memory performance at all testing times. The same measure benefited to a lesser extent from other doses. There also were significant improvements in accuracy of attention following the 333-mg dose. In vitro analysis confirmed cholinesterase inhibiting properties for the extracts.

**Conclusions**

The overall pattern of results is consistent with a dose-related benefit to processes involved in efficient stimulus processing and memory consolidation rather than retrieval or working memory efficiency. These findings extend those of the memory-enhancing effects of *Salvia* extracts in younger populations and warrant further investigation in larger series, in other populations and with different dosing regimes.

**Keywords** *Salvia* • Sage • Memory • Cognition • Cognitive decline • Acetylcholine • Cholinesterase • Attention • Age-related memory decline • Alzheimer’s disease

**Introduction**

Amongst medicinal plants, species of *Salvia* (sage) have a long-standing reputation as cognition enhancing agents (Kennedy and Scholey 2005; Imanshahidi and Hosseinzadeh 2006; Perry et al. 1999). The *Salvia* genus contains some 900 species of which three, *Salvia officinalis*, *S. lavandulaefolia* and *S. miltiorrhiza* are particularly notable.
Noninvasive Brain Stimulation in Stroke Rehabilitation

Brian R. Webster, Pablo A. Celnik, and Leonardo G. Cohen

Human Cortical Physiology Section and Stroke Neurorehabilitation Clinic, National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, Maryland 20892

Summary: Stroke is a common disorder that produces a major burden to society, largely through long-lasting motor disability in survivors. Recent studies have broadened our understanding of the processes underlying recovery of motor function after stroke. Bilateral motor regions of the brain experience substantial reorganization after stroke, including changes in the strength of interhemispheric inhibitory interactions. Our understanding of the extent to which different forms of reorganization contribute to behavioral gains in the rehabilitative process, although still limited, has led to the formulation of novel intervention strategies to regain motor function. Transcranial magnetic stimulation (TMS) and direct current stimulation (tDCS) electrical stimulation are noninvasive brain stimulation techniques that modulate cortical excitability in both healthy individuals and stroke patients. These techniques can enhance the effect of training on performance of various motor tasks, including those that mimic activities of daily living. This review looks at the effects of TMS and tDCS on motor cortical function and motor performance in healthy volunteers and in patients with stroke. Both techniques can either enhance or suppress cortical excitability, and may move to the clinical arena as strategies to enhance the beneficial effects of customary used neurorehabilitative treatments after stroke. Key Words: Stroke, motor cortex, rehabilitation, cortical stimulation, transcranial magnetic stimulation (TMS), transcranial direct current stimulation (tDCS), plasticity.

INTRODUCTION

An estimated 700,000 Americans suffered a stroke during 2005, incurring estimated costs related to their care of approximately $56.3 billion. Stroke is a leading cause of serious long-term disability, and approximately 1.1 million Americans with stroke had functional limitations in activities of daily living in 1999. The burden of stroke-related disability is predicted to increase in the coming decades in proportion to the expansion of the elderly population. Stroke case-fatality has declined, but stroke incidence has not, leading to rising numbers of stroke survivors.

After ischemic damage to motor areas of the brain, patients experience some degree of spontaneous recovery. Increasingly so since the advent of interventions implemented in the acute period after stroke—notably, use of tissue plasminogen activator (TPA) to dissolve blood clots. TPA represents an important advance in the fight against this disease, but so far has benefited a limited proportion of stroke patients. More than 50% of stroke survivors who reach the chronic stage experience permanent motor deficits. Repetitive task-oriented motor training represents the current standard in neurorehabilitation after chronic stroke. In recent years, new strategies in repetitive motor training have raised substantial interest, including constraint-induced therapy, bilateral arm training, body-weight support treadmill training, robotic assisted therapy, and use of virtual reality protocols.

MECHANISMS OF FUNCTIONAL RECOVERY

Studies of cortical plasticity after stroke suggest that the damaged cortex has the potential for extensive reorganization (for a review, see Ward and Cohen and Cincotti and Baron). Among possible mechanisms of neural plasticity contributing to functional recovery are dendritic sprouting over time, new synapse formation, and long-term potentiation (LTP) and depression (LTD). Reorganization after stroke may also involve undamaged areas of cortex taking on functions of the infarcted regions. Different forms of reorganization that may contribute to functional recovery include diaschisis, peri-infarct reorganization, activity in the ipsi-
Mirth and laughter elicited during brain stimulation

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Received May 30, 2011; Accepted November 30, 2011

ABSTRACT – There are few reports of laughter and/or mirth evoked by electrical stimulation of the brain. In this study, we present a patient with intractable epilepsy in whom mirth and laughter was consistently produced during stimulation of the left inferior frontal gyrus (opercular part) using stereotactically placed depth electrodes. A review of the literature shows that cortical sites that produce mirth when stimulated are located in the dominant hemisphere close to language areas or cortical negative motor areas.

KEY WORDS: brain stimulation, cortical mapping, mirth, laughter, language areas, negative motor areas, gelastic seizures

Electrical stimulation in epileptic patients undergoing pre-surgical evaluation with intracranial electrodes is routinely performed to determine the location of eloquent cortical areas. This provides a unique opportunity to study the functional anatomy of the human brain.

Laughter and mirth have been studied by researchers for centuries; yet their neuronal correlates remain poorly defined (Avid et al., 2003). There are few reports of laughter and mirth provoked by electrical stimulation of the brain. Arroyo et al. (1993) suggested that the motor program of laughter and the experience of mirth are dissociated. Based on their results, it was concluded that laughter is represented in the anterior cingulate gyrus and that mirth is a function of the temporal lobe. This was later supported by results published by Satow et al. (2003) and Sperli et al. (2006). Other reported data (Fried et al., 1998; Kroalak-Salmon et al., 2006; Schmitt et al., 2006) showed that laughter with and without mirth can be provoked by stimulation of the frontal cortex; in the pre-supplementary sensorimotor area (pre-SSMA), immediately anterior to face and hand representation in the rostral part of the supplementary sensorimotor area (SSMA), and the superior frontal gyrus.

In this manuscript, we present evidence that electrical stimulation of the left inferior frontal gyrus (opercular part) consistently elicited mirth and laughter in a patient with stereotactically placed depth electrodes for intractable epilepsy.
Effects of Brain-Derived Neurotrophic Factor (BDNF) and Electrical Stimulation on Survival and Function of Cochlear Spiral Ganglion Neurons in Deafened, Developing Cats

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ABSTRACT

Both neurotrophic support and neural activity are required for normal postnatal development and survival of cochlear spiral ganglion (SG) neurons. Previous studies in neonatal deafened cats demonstrated that electrical stimulation (ES) from a cochlear implant can promote improved SG survival but does not completely prevent progressive neural degeneration. Neurotrophic agents combined with an implant may further improve neural survival. Short-term studies in rodents have shown that brain-derived neurotrophic factor (BDNF) promotes SG survival after deafness and may be additive to trophic effects of stimulation. Our recent study in neonatal deafened cats provided the first evidence of BDNF neurotrophic effects in the developing auditory system over a prolonged duration Leake et al. (J Comp Neurol 519:1526–1545, 2011). Ten weeks of intracochlear BDNF infusion starting at 4 weeks of age elicited significant improvement in SG survival and larger soma size compared to controlateral. In the present study, the same deafening and BDNF infusion procedures were combined with several months of ES from an implant. After combined BDNF + ES, a highly significant increase in SG numerical density (>50% improvement re: controlateral) was observed, which was significantly greater than the neurotrophic effect seen with ES-only over comparable durations. Combined BDNF + ES also resulted in a higher density of myelinated radial nerve fibers within the osseous spiral lamina. However, substantial ectopic and disorganized sprouting of these fibers into the scala tympani also occurred, which may be deleterious to implant function. EABR thresholds improved (re: initial thresholds at time of implantation) on the chronically stimulated channels of the implant. Terminal electrophysiological studies recording in the inferior colliculus (IC) revealed that the basic cochlearotopic organization was intact in the midbrain in all studied groups. In deafened controls or after ES-only, lower IC thresholds were correlated with more selective activation widths as expected, but no such correlation was seen after BDNF + ES due to much greater variability in both measures.

Keywords: auditory deprivation, auditory nerve, BDNF, cochlear implant, cochlear spiral ganglion, electrical stimulation, neonatal deafness, primary afferents, neurotrophins

INTRODUCTION

The cochlear spiral ganglion (SG) cells are bipolar primary afferent neurons that relay auditory information from the hair cells to the central auditory system.
Electrical Stimulation in Epilepsy: Vagus Nerve and Brain Stimulation

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Opinion statement

Vagus nerve stimulation (VNS) for epilepsy is a well established and effective treatment for medically intractable epilepsy. VNS is indicated if resective epilepsy surgery is unsuccessful or is not an option. About 50% of patients with VNS have a seizure reduction greater than 50%, but less than 10% become seizure-free. VNS also has an alerting effect on patients and may allow a reduction in sedating medications. The major adverse event is hoarseness, but treatment is generally well tolerated. The therapeutic effect can be delayed; patients may improve several months after VNS implantation. Direct brain stimulation (DBS) is an emerging treatment for epilepsy. Scheduled stimulation is similar to brain stimulation in Parkinson's disease. Only the anterior thalamic nucleus has been studied in a larger randomized, controlled trial, in which patients with the stimulator turned on had a significantly reduced seizure frequency. Responsive stimulation applies an electrical stimulus at the site of seizure onset to terminate the seizure if one occurs. The seizure-onset zone must be well defined before implantation. Responsive stimulation requires seizure detection and application of a stimulus online. A large pivotal trial showed a significant reduction in seizure frequency. Both DBS and responsive neurostimulation are well tolerated, but there has been some concern about depression with DBS. Infection, hemorrhage, and lead breakage are adverse events possible with any type of stimulator. None of the brain stimulation devices have been approved by the US Food and Drug Administration, but final approval is expected soon. These devices are indicated for patients with bilateral seizure onset or seizure onset in eloquent areas. Although the initial trials of brain stimulation do not show overwhelming improvement in seizure frequency, the technology will improve with time as we continue to learn about the use of brain stimulation for epilepsy. Optimization of VNS has been going on for 10 years, and we need to ensure that brain stimulation is similarly developed further. In addition, sophisticated devices such as responsive neurostimulators can greatly enhance our understanding of the pathophysiology of epilepsy.
Power spectral density analysis of physiological, rest and action tremor in Parkinson’s disease patients treated with deep brain stimulation

Tjitske Heida*, Eva Christine Wentink and Enrico Marani

Abstract
Background: Observation of the signals recorded from the extremities of Parkinson’s disease patients showing rest and/or action tremor reveal a distinct high power resonance peak in the frequency band corresponding to tremor. The aim of the study was to investigate, using quantitative measures, how clinically effective and less effective deep brain stimulation protocols redistribute movement power over the frequency bands associated with movement, pathological and physiological tremor, and whether normal physiological tremor may reappear during those periods that tremor is absent.

Methods: The power spectral density patterns of rest and action tremor were studied in 7 Parkinson’s disease patients treated with (bilateral) deep brain stimulation of the subthalamic nucleus. Two tests were carried out: 1) the patient was sitting at rest; 2) the patient performed a hand or foot tapping movement. Each test was repeated four times for each extremity with different stimulation settings applied during each repetition. Tremor intermittency was taken into account by classifying each 3-second window of the recorded angular velocity signals as a tremor or non-tremor window.

Results: The distribution of power over the low frequency band (<3.5 Hz – voluntary movement), tremor band (3.5–7.5 Hz) and high frequency band (>7.5 Hz – normal physiological tremor) revealed that rest and action tremor show a similar power-frequency shift related to tremor absence and presence: when tremor is present most power is contained in the tremor frequency band; when tremor is absent lower frequencies dominate. Even under resting conditions a relatively large low frequency component became prominent, which seemed to compensate for tremor. Tremor absence did not result in the reappearance of normal physiological tremor.

Conclusion: Parkinson’s disease patients continuously balance between tremor and tremor suppression or compensation expressed by power shifts between the low frequency band and the tremor frequency band during rest and voluntary motor actions. This balance shows that the pathological tremor is either on or off, with the latter state not resembling that of a healthy subject. Deep brain stimulation can reverse this balance thereby either switching tremor on or off.

Keywords: Parkinson’s disease, Rest tremor, Action tremor, Kinetic tremor, Physiological tremor, Power spectral density, Deep brain stimulation

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Dopamine Measurement during Prolonged Deep Brain Stimulation: A Proof-of-Principle Study of Paired Pulse Voltammetry

Seungkeol Brian Park, Emily Jane Knight, Su-Yeun Chang, J. Luis Lujan, Dong Pyo Jang, Kevin E. Bennett and Kendal H. Lee

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Abstract

Purpose Deep Brain Stimulation (DBS) has been effective in treating various neurological and psychiatric disorders; however, its underlying mechanism hasn’t been completely understood. Fast scan cyclic voltammetry (FSCV) is a valuable tool to elucidate underlying neurotransmitter mechanisms of DBS, due to its sub-second temporal resolution and direct identification of analytes. However, since DBS-like high frequency stimulation evokes neurotransmitter release as well as extracellular pH shift, it is hard to isolate the neurotransmitter signal from the complex environment. Here we demonstrate the efficacy of a modified FSCV technique, Paired Pulse Voltammetry (PPV), in detecting dopamine (DA) release in the caudate nucleus during long-term electrical stimulation of the medial forebrain bundle (MFB) in the rat.

Methods Unlike traditional FSCV applying a single triangular waveform, PPV employs a binary waveform with a specific time gap (2.2 ms) in between the comprising pulses. DA measurement was performed with a carbon fiber microelectrode placed in the caudate nucleus and a twisted bipolar stimulating electrode in the MFB. PPV data was collected with the Wireless Instantaneous Neurochemical Concentration Sensing System (WINCS).

Results Using PPV, the detection of DA was evident throughout the long-term stimulation (5 minutes); however, without PPV, in vivo environmental changes including pH shift eventually obscured the characteristic oxidation current of DA at 0.6V.

Conclusions These results indicate that PPV can be a valuable tool to accurately determine DA dynamics in a complex in vivo environment during long-term electrical stimulation.

Keywords Deep brain stimulation (DBS), Fast scan cyclic voltammetry (FSCV), Paired pulse voltammetry (PPV), Dopamine (DA), Medial forebrain bundle (MFB)

INTRODUCTION

Deep Brain Stimulation (DBS) neurosurgery has now been widely performed throughout the world, achieving therapeutic success in various neurological and psychiatric conditions [1]. Among the most prominent disorders for which this treatment has proven effective are Parkinson’s disease, essential tremor, dystonia, and recently obsessive compulsive disorder [2-8]. Despite the efficacy of DBS for a wide variety of conditions, the precise mechanism of its therapeutic action is still incompletely understood. However, techniques such as fast scan cyclic voltammetry (FSCV) have been emerging as valuable tools for mechanistic studies of DBS [9]. FSCV is an established electrochemical technique, which typically involves the application of a linearly varying electrical potential to a carbon fiber micro-electrode (CFM) and measurement of the changes in current induced by the oxidation and reduction of neurochemicals. Using FSCV, neurochemicals can be differentiated from one another and the surrounding environment on the basis of the unique voltages at which
Sleeping in regularly may not be a good idea if you want to keep your brain sharp, according to a new study that found people in their 60s and 70s who slept on average 9 hours or more in a 24-hour period showed a more rapid decline in cognitive function over 3 years than counterparts who slept 6-8 hours.

Decline in cognitive function, such as memory and thinking, is a feature of Mild Cognitive Impairment (MCI), a known risk factor for dementia. The study, which was conducted by researchers from the University Hospital Madrid and Columbia University in New York, was published online recently in the *Journal of Psychiatric Research*.

The researchers, led by Dr. Julián Benito-León, looked at data from a large cohort of over 2,700 people in their 60s and 70s who were followed for 3 years.

At the beginning and end of the study period, the participants underwent assessment of brain function using the mini-mental state examination (MMSE), one of a battery of tests used to assess dementia.

Over the 3 years they were followed, the participants also filled in reports that included details of their sleeping patterns.
People who slept on average more than 9 hours a night showed double the amount of cognitive function decline, compared with people who slept 6-8 hours a night.

The results showed that 49% of participants were normal sleepers (they slept on average 6-8 hours over a 24-hour period, this was the "reference group"), 40% were long sleepers (9 or more hours) and 11% were short sleepers (5 hours or less).

Over the follow-up, the MMSE scores declined in all three groups, with long sleepers showing nearly double the amount of decline in cognitive function of normal sleepers.

The authors note that the "difference between long sleepers and the reference group was significant," and the result remained "robust," even when they took into account factors that might influence it, such as age, education, and smoking and drinking habits.

The researchers say further studies are needed to confirm these findings.

It is important to note finding a link does not establish that longer sleep actually causes the mental decline. There could be other explanations, and one question that could be explored is does mental decline cause people to sleep longer?

Another study published recently found that too much or too little sleep is linked to chronic diseases, such as diabetes, coronary heart disease, obesity and anxiety in those aged 45 and over.
WASHINGTON — High blood pressure, particularly in the arteries that supply blood to the head and neck, may be linked with declining cognitive abilities, according to a new study from Australia.

Researchers found that people with high blood pressure in the central arteries — including the aorta, the largest artery in the human body, and the carotid arteries in the neck — performed worse on tests of visual processing, and had slower thinking and poorer recognition abilities.

Typically, blood pressure measurements are taken from the brachial artery in the arm, but looking at the health of the central arteries may be a more sensitive way to assess cognitive abilities, said study researcher Matthew Pase, of the Center for Human Psychopharmacology at Swinburne University in Melbourne. The central arteries directly control bloodflow to the brain.

"If we can estimate the blood pressure in central arteries, we might be able to better predict cognitive function and cognitive decline," Pase said. [10 Odd Facts About the Brain]
Pase presented the findings here on May 24 at the annual meeting of the Association for Psychological Science.

**How it all works**

A beating heart pumps blood in spurts, but the central arteries are flexible, expanding and contracting to maintain steady bloodflow to the brain.

As people age, the central arteries stiffen, and with less elasticity, the brain receives more high-pressure blood, which may damage cognition, Pase said. [7 Ways the Mind and Body Change With Age](#)

In the study, Pase and his colleagues looked at whether associations between blood pressure and cognition were stronger for measurements taken in the arm, or the central arteries. The researchers examined 493 Australians between ages 20 and 82. The participants were mostly Caucasians, and all were nonsmokers with no history of stroke or [dementia](#), Pase said.

Study participants performed tasks to measure various types of [cognition](#), such as visual processing, working memory, recognition abilities and processing speed. The researchers also took blood pressure measurements from the arm and central arteries.

**Blood pressure and cognition**

The researchers found that high brachial blood pressure was linked to worse performance on the visual processing test, but high central blood pressure correlated to worse performance across several tests, including visual processing, recognition and processing speed.

"This suggests central blood pressure is a more sensitive predictor of cognitive aging," Pase said.

To expand upon these findings, Pase said he wants to look at whether reducing central blood pressure — which can be done by quitting smoking, doing regular exercise or limiting salt intake — might protect people against [mental deterioration](#).

The researchers will detail their results in an upcoming issue of the journal Psychological Science.
Brain plasticity and functional losses in the aged: scientific bases for a novel intervention.

Mahncke HW, Bronstone A, Merzenich MM.

Abstract

Aging is associated with progressive losses in function across multiple systems, including sensation, cognition, memory, motor control, and affect. The traditional view has been that functional decline in aging is unavoidable because it is a direct consequence of brain machinery wearing down over time. In recent years, an alternative perspective has emerged, which elaborates on this traditional view of age-related functional decline. This new viewpoint—based upon decades of research in neuroscience, experimental psychology, and other related fields—argues that as people age, brain plasticity processes with negative consequences begin to dominate brain functioning. Four core factors—reduced schedules of brain activity, noisy processing, weakened neuromodulatory control, and negative learning—interact to create a self-reinforcing downward spiral of degraded brain function in older adults. This downward spiral might begin from reduced brain activity due to behavioral change, from a loss in brain function driven by aging brain machinery, or more likely from both. In aggregate, these interrelated factors promote plastic changes in the brain that result in age-related functional decline. This new viewpoint on the root causes of functional decline immediately suggests a remedial approach. Studies of adult brain plasticity have shown that substantial improvement in function and/or recovery from losses in sensation, cognition, memory, motor control, and affect should be possible, using appropriately designed behavioral training paradigms. Driving brain plasticity with positive outcomes requires engaging older adults in demanding sensory, cognitive, and motor activities on an intensive basis, in a behavioral context designed to re-engage and strengthen the neuromodulatory systems that control learning in adults, with the goal of increasing the fidelity, reliability, and power of cortical representations. Such a training program would serve a substantial unmet need in aging adults. Current treatments directed at age-related functional losses are limited in important ways. Pharmacological therapies can target only a limited number of the many changes believed to underlie functional decline. Behavioral approaches focus on teaching specific strategies to aid higher order cognitive functions, and do not usually aspire to fundamentally change brain function. A brain-plasticity-based training program would potentially be applicable to all aging adults with the promise of improving their operational capabilities. We have constructed such a brain-plasticity-based training program and conducted an initial randomized controlled pilot study to evaluate the feasibility of its use by older adults. A main objective of this initial study was to estimate the effect size on standardized neuropsychological measures of memory. We found that older adults could learn the training program quickly, and could use it entirely unsupervised for the majority of the time required. Pre- and posttesting documented a significant improvement in memory within the training group (effect size 0.41, p<0.0005), with no significant within-group changes in a time-matched computer using active control group, or in a no-contact control group. Thus, a brain-plasticity-based intervention targeting normal age-related cognitive decline may potentially offer benefit to a broad population of older adults.
HEARING LOSS ACCELERATES BRAIN FUNCTION DECLINE IN OLDER ADULTS

Release Date: 01/23/2013

Older adults with hearing loss are more likely to develop problems thinking and remembering than older adults whose hearing is normal, according to a new study by hearing experts at Johns Hopkins.

In the study, volunteers with hearing loss, undergoing repeated cognition tests over six years, had cognitive abilities that declined some 30 percent to 40 percent faster than in those whose hearing was normal. Levels of declining brain function were directly related to the amount of hearing loss, the researchers say. On average, older adults with hearing loss developed a significant impairment in their cognitive abilities 3.2 years sooner than those with normal hearing.

The findings, to be reported in the JAMA Internal Medicine online Jan. 21, are among the first to emerge from a larger, ongoing study monitoring the health of older blacks and whites in Memphis, Tenn., and Pittsburgh, Pa. Known as the Health, Aging and Body Composition, or Health ABC study, the latest report on older adults involved a subset of 1,984 men and women between the ages of 75 and 84, and is believed to be the first to gauge the impact of hearing loss on higher brain functions over the long term. According to senior study investigator and Johns Hopkins otologist and epidemiologist Frank Lin, M.D., Ph.D., all study participants had normal brain function when the study began in 2001, and were initially tested for hearing loss, which hearing specialists define as recognizing only those sounds louder than 25 decibels.

“Our results show that hearing loss should not be considered an inconsequential part of aging, because it may come with some serious long-term consequences to healthy brain functioning,” says Lin, an assistant professor at the Johns Hopkins University School of Medicine and the university's Bloomberg School of Public Health.

“Our findings emphasize just how important it is for physicians to discuss hearing with their patients and to be proactive in addressing any hearing declines over time,” says Lin. He estimates that as many as 27 million Americans over age 50, including two-thirds of men and women aged 70 years and older, suffer from some form of hearing loss. More worrisome, he says, only 15 percent of those who need a hearing aid get one, leaving much of the problem and its consequences untreated.

Possible explanations for the cognitive slide, Lin says, include the ties between hearing loss and social isolation, with loneliness being well established in previous research as a risk factor for cognitive decline. Degraded hearing may also force the brain to devote too much of its energy to processing sound, and at the expense of energy spent on memory and thinking. He adds there may also be some common, underlying damage that leads to both hearing and cognitive problems.

Lin and his team already have plans under way to launch a much larger study to determine if use of hearing aids or other devices to treat hearing loss in older adults might forestall or delay cognitive decline.
In the latest study, which began in 1997, all participants were in good general physical health at the time. Hearing tests were given to volunteers in 2001, during which they individually listened to a range of soft and loud sounds, from 0 decibels to 100 decibels, in a soundproof room.

Brain functioning was also assessed in 2001, using two well-recognized tests of memory and thinking ability, known as the Modified Mini-Mental State (3MS) and Digit Symbol Substitution (DSS), respectively. Included in the 3MS test, study participants were asked to memorize words, given commands or instructional tasks to follow, and asked basic questions as to the correct year, date and time. In the DSS test, study participants were asked to match specific numbers to symbols and timed on how long it took them to complete the task.

Both types of tests were repeated for each study participant three more times until the study ended in 2007, to gauge cognitive decline. Factors already known to contribute to loss of brain function were accounted for in the researchers’ analysis, including age, high blood pressure, diabetes and stroke.

Funding support for this study and the Health ABC study was provided by the Intramural Research Program of the National Institute on Aging, part of the National Institutes of Health (NIH). Corresponding grant numbers are N01-AG62101, N01-AG62103, N01-AG62106, R01-AG028050, R01-NR012459, P30-AG02133 and K34-DC0111279. Additional research support was provided by the Eleanor Schwartz Charitable Foundation and a Triological Society and American College of Surgeons Clinician-Scientist Award.

In addition to Lin, other Johns Hopkins researchers involved in this study were Jin Xia, M.S., and Qian-Li Xue, Ph.D. Other study co-investigators included Kristine Yaffe, M.D., and Hilsa Ayonayon, Ph.D., at the University of California, San Francisco; Tamara Harris, M.D., M.S., Luigi Ferrucci, M.D., Ph.D., and Eleanor Simonsick, Ph.D., at the National Institute on Aging, in Baltimore; Elizabeth Purchase Helzner, Ph.D., at the State University of New York Downstate Medical Center, in Brooklyn; and Suzanne Satterfield, M.D., Dr.PH., at the University of Tennessee, in Memphis.
**Table 1**  
*Potential laboratory studies that may be used to evaluate a patient with cognitive impairment*  

**Laboratory studies for which clinical evidence exists to include in general evaluation**

- Complete blood cell count
- Glucose level
- Thyroid function tests
- Serum electrolyte panel
- Blood urea nitrogen/creatinine ratio
- Serum B₁₂ levels
- Liver function tests

**Studies for which no evidence exists to include in general evaluation**

- Syphilis screening
- Linear or volumetric MRI or CT measurement strategies
- Single photon emission computed tomography
- Genetic testing for dementia with Lewy bodies or Creutzfeldt-Jakob disease
- APOE genotyping for Alzheimer disease
- Electroencephalogram
- Lumbar puncture

**Studies with not enough evidence to support or refute**

- Positron emission tomography
- Genetic markers for Alzheimer disease not listed in the guidelines
- Cerebrospinal fluid or other biomarkers for Alzheimer disease
- \( \tau \) Mutations in patients with frontotemporal dementia
- Alzheimer disease gene mutations in patients with frontotemporal dementia

**Other laboratory studies (based on clinical suspicion)**

- HIV testing
- Urine toxicology screen (substance use disorder)
- Carbohydrate-deficient transferrin and \( \gamma \)-glutamyl transferase (alcohol use disorder)

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Based on American Academy of Neurology recommendations. ⁴⁶
Brain function can start declining 'as early as age 45'

Individuals were tested for memory, vocabulary and aural and visual comprehension skills

The brain's ability to function can start to deteriorate as early as 45, suggests a study in the British Medical Journal. University College London researchers found a 3.6% decline in mental reasoning in women and men aged 45-49. They assessed the memory, vocabulary and comprehension skills of 7,000 men and women aged 45 to 70 over 10 years.

The Alzheimer's Society said research was needed into how changes in the brain could help dementia diagnoses. Previous research had suggested that cognitive decline does not begin much before the age of 60. But the results of this study show that it could in fact begin in middle age.

This is important, the researchers say, because dementia treatments are more likely to work at the time when individuals start to experience mental impairment. The UCL researchers tested the cognitive functions of 5,198 men and 2,192 women aged 45 to 70, who were all UK civil servants, from 1997 to 2007. Individuals were tested for memory, vocabulary and aural and visual comprehension skills. Differences in education level were taken into account.

Mid-life crisis
The results of the tests show that cognitive scores declined in all categories except vocabulary - and there was a faster decline in older people. The study found a 9.6% decline in mental reasoning in men aged 65-70 and a 7.4% decline for women of the same age. For men and women aged 45-49, there was a 3.6% decline. Professor Archana Singh-Manoux from the Centre for Research in Epidemiology and Population Health in France, who led the research team at University College London, said the evidence from the study showed that dementia involved cognitive decline over two to three decades.
Dr Anne Corbett, Alzheimer’s Society: 'There are things people can do to reduce their chances of getting dementia later down the line' "We now need to look at who experiences cognitive decline more than the average and how we stop the decline. Some level of prevention is definitely possible. "Rates of dementia are going to soar and health behaviours like smoking and physical activity are linked to levels of cognitive function. "It’s important to identify the risk factors early. If the disease has started in an individual's 50s but we only start looking at risk in their 60s, then how do you start separating cause and effect?"

Lifestyle choices

If the disease has started in an individual's 50s but we only start looking at risk in their 60s, then how do you start separating cause and effect?"

Professor Archana Singh-ManouxUCL

Dr Anne Corbett, research manager at the Alzheimer’s Society, said the study added to the debate on when cognitive decline began, but it left some questions unanswered. "The study does not tell us whether any of these people went on to develop dementia, nor how feasible it would be for GPs to detect these early changes. "More research is now needed to help us fully understand how measurable changes in the brain can help us improve diagnosis of dementia." Dr Simon Ridley, head of research at Alzheimer’s Research UK, said he wanted to see similar studies carried out in a wider population sample.

He added: "Previous research suggests that our health in mid-life affects our risk of dementia as we age, and these findings give us all an extra reason to stick to our New Year’s resolutions. "Although we don’t yet have a sure-fire way to prevent dementia, we do know that simple lifestyle changes - such as eating a healthy diet, not smoking, and keeping blood pressure and cholesterol in check - can all reduce the risk of dementia." Professor Lindsey Davies, president of the Faculty of Public Health, said that people should not wait until their bodies and minds broke down before taking action.

"We need only look at the problems that childhood obesity rates will cause if they are not addressed to see how important it is that we take 'cradle to grave' approach to public health."
A forgotten name or date the mistake is often written off as a ‘senior moment’, an unavoidable consequence of a decline in brain function due to ageing. Well, it turns out that such instances may simply be down to older brains taking longer to churn through the large stores of knowledge they have accumulated.

Researchers at the University of Tuebingen in Germany programmed a computer to act as a human, reading a certain amount each day and learning new things along the way. After
reading just a limited amount, the computer’s performance on cognitive tests resembled that of a young adult.

However, when the same computer was exposed to a lifetime of data, its performance looked more like that of an older adult. Often it was slower, not because its processing capacity was lower, but because it had more data to process, and that processing takes time.

"Imagine someone who knows two people's birthdays and can recall them almost perfectly," says Dr Michael Ramscar, the study’s leader. "Would you really want to say that person has a better memory than a person who knows the birthdays of 2000 people, but can ‘only’ match the right person to the right birthday nine times out of ten?"

"Technology now allows researchers to make quantitative estimates about the number of words an adult can be expected to learn across a lifetime, enabling the team to separate the challenge that increasing knowledge poses to memory from the actual performance of memory itself,” he added.
Physical basis of cognitive alterations in alzheimer's disease: Synapse loss is the major correlate of cognitive impairment

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Abstract

We present here both linear regressions and multivariate analyses correlating three global neuropsychological tests with a number of structural and neurochemical measurements performed on a prospective series of 15 patients with Alzheimer's disease and 9 neuropathologically normal subjects. The statistical data show only weak correlations between psychometric indices and plaques and tangles, but the density of neocortical synapses measured by a new immunocytochemical/densitometric technique reveals very powerful correlations with all three psychological assays. Multivariate analysis by stepwise regression produced a model including midfrontal and inferior parietal synapse density, plus inferior parietal plaque counts with a correlation coefficient of 0.96 for Mattis's Dementia Rating Scale. Plaque density contributed only 26% of that strength.
Cognitive disorders can be caused by all sorts of brain problems, including tumors, strokes, closed-head injuries, infections, exposure to neurotoxins (i.e., substances that are toxic to the brain), genetic factors, and disease. The specific type of cognitive disorder someone develops depends on the part of the brain that is affected. For instance, a tumor that grows in the brain’s speech centers will result in problems with communication. Similarly, an infection in the brain's motor centers will cause problems with movement.

Tumors are masses of cells that grow and infiltrate the body. These masses of cells can be either benign (i.e., they will stop growing once they are removed via surgery) or malignant (i.e., they are difficult to remove and will continue to grow and spread). Both benign and malignant tumors in the brain can cause impaired cognitive functioning, depending on their size and location.

Even the most skilled surgeon cannot remove a benign tumor without causing some damage to surrounding brain areas. As a result, someone who has had a benign tumor removed may still experience residual weakness or numbness, for example. Individuals with malignant tumors will experience cognitive problems as the cell mass presses on and destroys healthy tissue in the brain and spinal cord, blocks the fluid that flows around and through the brain, and/or causes swelling due to accumulation of fluid. Malignant tumors are often lethal.
Strokes - disruptions in the blood supply to the brain - are one of the most common causes of brain damage. Strokes are caused by blockages to blood vessels (ischemic strokes), or when a blood vessel bursts (a hemorrhagic stroke). The risk factors for stroke include age, family history, heart disease, uncontrolled diabetes, high blood pressure, and smoking. Common cognitive effects of stroke include impaired memory, language difficulties, and paralysis, but depend on the part of the brain that is affected. For more information about stroke, please see our related topic center.

Closed head injuries are blows to the head that do not penetrate the skull (e.g., when someone hits his or her head during a car accident). Concussions (when the brain bounces against the skull), hematomas (brain bruises or bleeding), and traumatic brain injuries all all types of closed head injuries. Again, the severity and type of cognitive impairment caused by closed head injuries depends on the portion of the brain that is injured. More information about traumatic brain injuries can be found at the end of this article, by clicking here.

Infections can also cause cognitive disorders. Both bacteria and viruses (e.g., the virus that causes rabies) can disrupt brain functioning. One of the most common forms of brain infection is meningitis, an inflammation of the meninges, the protective covering that surrounds the brain and the central nervous system. Meningitis can cause deafness, other forms of cognitive impairment, and in severe cases, death.

Repeated and/or significant exposure to toxic chemicals (neurotoxins) such as metals (e.g., lead, mercury), drugs (e.g., cocaine, alcohol), or other substances (e.g., paint, glue, etc.) can cause cognitive impairment. The type of cognitive impairment created by neurotoxins depends on the type of toxin, the degree of exposure (how much of the substance was taken in, and for how long), and when the exposure occurred (whether the person affected was an infant, child, or adult). Typically, young children exposed to neurotoxins are more likely to develop cognitive disorders (because their brains are experiencing more rapid development) than adults.

Some individuals who develop cognitive impairment have inherited a problem in their genetic makeup. For instance, individuals with Down syndrome have an extra 21st chromosome. People with this syndrome often have mental retardation (intellectual functioning that is significantly below average, combined with an impaired ability to adapt to the demands of everyday functioning). For more information on Mental Retardation, please see our topic center describing Mental Illnesses and Disorders of Childhood.
Diseases that cause cognitive disorders can result from any one (or a combination) of the factors listed above. For instance, Huntington's Disease (a disorder that affects thinking, emotions, and movement), and multiple sclerosis (a movement disorder created when the body attacks the lining of brain cells, called myelin, which decreases the brain's ability to quickly and efficiently deliver messages) both have a strong genetic component. In contrast, Parkinson's Disease (a movement disorder described below) and Epilepsy (a disorder in which clusters of brain cells signal abnormally and cause seizures; see our related topic center) can have a host of causes, including defective genes, brain infections, tumors, etc.

Brain aging is conclusively linked to genes

November 4, 2013 -- Texas Biomedical Research Institute

For the first time in a large study sample, the decline in brain function in normal aging is conclusively shown to be influenced by genes, say American researchers.

Scientists documented profound aging effects from young adulthood to old age, on neurocognitive ability. Genetic material shared amongst biological relatives appears to predict the observed changes in brain function with age.

Credit: © Barabas Attila / Fotolia

For the first time in a large study sample, the decline in brain function in normal aging is conclusively shown to be influenced by genes, say researchers from the Texas Biomedical Research Institute in San Antonio and Yale University.
"Identification of genes associated with brain aging should improve our understanding of the biological processes that govern normal age-related decline," said John Blangero, Ph.D., a Texas Biomed geneticist and the senior author of the paper. The study, funded by the National Institutes of Health (NIH), is published in the November 4, 2013 issue of the Proceedings of the National Academy of Sciences. David Glahn, Ph.D., an associate professor of psychiatry at the Yale University School of Medicine, is the first author on the paper.

In large pedigrees including 1,129 people aged 18 to 83, the scientists documented profound aging effects from young adulthood to old age, on neurocognitive ability and brain white matter measures. White matter actively affects how the brain learns and functions. Genetic material shared amongst biological relatives appears to predict the observed changes in brain function with age. Participants were enrolled in the Genetics of Brain Structure and Function Study and drawn from large Mexican Americans families in San Antonio. Brain imaging studies were conducted at the University of Texas Health Science Center at San Antonio Research Imaging Institute directed by Peter Fox, M.D.

"The use of large human pedigrees provides a powerful resource for measuring how genetic factors change with age," Blangero said.

By applying a sophisticated analysis, the scientists demonstrated a heritable basis for neurocognitive deterioration with age that could be attributed to genetic factors. Similarly, decreasing white matter integrity with age was influenced by genes. The investigators further demonstrated that different sets of genes are responsible for these two biological aging processes.

"A key advantage of this study is that we specifically focused on large extended families and so we were able to disentangle genetic from non-genetic influences on the aging process," said Glahn.

Story Source:
The above story is based on materials provided by Texas Biomedical Research Institute. Note: Materials may be edited for content and length.

Journal Reference:

Mild Cognitive Impairment

Mild cognitive impairment (MCI) causes a slight but noticeable and measurable decline in cognitive abilities, including memory and thinking skills. A person with MCI is at an increased risk of developing Alzheimer's or another dementia.
About Mild Cognitive Impairment
Mild cognitive impairment causes cognitive changes that are serious enough to be noticed by the individuals experiencing them or to other people, but the changes are not severe enough to interfere with daily life or independent function.

Because the changes caused by MCI are not severe enough to affect daily life, a person with MCI does not meet diagnostic guidelines for dementia. However, those with MCI have an increased risk of eventually developing Alzheimer's or another type of dementia. However, not all people with MCI get worse and some eventually get better.

Learn more: Key Types of Dementia, What Is Alzheimer's?, Alzheimer's Risk Factors

Symptoms
Experts classify Mild cognitive impairment based on the thinking skills affected:

- **MCI that primarily affects memory is known as "amnestic MCI."** With amnestic MCI, a person may start to forget important information that he or she would previously have recalled easily, such as appointments, conversations or recent events.

- **MCI that affects thinking skills other than memory is known as "nonamnestic MCI."** Thinking skills that may be affected by nonamnestic MCI include the ability to make sound decisions, judge the time or sequence of steps needed to complete a complex task, or visual perception.

Diagnosis
Mild cognitive impairment is a "clinical" diagnosis representing a doctor's best professional judgment about the reason for a person's symptoms. There are currently no tests or procedures to demonstrate conclusively that a person has MCI. It's also not

Prevalence of MCI
Long-term studies suggest that 10 to 20 percent of those aged 65 and older may have MCI.

Progress in MCI Diagnosis
The Alzheimer's Association partnered with the National Institute on Aging (NIA) to convene expert workgroups to update the diagnostic criteria and guidelines for MCI due to Alzheimer's disease.
yet possible to determine the underlying cause of MCI in a specific person.

A medical workup for MCI includes the following core elements:

- **Thorough medical history**, where the physician documents current symptoms, previous illnesses and medical conditions, and any family history of significant memory problems or dementia.

- **Assessment of independent function and daily activities**, which focuses on any changes from a person's usual level of function.

- **Input from a family member or trusted friend** to provide additional perspective on how function may have changed.

- **Assessment of mental status** using brief tests designed to evaluate memory, planning, judgment, ability to understand visual information and other key thinking skills.

- **In-office neurological examination** to assess the function of nerves and reflexes, movement, coordination, balance and senses.

- **Evaluation of mood** to detect depression; symptoms may include problems with memory or feeling “foggy.” Depression is widespread and may be especially common in older adults.

- **Laboratory tests** including blood tests and imaging of the brain's structure.

If the workup doesn't create a clear clinical picture, the doctor may recommend neuropsychological testing, which involves a series of written or computerized tests to evaluate specific thinking skills.

**Causes and risks**

The causes of mild cognitive impairment are not yet completely understood. Experts believe that many cases — but not all — result from brain changes occurring in the very early stages of Alzheimer's disease or other dementias.

The risk factors most strongly linked to MCI are the same as those for
dementia: advancing age, family history of Alzheimer's or another dementia, and conditions that raise risk for cardiovascular disease.

Learn more: [Dementia Risk and Prevention](#)

### Help is available

The Alzheimer's Association can help you learn more about MCI, Alzheimer’s disease and dementia, and help you find local support services.

- Call our [24/7 Helpline](#): 800.272.3900
- Locate a support group in your community
- Join our [online community](#)
- Visit our [Virtual Library](#)

### Treatment and outcomes

No medications are currently approved by the U.S. Food and Drug Administration (FDA) to treat mild cognitive impairment. Drugs approved to treat symptoms of Alzheimer's disease have not shown any lasting benefit in delaying or preventing progression of MCI to dementia.

The following coping strategies may be helpful for those with MCI. Some studies suggest that these strategies may help slow decline in thinking skills, although more research is needed to confirm their effect.

- **Exercise** on a regular basis to benefit your heart and blood vessels, including those that nourish your brain.

- **Control cardiovascular risk factors** to protect your heart and blood vessels, including those that support brain function.

- **Participate in mentally stimulating and socially engaging activities**, which may help sustain brain function.

Experts recommend that a person diagnosed with MCI be re-evaluated every six months to determine if symptoms are staying the same, improving or growing worse.

MCI increases the risk of later developing dementia, but some people with MCI never get worse. Others with
MCI later have test results that return to normal for their age and education.

It's not yet possible to tell for certain what the outcome of MCI will be for a specific person or to determine the underlying cause of MCI from a person's symptoms.

Researchers hope to increase the power to predict MCI outcomes by developing new diagnostic tools to identify and measure underlying brain changes linked to specific types of dementia. Stay informed about research investigating MCI, Alzheimer’s and related dementias. [Sign up for enews today.](#)
The Role of Phytochemicals in the Treatment and Prevention of Dementia

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Abstract

Dementia pathologies such as Alzheimer’s disease (AD) are reaching epidemic proportions, yet they are not successfully managed by effective symptomatic treatments. Only five drugs have been developed to alleviate cognitive symptoms, and more effective and safe treatments are needed for both the cognitive symptoms and behavioural and psychological symptoms of dementia (BPSD). As two of these licensed drugs (cholinesterase inhibitors [ChEIs]) are naturally derived (galantamine and rivastigmine), the potential for plants to yield new therapeutic agents has stimulated extensive research to discover new ChEIs together with plant extracts, phytochemicals and their derivatives with other mechanistic effects relevant to dementia treatment. This review presents the potential and actual therapeutic strategies for dementia in relation to the known mechanisms of dementia pathology. Phytochemicals that have shown mechanistic effects relevant to the pathological targets in dementia are discussed, with an emphasis on those showing positive clinical trial evidence.
Functional and structural disruption in neurons and/or glia of:
- Cellular signalling
- Gene transcription and mRNA translation
- DNA and/or histone epigenetic codes
- Firing rate and patterns (LTP and LTD)
- Dendritic spines, synaptic plasticity and neurogenesis
- Neuromodulator release

Universal domains:
- Attention, working memory, executive function
- Procedural learning and memory
- Speed of processing
- Fear-extinction learning
- Semantic memory

Higher domains:
- Episodic memory
- Social cognition
- Theory of mind
- Verbal learning and memory
- Language (use and understanding)

Focal and distributed network perturbation:
- Interregional dysconnectivity
- Local overconnectivity
- Collapse of small-world configurations
- Disorganization and desynchronization
- Disrupted γ- and θ-oscillations

Multiple spatial scales: molecules to cerebral circuits

Multiple time scales: milliseconds to years
Its spring, which means it’s the season for fresh, juicy berries. And that’s good news for your brain.

Researchers report in the journal *Annals of Neurology* that women who ate berries more frequently over a period of years showed slower decline in brain functions such as memory and attention when they got older than women who ate them less often. The findings don’t confirm that eating berries can prevent dementia associated with aging, or slow down Alzheimer’s, but they suggest that the fruits may play a part in keeping brains healthy.

The protective effect of blueberries and strawberries isn’t an entirely new finding. But previous studies have involved animals and only a small number of people, which left open the possibility that it wasn’t the berries, but something else that might be influencing how quickly the brain lost its executive functions.

*(MORE: Flavonoids May Help Fight Parkinson’s)*
In the current analysis, Elizabeth Devore, an instructor in medicine at Brigham and Women’s Hospital, and her colleagues addressed the gap in the research by reviewing the eating habits of a single cohort of 16,000 women participating in the Nurses Health Study. During their 50s and 60s, every four years the women answered questions by phone about what they ate. And in their 70s, they came into the lab for six different cognitive function tests. Devore and her team also had information on the women’s education, income and other socioeconomic factors that can affect cognitive function.

Their findings confirmed that women who ate berries at least once a week were able to slow down their cognitive decline by about 1.5 to 2.5 years. For blueberries, the effect started with about a half cup of berries each week; for strawberries, it took about a cup of the fruit per week. This effect persisted even after the scientists accounted for the fact that berry-eaters might also have other brain-healthy habits or characteristics, such as having more education and engaging in intellectually satisfying pursuits such as learning new languages or maintaining a rich network of social connections. “In the end, we did not see a lot of confounding from these factors,” says Devore.

(SPECIAL: What Health Experts Eat For Breakfast)

She and her colleagues focused their attention on berries because rodent studies showed that the key compound in berries, a flavonoid called anthocyanidin, could seep through the blood and into brain tissues — specifically concentrating in the hippocampus, which is responsible for learning and memory. As an antioxidant, flavonoids also fight inflammation and oxidation, both processes that affect aging brain cells.

The study is only the first to track berry consumption long term until cognitive decline set in, and the findings will need to be repeated and confirmed. But in the meantime, says Devore, it makes sense to add blueberries and strawberries to your diet, frozen or fresh. “I don’t think there are many downsides to that. The availability of berries and access to this kind of intervention is great as a public health message.” And a tasty one too.

HOW TO detect + Treat Alzheimer’s disease

The scientists note that this test could be utilized by therapists who don’t have the staff or equipment to conduct more advanced tests.

Written by Desire’ Dubounet 10-24-2013

According to a news release from the University of Florida, scientists have revealed that THE SMELL of peanut butter may help spot Alzheimer’s disease.
Jennifer Stamps, a graduate student in the University of Florida McKnight Brain Institute Center for Smell and Taste, recognized while working with Dr. Kenneth Mailman, a professor of neurology and health psychology in the University of Florida College of Medicine’s department of neurology, that patients should be tested for their sense of smell.

The ability to smell is connected with the first cranial nerve and is typically one of the first things to be lost in cognitive decline in Alzheimer’s. “Dr. Heilman said, ‘If you can come up with something quick and inexpensive, we can do it,’” Stamps recalled. She chose peanut since it is a “pure odorant” that is only recognized by the olfactory nerve.

To measure a person’s sense of smell with peanut butter, a therapist will hold a ruler next to a tablespoon of peanut butter and move the spoon up the ruler until the patient could recognize the odor with only one nostril. The same technique was then performed on the other nostril.

The scientists discovered that patients in the early stages of Alzheimer’s disease had a noteworthy difference in recognizing smell between the left and right nostril – the left nostril was unable to identify the smell until it was an average of 10 centimeters closer to the nose than the right nostril had made the identification in patients with Alzheimer’s disease.

Of the 24 patients observed who had mild cognitive impairment, only 10 patients confirmed a left nostril impairment and 14 patients did not. “At the moment, we can use this test to confirm diagnosis,” Stamps posited. “But we plan to study patients with mild cognitive impairment to see if this test might be used to predict which patients are going to get Alzheimer’s disease.”

The scientists note that this test could be used by clinicians who don’t have the staff or equipment to conduct more expensive tests. The first parts in the brain to be affected in people with Alzheimer’s disease is the front part of the temporal lobe that has developed from the smell system, and this part of the brain is related with generating new memories.

“We see people with all kinds of memory disorders,” Heilman added. “This can become an important part of the evaluation process.” The research’s findings are defined in better detail in the “Journal of the Neurological Sciences”

About 5.2 million Americans have Alzheimer’s or another form of dementia, according to the Alzheimer’s Association, with about 13.8 million cases expected by 2050. The disease is marked by declines in cognitive function and memory skills, and people aren’t typically diagnosed until they take mental status exams or doctors rule out other diseases that cause dementia-like symptoms. Alzheimer’s disease is difficult to diagnose before symptoms start showing up, because there is no single test that can definitively determine whether a person has the degenerative brain disease. Could a scoop of peanut butter and a ruler become that elusive early detection test?

A Mental test can be done by listing 7 common words not visible in the room at the time of the test. Ask the client to use each word in a sentence. Do not tell them this is a memory test. An item might be an umbrella, the client might say “I hit the dog with my umbrella”. If the use of a word inappropriately in the test is not Alzh positive but it is concerning. Then surprise the client and ask them to remember the 7 words. If 0 words are remembered the test is Alzh positive. If the last word is remembered then still possibly Alzh positive. 2 words remembered the client is not fully Alzh positive, but possibly senile.
Early Warning Signs: When to Call the Doctor About Alzheimer’s

Are you worried about an older loved one’s memory or behavior? Has your mom been getting lost while running errands? Has your dad started to ask the same questions, over and over? Signs of the early stages of Alzheimer’s disease aren’t always clear-cut -- after all, it can be hard to distinguish them from age-related memory changes.

To help guide you, here are the Alzheimer’s warning signs to watch for, along with advice about seeing a doctor and getting a diagnosis.

Alzheimer Disease Warning Signs

Many people confuse Alzheimer’s disease with dementia. What’s the difference? Alzheimer’s is a disease; dementia is a group of symptoms that include loss of memory, thinking, and reasoning skills. However, dementia isn’t always caused by Alzheimer’s disease; it can be result from other conditions as well.

Although some memory changes may be age-related, memory problems that interfere with daily life are not. According to experts, common early signs of Alzheimer’s disease or other dementias include:

- Memory loss. Although older memories might seem unaffected, people with dementia might forget recent experiences or important dates or events that interferes with daily life. Anyone can forget some details from a recent event or conversation or recall them later. People with dementia might forget the entire thing.
- Repetition. People with dementia may repeat stories, sometimes word for word. They may keep asking the same questions, no matter how many times they’re answered.
- Language problems. We all struggle to remember a word occasionally. People with dementia can have profound problems remembering even basic words. Their way of speaking may become contorted and hard to follow.
- Personality changes. People with dementia may have sudden mood swings. They might become emotional - upset or angry - for no particular reason. They might become withdrawn or stop doing things they usually enjoy. They could become uncharacteristically suspicious of family members -- or trusting of telemarketers.
- Disorientation and confusion. People with dementia may get lost in places they know very well, like their own neighborhoods. They may have trouble completing basic and familiar tasks, like cooking dinner or shaving.
- Lack of hygiene. Sometimes this is the most obvious sign of Alzheimer’s disease. People who have dressed smartly every day of their lives might start wearing stained clothing or stop bathing.
- Odd behavior. We all misplace our keys from time to time. People with Alzheimer's disease and other dementias are prone to placing objects in odd and wholly inappropriate places. They might put a toothbrush in the fridge or milk in the cabinet under the sink.

If your loved one is exhibiting any of these Alzheimer’s warning signs, don't panic. Having these symptoms doesn’t mean that your loved one necessarily has Alzheimer’s disease. But you need to schedule an appointment with the doctor for an evaluation.
10 warning signs of Alzheimer's:

1. **Memory loss that disrupts daily life**

   One of the most common signs of Alzheimer's is memory loss, especially forgetting recently learned information. Others include forgetting important dates or events; asking for the same information over and over; increasingly needing to rely on memory aids (e.g., reminder notes or electronic devices) or family members for things they used to handle on their own.

   **What's a typical age-related change?**
   Sometimes forgetting names or appointments, but remembering them later.

2. **Challenges in planning or solving problems**

   Some people may experience changes in their ability to develop and follow a plan or work with numbers. They may have trouble following a familiar recipe or keeping track of monthly bills. They may have difficulty concentrating and take much longer to do things than they did before.

   **What's a typical age-related change?**
   Making occasional errors when balancing a checkbook.
3 Difficulty completing familiar tasks at home, at work or at leisure

People with Alzheimer's often find it hard to complete daily tasks. Sometimes, people may have trouble driving to a familiar location, managing a budget at work or remembering the rules of a favorite game.

What's a typical age-related change?
Occasionally needing help to use the settings on a microwave or to record a television show.

4 Confusion with time or place

People with Alzheimer's can lose track of dates, seasons and the passage of time. They may have trouble understanding something if it is not happening immediately. Sometimes they may forget where they are or how they got there.

What's a typical age-related change?
Getting confused about the day of the week but figuring it out later.
5 Trouble understanding visual images and spatial relationships

For some people, having vision problems is a sign of Alzheimer’s. They may have difficulty reading, judging distance and determining color or contrast, which may cause problems with driving.

What’s a typical age-related change?
Vision changes related to cataracts.

6 New problems with words in speaking or writing

People with Alzheimer’s may have trouble following or joining a conversation. They may stop in the middle of a conversation and have no idea how to continue or they may repeat themselves. They may struggle with vocabulary, have problems finding the right word or call things by the wrong name (e.g., calling a “watch” a “hand-clock”).

What’s a typical age-related change?
Sometimes having trouble finding the right word.
A person with Alzheimer's disease may put things in unusual places. They may lose things and be unable to go back over their steps to find them again. Sometimes, they may accuse others of stealing. This may occur more frequently over time.

What's a typical age-related change?
Misplacing things from time to time and retracing steps to find them.

People with Alzheimer's may experience changes in judgment or decision-making. For example, they may use poor judgment when dealing with money, giving large amounts to telemarketers. They may pay less attention to grooming or keeping themselves clean.

What's a typical age-related change?
Making a bad decision once in a while.
Withdrawal from work or social activities

A person with Alzheimer’s may start to remove themselves from hobbies, social activities, work projects or sports. They may have trouble keeping up with a favorite sports team or remembering how to complete a favorite hobby. They may also avoid being social because of the changes they have experienced.

What's a typical age-related change?
Sometimes feeling weary of work, family and social obligations.

Changes in mood and personality

The mood and personalities of people with Alzheimer’s can change. They can become confused, suspicious, depressed, fearful or anxious. They may be easily upset at home, at work, with friends or in places where they are out of their comfort zone.

What's a typical age-related change?
Developing very specific ways of doing things and becoming irritable when a routine is disrupted.
Alzheimer’s Diagnostic Tests

Diagnosing Alzheimer’s will likely involve several types of evaluations and may take more than one day. In many cases, specialists may be seen, such as a neurologist, psychologist or psychiatrist, in addition to your primary care doctor, as they may have the knowledge and training needed to evaluate symptoms correctly, accurately, and efficiently.

Evaluations commonly performed include:

Medical history: an interview or questionnaire to identify past medical problems, difficulties in daily activities and any medications (prescriptions, vitamins, supplements and over-the-counter medications), among other things. It is important to inform the doctor of any family history of Alzheimer’s or other related medical issues. The doctor may wish to speak to a close family member to supplement information, as it is important to get a thorough picture of a person’s medical history.

Physical examination: should include evaluations of hearing and sight, heart and lungs, as well as temperature, blood pressure and pulse readings. The doctor might also ask about diet and nutrition and use of alcohol and tobacco products.

Standard laboratory tests: might include blood and urine tests designed to help eliminate other possible conditions. These will measure things like blood count, thyroid and liver function, and levels of glucose and other blood-based indicators of illness. A depression screening should also be conducted. In some cases, a small sample of spinal fluid may be collected for testing.

Neuropsychological testing: Doctors use a variety of tools to assess memory, problem-solving, attention, vision–motor coordination and abstract thinking, such as performing simple calculations in your head. The goal is to better characterize the types of cognitive symptoms present, which might provide clues to the underlying cause. The most commonly used test is called a mini–mental state exam, or MMSE. During the MMSE, the doctor or health professional will ask a number of questions which test a variety of common mental skills. Some examples of questions on the MMSE will ask about the date or the person’s location and also ask the person to count backward or copy a drawn figure.

Brain–imaging scan: MRI and CT scans look at the structure of the brain and are used to rule out brain tumors or blood clots in the brain as the reason for symptoms. PET scans can look at how certain parts of the brain are working or how active they are. Many scientists are trying to determine if other brain–imaging techniques might be able to identify telltale signs of early Alzheimer’s reliably enough to be used as diagnostic tools.

While we have yet to find a cure for Alzheimer’s, or a common medicine that can reverse its effects, a number of natural Alzheimer’s treatments have shown promise in terms of slowing down disease progression and enhancing quality of life Alzheimer’s patients:
Natural Alzheimer’s Treatment #1: Omega-3 fatty acids

Found primarily in fish oil, this ingredient on the list of natural Alzheimer’s treatments has been shown to slow down cognitive degeneration. University of California researchers experimented with mice bred to develop Alzheimer’s symptoms. They found that a DHA diet decreased the presence of specific proteins responsible for neural damage in the brains of these test subjects. The study indicates that DHA supplementation may be helpful in suspending the progression of Alzheimer’s symptoms. DHA is a type of omega-3 fatty acid found in eggs, fish, organ meats and algae.

Natural Alzheimer’s Treatment #2: Vitamin E supplements

A 2009 study presented at the American Geriatrics Society Annual Scientific Meeting showed that a therapy combining high vitamin E doses with a cholinesterase inhibitors slowed down the declining ability of Alzheimer’s patients to perform routine functions. Vitamin E is a viable alternative to other Alzheimer’s treatments but medical providers caution that large doses can be risky. This natural Alzheimer’s treatment should be pursued only under strict supervision by a health care provider. Food sources of vitamin E include nuts, seeds, broccoli and other greens as well as fruit like mangoes.

Natural Alzheimer’s Treatment #3: Lifestyle changes involving diet and exercise

A Mediterranean diet based on whole grains, fish, nuts, fruits, vegetables and healthy oils has been proven to benefit both heart and brain function. In conjunction with regular physical activity, this diet has been shown to reduce cognitive decline and to prevent its early onset. Proper nutrition and staying physically and mentally fit shows promise in slowing the progression of Alzheimer’s symptoms, along with a host of other benefits outside of memory function.

Natural Alzheimer’s Treatment #4: Sensory therapy

With declining cognitive abilities, Alzheimer’s patients can find new ways to communicate with caregivers through various sensory activities. Drama and music are often provided in long-term care facilities as a means of encouraging communication and relaxing the patient. Dance is a low impact physical activity that gives patients a sensory experience. Art activities such as pottery, done in a group setting or as an individual project is another sensory skill that that helps stimulate the mind and work to slow the progression of this disease when used in combination with other Alzheimer’s treatments.

Natural Alzheimer’s Treatment #5: Electro - Acupuncture

The National Institutes of Health and the World Health Organization recognize the efficacy of acupuncture in treating a variety of medical conditions. Limited studies conducted by Wellesley College researchers found that patients affected by mild to moderate Alzheimer’s symptoms reacted positively to acupuncture treatment. Depression and anxiety scores and thinking skills showed a marked improvement. A separate study performed by Hong Kong researchers found enhanced cognitive abilities in Alzheimer’s patients after a series of acupuncture treatments.
**Natural Alzheimer's Treatment #5: Alternative Brain Fuel Coconut Oil**

In this case, insulin problems prevent brain cells from accepting glucose, their primary fuel. Without it, they eventually die. But there is an alternative fuel -- ketones, which cells easily accept. Ketones are metabolized in the liver after you eat medium chain triglycerides, found in coconut oil. Dr. Newport added coconut oil to her husband Steve's diet. Just two weeks later, he took the clock test again and demonstrated stunning improvement.

"I thought at the time, was it just good luck? Was it a lot of prayer? Was it the coconut oil?" she said. "And I thought, well, we're going to keep the coconut oil going." Three weeks later, Steve took the clock test a third time and continued to perform better on it.

And it wasn't just intellectually, he also improved emotionally and physically. "He was not able to run. He was able to run again," she recalled. "He could not read for about a year and a half, but after two or three months he was able to read."

"Instead of being very sluggish, not talking very much in the morning, he would come out in the morning with energy, talkative, and joking, and he could find his water and his utensils," Dr. Newport said. She documented Steve's success in a book titled, Alzheimer's Disease: What If There Was A Cure?
THE BENEFITS OF COCONUT WATER

DID YOU KNOW?

- MINERALS
- VITAMINS
- ELECTROLYTES
- ALKALIZES SYSTEM
- AIDS DIGESTION
- HELPS WITH DIABETES
- ANTIBACTERIAL
- ANTIFUNGAL

Coconut water was used in the 2nd World War as a blood substitute when blood plasma was low.
TREATING ALZHEIMER'S DISEASE with SCIO

Part of the Following:

Large Scale Study of the Safety and Efficacy
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Abstract:

This study demonstrates the safety and effective qualities of the SCIO device used in a large scale study. A large scale study of over 103,000 patients with over 310,000 patient visits reported their diseases. Many of them reported this disease. And the results of their therapy are reported in this study.

Introduction:

Over View:

This Large scale research was designed to produce a extensive study of people with a wide variety of diseases to see who gets or feels better while using the SCIO for stress reduction and patient monitoring. The SCIO is a evoked potential Universal Electro-Physiological Medical apparatus that gauges how a individual reacts to miscellaneous homeopathic substances. The device is registered in Europe, America, Canada, S Africa, Australia, S. America, Mexico and elsewhere. The traditional software is fully registered. Some additional functions where determined by the manufacturer to be worthy of evaluation. Thus a study was necessary to determine safety and efficacy. (As a result of these studies these additional functions are now registered within the EC)

A European ethics committee was officially registered and governmental permission attained to do the insignificant risk study. Qualified registered and or licensed Biofeedback therapists where enlisted to perform the study. Therapists were enrolled from all over the world including N. America, Europe, Africa, Australia, Asia, and S. America. They were trained in the aspects of the study and how to attain informed consent and transmit the results to the ethics committee or IRB (Institutional Review Board).

2,569 therapists enlisted in the study. There were 103,680 patients. 69% had more than one visit. 43% had over two visits. There were over 310,000
patient visits recorded. The therapists were trained and supervised by medical staff. They were to perform the SCIO therapy and analysis. They were to report any medical suspected or confirmed diagnosis. Therapists personnel are not to diagnose outside of the realm of their scope of practice. Then the therapist is to inquire on any reported changes during the meeting and on follow-ups any measured variations. It must be pointed out that the Therapists were free to do any additional therapies they wish such as homeopathy, nutrition, exercise, etc. Therapists were told to not recommend synthetic drugs. Thus the evaluation was not reduced to just the device but to the total effect of seeing a SCIO therapist.

Part 1. The emphasis was on substantiating safety followed by efficacy of the SCIO.

Part 2. Proving the efficacy of the SCIO on diseases (emphasis on degenerative disease)

Part 3. Proving the efficacy of the SCIO on the avant garde therapies of Complementary Med

Part 4. QQC standardization

Methods and Materials:

SCIO Device:

The SCIO is an evoked potential Universal Electro-Physiological Medical device that measures how a person reacts to items. It is designed to measure reactions for allergy, homeopathy, nutrition, sarcodes, nosodes, vitamins, minerals, enzymes and many more items. Biofeedback is used for pre-diagnostic work and or therapy.

The QXCI software will allow the unconscious of the patient to guide to repair electrical and vibrational aberrations in your body. For complete functional details and pictures, see appendix.

Subspace Software:

The QXCI software is designed for electro-physiological connection to the patient to allow reactivity testing and rectification of subtle abnormalities of the body electric. If a patient is not available a subspace or distance healing link has been designed for subspace therapeutics. Many reports of the success of the subspace have been reported and thus the effectiveness and the safety of the subspace link is part of this
test. Many companies have tried to copy the subspace of Prof. Nelson and their counterfeit attempts have ended in failure.

**SOC Index :**

The SCIO interview opens with a behavioral medicine interview. This is called the SOC Index. Named after the work of Samuel Hahnemann the father of homeopathy, he said that the body heals itself with it’s innate knowledge. But the patient can suppress or obstruct the healing process with some behavior. Hahnemann said that the worst way to interfere with the healing natural process was Allopathy or synthetic drugs. Theses upset the natural healing process by unnatural intervention and regulation disturbance. Other ways to Suppress or Obstruct the Cure are smoking, mercury amalgams, stress, lack of water, exercise and many others. This behavioral survey then gives an index of SOC.

The scores relate to the risk of Suppression and Obstruction to the natural Cure. The higher the scores the more the Suppression and or Obstruction. The scores of 100 or lower are ideal. A copy of the SOC index questions appear in the appendix.

**Study Technicians :**

The study technicians were educated and supervised by medical officers. The study technicians were to execute the SCIO therapy and analysis. All were trained to the standards of the International Medical University of Natural Education. Therapists from all over the world including N. America, Europe, Africa, Australia, Asia, S. America and elsewhere were enlisted to perform the study according to the Helsinki study ethics regulations.

They were to chronicle any medical suspected or confirmed diagnosis. Therapists personnel are not to diagnose outside of the realm of their scope of practice. Then the study technician is to inquire on any disclosed observations during the test and on follow-ups report any measured changes.

To test the device as subspace against the placebo effect, two of the 2,500+ therapists were given placebo SCIO devices that were totally outwardly the same but were not functional. These two blind therapists were then assigned 35 patients each (only 63 showed). This was to assess the double blind factor of the placebo effect as compared to the device. Thus the studied groups were A. placebo group, B. subspace group, and C. attached harness group.

Cross placebo group manipulation was used to further evaluate the effect.
Important Questions: these are the key questions of the study

1. Define Diseases or Patient Concerns
2. Percentage of Improvement in Symptoms
3. Percentage of Improvement in Feeling Better
4. Percentage of Improvement Measured
5. Percentage of Improvement in Stress Reduction
6. Percentage of Improvement in SOC Behavior
7. What Measured+How (relevant measures to the patient’s health situation)
8. If Patient worsened please describe in detail involving SOC

After the patient visit is was complete the data was e-mailed to the Ethics Committee or IRB for storage and then analysis. This maneuver minimized the risk of data loss or tampering. Case studies were reported separately in the disease analysis.

MEDICAL DETAILS

Pre-senile dementia with hyaline degeneration of the smaller blood vessels of the brain. Similar to senility.

- Progressive mental deterioration (personality changes, progressive dementia, amnesia, decreased attention span, faulty concentration, loss of abstract thinking, hyperactivity, irritability, difficulty comprehending written and verbal speech)
- Motor disturbances (expressive and receptive aphasia, echolalia, apraxia, spatial disorientation, repetitive movements, slow reflexes, shuffling gait, incontinence)

Mental test can be done by listing 7 common words ask the client to use each word in a sentence. If the use of two or more words are inappropriate then the test is not positive but concerning.

Then ask the client to remember the 7 words. If 6 or less words are remembered the test is positive.

In most cases personal appearance is fine and their room is also well kept without help, although they are disorientated.
Results:

Before we review the direct disease improvement profiles, we need to review the overall results. The first most basic of question in the results is the basic feedback of the generic patient conditions.

1. Percentage of Improvement in Symptoms
2. Percentage of Improvement in Feeling Better
3. Percentage of Improvement Measured
4. Percentage of Improvement in Stress Reduction
5. Percentage of Improvement in SOC Behavior

The SOC index gives us great insight to this study. Each disease has a different cut off where the ability of the SCIO to help was compromised. As a general index scores of 200 + where much less successful.

ALZHEIMER'S DISEASE

This groups significant SOC cut off was 90.

The Large scale study had over 98,000 patients and 275,000 patient visits we have direct evidence of the safety and efficacy. A placebo group was used for the large scale test to help validate the results.

This disease group total number of patients was 219

Subspace Treatment 58 patients, 161 SCIO Harness Patients

OVERALL ASSESSMENT

A. Subspace Treatment 78 patient visits

There were 2 cases of patients who reported a negative Improvement.

None of these cases reported any major difficulty.

There were

2 cases reporting no improvement of Symptoms, .025% of Subgroup
3 cases reporting no improvement in feeling better, .032% of Subgroup
5 cases reporting no improvement in stress reduction .047% of Subgroup

10%---- Percentage of Improvement in Symptoms

4 %--- Percentage of Improvement in Feeling Better

12%---- Percentage of Improvement Measured

21%-- Percentage of Improvement in Stress Reduction

0 %---- Percentage of Improvement in SOC Behavior

B. SCIO Harness Treatment 310 patient visits

There were 1 case of patients who reported a negative Improvement. None of these cases reported any major difficulty. There were

3 cases reporting no improvement of Symptoms, .014 % of Subgroup
1 cases reporting no improvement in feeling better, .006% of Subgroup
3 cases reporting no improvement in stress reduction .013 % of Subgroup

44%---- Percentage of Improvement in Symptoms

55%--- Percentage of Improvement in Feeling Better

69%---- Percentage of Improvement Measured

58%-- Percentage of Improvement in Stress Reduction

34%---- Percentage of Improvement in SOC Behavior

CASE STUDY REPORT CONDENSATION:

"1999 2 Budapest Hu.

A 48 year old man presents with Alzheimer’s. After one session the Alzheimer’s starts to abate. After just three sessions the Alzheimer’s is gone."
“My client is a female 54 years old. She has been diagnosed with Alzheimer’s. When she first came for a biofeedback session she had blank look in her eyes and was very quiet. She was not able to tell me her birthday and other input information. After 5 sessions on the EPFX she is like a different person. She is alert and her eyes are shining. She is remembering and communication with others a lot better. Her family informed me that her whole outlook on life is better.

Mississippi, U.S.A."

“I have been in practice with the EPFX device since May 2007. My first client outside of myself and family members is an elderly gentleman. He is 75 years old, and was in fairly poor health when I began working with him. He had to walk with a cane because of the pain in his back and hips. His doctors had diagnosed him with Alzheimer's disease 10 years ago when his memory started to fail. Around the same time frame, give or take a few years, he was having difficulty with Trigeminal neuralgia. When I started working with him, he was taking Trileptal 600 mg 2x daily, along with four other prescription medications for various ailments. He commented before we began the sessions that he did not think he had Alzheimer's disease, he knew there was something wrong, but that was an incorrect diagnosis in his mind. This is his personal testimonial after only 3 months of sessions on the EPFX device.

"Quantum Healing has really helped me. After 3 months of weekly Biofeedback session and minor alterations in my diet I have got to where I hardly use a cane to get around, also I'm relieved of most of my pain, and my thought process has improved. I highly recommend it!"

Shortly after he wrote that testimony, he went to a new Neurologist that told him the prescription drugs he was taking causes symptoms of Alzheimer's disease. He also offered an alternative to taking the drug. It was slightly invasive because it involved blocking the Trigeminal nerve to stop the pain, rather than taking the drug. He agreed to do the procedure, and within 2 months was off the drug.

Utah, U.S.A."

**USUAL or CUSTOMARY TREATMENT PLAN:**

Metex; Brain Liquescence; Phosphatidyl Choline; Fatty Acid Liquescence; Serotonin_Dopamine Liquescence, Curry, Mustard, Tumeric,

Brain Balance therapy
SCIO TREATMENT SUGGESTED

**Color** - set patient's favorite if desired, or choose color by chakra that is deficient

**Cosmic**: set 1 for physical body, 2 for astral, 3 for etheric, 4 for mental, 5 for cosmic, 6 for other

**Magnetic Method** - 1+10 is universal, 7 for detox, 8 for regrowth of new tissue, 3 for injury, 2 for metabolic correction, 5 for inflammation, 6 for infection, 9 for psych stress, 2 for energy stimulation

**Frequency** - 1k, 555hz, 33hz, 1111hz, 55-1200hz, Auto Trivector for 30 min once a month in early stages once a week in later stage.
Discussion:

The results show significant improvement in symptoms and feeling better. The Collective results show a dramatic benefit to the SCIO therapist visit.

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The SCIO will improve the body electric VARHOPE by five% as an average after just one session. The AutoFocusing Harmonic therapies of the Cybernetic Loop of measuring, stimulating, re-measuring, all guided at maximizing the body electric potential will improve your body electric by an average of five%. Improvements of Voltage, Amperage and thus power. Improvements of Resistance and Hydration that means improved enzyme and osmosis transfer of nutrients and detoxification. Improvements in Oxidation meaning more endurance. And improvement in Ph meaning more health. No wonder there are a mile long list of testimonials. Now we can understand why the sport athletes get such great results. A five% improvement is a great edge for a professional sportsman. The patented and proprietary process of the SCIO and QDC have been proven on the world scientific stage to work wonders of improving and stabilizing the body electric.

If you need more information on the SCIO and purchase details please get in touch with us
Maitreya Kft.
tel: +3613036043 | web: www.qxsubspace.com | e-mail: info@qxsubspace.com
CURRY POWDER
Stimulates the mind and prevents alzheimers while cleaning the kidney

HEALTH BENEFITS of WALKING

- 20 minutes a day will burn 7 pounds of body fat a year
- 45 minutes a day halved risk of catching a cold
- 1 minute can extend life by 1.5+ minutes
- 20 minutes a week can extend life by several years

DEMENTIA
Seniors who walk 5-9 miles/week are less likely to suffer from mental decline as they age, including dementia.

DIABETES
Walking 30 minutes/day, 5 days/week, along with moderate diet changes, can halve the risk of Type 2 Diabetes.

HEART DISEASE
Walking 30 minutes/day, 5 days/week can halve the risk of heart disease and reduce stress, cholesterol, and blood pressure.

ARTHRITIS
Walking can reduce pain and improve function, mobility, mood, and quality of life, without worsening symptoms.

DEPRESSION
Walking triggers endorphins, promotes relaxation, and prevents anxiety and depression.

WALKING 1.5 HOURS/ WEEK REDUCES MORTALITY BY 69% IN WOMEN WITH BREAST CANCER
WOMEN WHO WALK FOR 1 HOUR/ DAY, 5 DAYS/A WEEK AND CONSUME 1,500 CALORIES/DAY CAN LOSE AND KEEP OFF 10 LBS.
WALKING 30 MIN/ DAY, 4 DAYS/A WEEK CAN REDUCE THE RISK OF DIABETES BY NEARLY 60%.
PROSTATE CANCER PATIENTS WHO WALK 30 MIN/NIGHT HAVE NEARLY 50% LOWER MORTALITY RISK.
WOMEN WHO WALK REGULARLY ARE 51% LESS LIKELY TO DEVELOP COLON CANCER THAN THOSE WHO EXERCISE LESS THAN ONE HOUR A WEEK.
Health benefits of Apples

- **Neurological**
  - Prevention of dementia

- **Cardiovascular**
  - Decreased cholesterol level

- **Lungs**
  - Decreased cancer risk

- **Colon**
  - Decreased cancer risk

- **Systemic**
  - Prevention of overweight

- **Prostate**
  - Decreased cancer risk
Health Benefits of Pomegranates

- Keeps blood platelets from sticking together
- Increases oxygen levels to heart
- Anti-inflammatory
- May help combat erectile dysfunction
- Helps lower blood pressure
- Shown to inhibit breast cancer, prostate cancer, colon cancer, and leukemia
- Prevents vascular changes that promote tumor growth in lab animals
- Helps with depression
- Powerful, nutrient-dense food high in antioxidants
- Potent immune support
- May protect against osteoporosis
- May prevent & slow Alzheimer’s
- May reduce PSA levels
- Raises HDL levels
- Enhances oral health

Antioxidant Pomegranate Smoothie | Serves: 2

- 8 C organic baby spinach
- 1 C pomegranate juice
- 1 C blueberries, frozen
- 1 C strawberries, frozen
- 8 dates, cut in half
- 2 tbsp flaxseeds, ground
- 1/2 avocado, optional

Instructions:
- Use organic ingredients.
- Blend all ingredients together. Delish!

11 Health Benefits of Pomegranate Juice 😊

1. Fights Breast Cancer
2. Lung Cancer Prevention
3. Slows Prostate Cancer
4. Keeps PSA Levels Stable
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Aging brain

Age is a major risk factor for most common neurodegenerative diseases, including Mild cognitive impairment, Alzheimer's disease, cerebrovascular disease, Parkinson's disease and Lou Gehrig's disease. While much research has focused on diseases of aging, there are few informative studies on the molecular biology of the aging brain (usually spelled ageing brain in British English) in the absence of neurodegenerative disease or the neuropsychological profile of healthy older adults. However, research does suggest that the aging process is associated with several structural, chemical, and functional changes in the brain as well as a host of neurocognitive changes. This page is devoted to reviewing the changes associated with healthy aging.

Structural Changes

Aging entails many physical, biological, chemical, and psychological changes. Therefore, it is logical to assume the brain is no exception to this phenomenon. Computed Tomography (CT) studies have found that the cerebral ventricles expand as a function of age, and this process is known as ventriculomegaly. More recent MRI studies have reported age-related regional decreases in cerebral volume. Regional volume reduction is not uniform; some brain regions shrink at a rate of up to 1% per year, whereas others remain relatively stable until the end of the life-span. The brain is very complex, and is composed of many different areas and types of tissue, or matter. The different functions of different tissues in the brain may be more or less susceptible to age-induced changes. The brain matter can be broadly classified as either grey matter, or white matter. Grey matter consists of cell bodies in the cortex and subcortical nuclei, whereas white matter consists of tightly packed myelinated axons connecting the neurons of the cerebral cortex to each other and with the periphery.

Loss of Neural Circuits and Brain Plasticity

Brain plasticity refers to the brain's ability to change structure and function. This ties into that old phrase, "if you don't use it, you lose it," which is another way of saying, if you don't use it, your brain will devote less somatotopic space for it. One proposed mechanism for the observed age-related plasticity deficits in animals is the result of age-induced alterations in calcium regulation. The changes in our abilities to handle calcium will ultimately influence neuronal firing and the ability to propagate action potentials, which in turn would affect the ability of the brain to alter its structure or function (i.e. its plastic nature). Due to the complexity of the brain, with all of its structures and functions, it is logical to assume that some areas would be more vulnerable to aging than others. Two circuits worth mentioning here are the hippocampal and neocortical circuits. It has been suggested that age-related cognitive decline is due in part not to neuronal death but to synaptic alterations. Evidence in support of this idea from animal work has also suggested that this cognitive deficit is due to
functional and biochemical factors such as changes in enzymatic activity, chemical messengers, or gene expression in cortical circuits. 

**Thinning of the Cortex**

Advances in MRI technology have provided the ability to see the brain structure in great detail in an easy, non-invasive manner in vivo. Bartzokis *et al.*, has noted that there is a decrease in grey matter volume between adulthood and old age, whereas white matter volume was found to increase from age 19-40, and decline after this age. Studies using Voxel-based morphometry have identified areas such as the insula and superior parietal gyri as being especially vulnerable to age-related losses in grey matter of older adults. Sowell *et al.*, reported that the first 6 decades of an individual's life were correlated with the most rapid decreases in grey matter density, and this occurred over dorsal, frontal, and parietal lobes on both interhemispheric and lateral brain surfaces. It is also worth noting that areas such as the cingulate gyrus, and occipital cortex surrounding the calcarine sulcus appear exempt from this decrease in grey matter density over time. Age effects on grey matter density in the posterior temporal cortex appear more predominantly in the left versus right hemisphere, and were confined to posterior language cortices. Certain language functions such as word retrieval and production were found to be located to more anterior language cortices, and deteriorate as a function of age. Sowell *et al.*, also reported that these anterior language cortices were found to mature and decline earlier than the more posterior language cortices. It has also been found that the width of sulcus not only increases with age, but also with cognitive decline in the elderly.

**Age-Related Neuronal Morphology**

There is converging evidence from cognitive neuroscientists around the world that age-induced cognitive deficits may not be due to neuronal loss or cell death, but rather may be the result of small region-specific changes to the morphology of neurons. Studies by Duan *et al.*, have shown that dendritic arbors and dendritic spines of cortical pyramidal neurons decrease in size and/or number in specific regions and layers of human and non-human primate cortex as a result of age (Duan *et al.*, 2003; morph). Interestingly, a 46% decrease in spine number and spine density has been reported in humans older than 50 compared with younger individuals. An electron microscopy study in monkeys reported a 50% loss in spines on the apical dendritic tufts of pyramidal cells in prefrontal cortex of old animals (27–32 years old) compared with young ones (6–9 years old).

**Neurofibrillary Tangles**

Age-related neuro-pathologies such as Alzheimer's disease, Parkinson's disease, diabetes, hypertension and arteriosclerosis make it difficult to distinguish the normal patterns of aging. One of the important differences between normal aging and pathological aging is the location of neurofibrillary tangles. Neurofibrillary tangles are composed of paired helical filaments (PHF). In normal, non-demented aging, the number of tangles in each affected cell body is relatively low and restricted to the
olfactory nucleus, parahippocampal gyrus, amygdala and entorhinal cortex. As the non-demented individual ages, there is a general increase in the density of tangles, but no significant difference in where tangles are found. The other main neurodegenerative contributor commonly found in the brain of patients with AD is amyloid plaques. However, unlike tangles, plaques have not been found to be a consistent feature of normal aging.

**Role of Oxidative Stress**

Cognitive impairment has been attributed to oxidative stress, inflammatory reactions and changes in the cerebral microvasculature. The exact impact of each of these mechanisms in affecting cognitive aging is unknown. Oxidative stress is the most controllable risk factor and is the best understood. The online Merriam-Webster Medical Dictionary defines oxidative stress as, "physiological stress on the body that is caused by the cumulative damage done by free radicals inadequately neutralized by antioxidants and that is to be associated with aging." Hence oxidative stress is the damage done to the cells by free radicals that have been released from the oxidation process.

Compared to other tissues in the body, the brain is deemed unusually sensitive to oxidative damage. Increased oxidative damage has been associated with neurodegenerative diseases, mild cognitive impairment and individual differences in cognition in healthy elderly people. In ‘normal aging’, the brain is undergoing oxidative stress in a multitude of ways. The main contributors include protein oxidation, lipid peroxidation and oxidative modifications in nuclear and mitochondrial DNA. Oxidative stress can damage DNA replication and inhibit repair through many complex processes, including telomere shortening in DNA components. Each time a somatic cell replicates, the telomeric DNA component shortens. As telomere length is partly inheritable, there are individual differences in the age of onset of cognitive decline.

**DNA Damage**

At least 25 studies have demonstrated that DNA damages accumulate with age in the mammalian brain. These DNA damages include the oxidized nucleoside 8-hydroxydeoxyguanosine (8-OHdG), single- and double-strand breaks, DNA-protein crosslinks and malondialdehyde adducts (reviewed in Bernstein et al.). Increases in DNA damages with age have been reported in the brains of mouse, rat, gerbil, rabbit, dog, and human. Young 4-day-old rats have about 3,000 single-strand breaks and 156 double-strand breaks per neuron, whereas in rats older than 2 years the level of damage increases to about 7,400 single-strand breaks and 600 double-strand breaks per neuron.

Lu et al. studied the transcriptional profiles of the human frontal cortex of individuals ranging from 26 to 106 years of age. This led to the identification of a set of genes whose expression was altered after age 40. They further found that the promoter sequences of these particular genes accumulated oxidative DNA damages, including 8-OHdG, with age (see DNA damage theory of aging). They concluded that DNA damage may
reduce the expression of selectively vulnerable genes involved in learning, memory and neuronal survival, initiating a pattern of brain aging that starts early in life.

### Chemical changes

In addition to the structural changes that the brain incurs with age, the aging process also entails a broad range of biochemical changes. More specifically, neurons communicate with each other via specialized chemical messengers called **neurotransmitters**. Several studies have identified a number of these neurotransmitters, as well as their **receptors**, that exhibit a marked alteration in different regions of the brain as part of the normal aging process.

#### Dopamine

An overwhelming number of studies have reported age-related changes in **dopamine** synthesis, **binding sites**, and number of receptors. Studies using **positron emission tomography** (PET) in living human subjects have shown a significant age-related decline in dopamine synthesis, \[^{[21]}\] notably in the **striatum** and **extrastratal** regions (excluding the **midbrain**). \[^{[22]}\] Significant age-related decreases in dopamine receptors **D\(_1\)**, **D\(_2\)**, and **D\(_3\)** have also been highly reported. \[^{[23][24][25][26][27]}\] A general decrease in **D\(_1\)** and **D\(_2\)** receptors has been shown, \[^{[25]}\] and more specifically a decrease of **D\(_1\)** and **D\(_2\)** receptor binding in the **caudate nucleus** and **putamen**. \[^{[24][27]}\] A general decrease in **D\(_1\)** receptor density has also been shown to occur with age. Significant age-related declines in dopamine receptors, **D\(_2\)** and **D\(_3\)** were detected in the **anterior cingulate cortex**, **frontal cortex**, lateral temporal cortex, **hippocampus**, medial temporal cortex, **amygdala**, **medial thalamus**, and lateral thalamus. \[^{[23]}\] One study also indicated a significant inverse correlation between dopamine binding in the occipital cortex and age. \[^{[24]}\] Postmortem studies also show that the number of **D\(_1\)** and **D\(_2\)** receptors decline with age in both the caudate nucleus and the putamen, although the ratio of these receptors did not show age-related changes. \[^{[26]}\] The loss of dopamine with age is thought to be responsible for many neurological symptoms that increase in frequency with age, such as decreased arm swing and increased **rigidity**. \[^{[28]}\] Changes in dopamine levels may also cause age-related changes in cognitive flexibility. \[^{[28]}\]

#### Serotonin

Decreasing levels of different **serotonin** receptors and the **serotonin transporter**, 5-HTT, have also been shown to occur with age. Studies conducted using PET methods on humans, in vivo, show that levels of the **S\(_2\)** receptor in the caudate nucleus, putamen, and frontal cerebral cortex, decline with age. \[^{[27]}\] A decreased binding capacity of the 5-HT\(_2\) receptor in the frontal cortex was also found, \[^{[28]}\] as well as a decreased binding capacity of the serotonin transporter, 5-HHT, in the thalamus and the midbrain. \[^{[29]}\] Postmortem studies on humans have indicated decreased binding capacities of serotonin and a decrease in the number of **S\(_1\)** receptors in the frontal cortex and hippocampus as well as a decrease in affinity in the putamen. \[^{[29]}\]
Glutamate

Glutamate is another neurotransmitter that tends to decrease with age. Studies have shown older subjects to have lower glutamate concentration in the motor cortex compared to younger subjects. A significant age-related decline especially in the parietal gray matter, basal ganglia, and to a lesser degree, the frontal white matter, has also been noted. Although these levels were studied in the normal human brain, the parietal and basal ganglia regions are often affected in degenerative brain diseases associated with aging and it has therefore been suggested that brain glutamate may be useful as a marker of brain diseases that are affected by aging.

Neuropsychological Changes

Changes in Orientation

Orientation is defined as the awareness of self in relation to one's surroundings. Often orientation is examined by distinguishing whether a person has a sense of time, place, and person. Deficits in orientation are one of the most common symptoms of brain disease, hence tests of orientation are included in almost all medical and neuropsychological evaluations. While research has primarily focused on levels of orientation among clinical populations, a small number of studies have examined whether there is a normal decline in orientation among healthy aging adults. Results have been somewhat inconclusive. Some studies suggest that orientation does not decline over the lifespan. For example, in one study 92% of normal elderly adults (65–84 years) presented with perfect or near perfect orientation. However some data suggest that mild changes in orientation may be a normal part of aging. For example, Sweet and colleagues concluded that "older persons with normal, healthy memory may have mild orientation difficulties. In contrast, younger people with normal memory have virtually no orientation problems" (p. 505). So although current research suggests that normal aging is not usually associated with significant declines in orientation, mild difficulties may be a part of normal aging and not necessarily a sign of pathology.

Changes in Attention

Many older adults notice a decline in their attentional abilities. Attention is a broad construct that refers to "the cognitive ability that allows us to deal with the inherent processing limitations of the human brain by selecting information for further processing" (p. 334). Since the human brain has limited resources, people use their attention to zone in on specific stimuli and block out others.

If older adults have fewer attentional resources than younger adults, we would expect that when two tasks must be carried out at the same time, older adults' performance will decline more than that of younger adults. However, a large review of studies on cognition and aging suggest that this hypothesis has not been wholly supported. While some studies have found that older adults have a more difficult time encoding and retrieving information when their attention is divided, other studies have not found meaningful differences from
younger adults. Similarly, one might expect older adults to do poorly on tasks of sustained attention, which measure the ability to attend to and respond to stimuli for an extended period of time. However, studies suggest that sustained attention shows no decline with age. Results suggest that sustained attention increases in early adulthood and then remains relatively stable, at least through the seventh decade of life. More research is needed on how normal aging impacts attention after age eighty.

It is worth noting that there are factors other than true attentional abilities that might relate to difficulty paying attention. For example, it is possible that sensory deficits impact older adults' attentional abilities. In other words, impaired hearing or vision may make it more difficult for older adults to do well on tasks of visual and verbal attention.

Changes in memory

Main article: Memory and aging

There have been many different types of memory identified in humans, such as episodic, semantic, strategic, working, source spatial, and non-declarative. Studies done by Rapp et al., have found that memory functions, more specifically those associated with the medial temporal lobe are especially vulnerable to age-related decline. A number of studies utilizing a variety of methods such as histological, structural imaging, functional imaging, and receptor binding have supplied converging evidence that the frontal lobes and frontal-striatal dopaminergic pathways are especially affected by age-related processes resulting in memory changes.

Genetic changes

Variation in the effects of aging among individuals can be attributed to both genetic and environmental factors. As in so many other science disciplines, the nature and nurture debate is an ongoing conflict in the field of cognitive neuroscience. The search for genetic factors has always been an important aspect in trying to understand neuro-pathological processes. Research focused on discovering the genetic component in developing AD has also contributed greatly to the understanding the genetics behind normal or "non-pathological" aging.

The human brain shows a decline in function and a change in gene expression. This modulation in gene expression may be due to oxidative DNA damage at promoter regions in the genome. Genes that are down-regulated over the age of 40 include:

- GluR1 AMPA receptor subunit
- NMDA R2A receptor subunit (involved in learning)
- Subunits of the GABA-A receptor
- Genes involved in long-term potentiation e.g. calmodulin 1 and CAM kinase II alpha.
- Calcium signaling genes
- Synaptic plasticity genes
- Synaptic vesicle release and recycling genes

Genes that are upregulated include:

- Genes associated with stress response and DNA repair
- Antioxidant defence

**Delaying the Effects of Aging**

The process of aging may be inevitable, however one may potentially delay the effects and severity of this progression. While there is no consensus of efficacy, the following are reported as delaying cognitive decline:

- High level of education
- Physical exercise
- Staying intellectually engaged, i.e. reading and mental activities (such as crossword puzzles)
- Maintaining social and friendship networks
- Maintaining a healthy diet, including omega-3 fatty acids, and protective antioxidants.

"Super Agers"

Longitudinal research studies have recently conducted genetic analyses of centenarians and their offspring to identify biomarkers as protective factors against the negative effects of aging. In particular, the cholesteryl ester transfer protein (CETP) gene is linked to prevention of cognitive decline and Alzheimer's disease. Specifically, valine CETP homozygotes but not heterozygotes experienced a relative 51% less decline in memory compared to a reference group after adjusting for demographic factors and APOE status.

**Cognitive Reserve**

*Main article: Cognitive reserve*

The ability of an individual to demonstrate no cognitive signs of aging despite an aging brain is called cognitive reserve. This hypothesis suggests that two patients might have the same brain pathology, with one person experiencing noticeable clinical symptoms, while the other continues to function relatively normally. Studies of cognitive reserve explore the specific biological, genetic and environmental differences which make one person susceptible to cognitive decline, and allow another to age more gracefully.

**Nun Study**

*Main article: Nun Study*

A study funded by the National Institute of Aging followed a group of 678 Roman Catholic sisters and recorded the effects of aging. The researchers used autobiographical essays collected as the nuns joined their
Sisterhood. Findings suggest that early idea density, defined by number of ideas expressed and use of complex prepositions in these essays, was a significant predictor of lower risk for developing Alzheimer’s disease in old age. Lower idea density was found to be significantly associated with lower brain weight, higher brain atrophy, and more neurofibrillary tangles.

**Hypothalamus Inflammation and GnRH**

In a very recent study (published May 1, 2013), it is suggested that the inflammation of the hypothalamus may be connected to our overall aging bodies. They focused on the activation of the protein complex NF-κB in mice test subjects, which showed increased activation as mice test subjects aged in the study. This activation not only affects aging, but affects a hormone known as GnRH, which has shown new anti-aging properties when injected into mice outside the hypothalamus, while causing the opposite effect when injected into the hypothalamus. It'll be some time before this can be applied to humans in a meaningful way, as more studies on this pathway are necessary to understand the mechanics of GnRH's anti-aging properties.

Compare with the analog in computer science: software aging

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