Cognitive Enhancement

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Cognitive enhancement is a special topic. The articles cited discuss recent research on the use of natural supplements to enhance mental and cognitive performance in healthy subjects. This protocol is written to support people who wish to boost their mental performance so that they may accomplish more in their lives.

Few research articles focus on performance enhancement in healthy people. Most examine drugs and supplements to combat diseases. The same supplements are often used for both, but the motivation is not the same.

Innovative Drug Strategies

Piracetam

Piracetam is considered to be the "father" of nootropic drugs (cognitive enhancers.) Piracetam has been shown to improve a whole series of mental activities, especially higher cortical functions. It can improve your intelligence, concentration, memory and creativity. Piracetam is a cyclic derivative (2-oxo-pyrrolidine acetamide) of the amino acid GABA (gamma amino butyric acid). Although GABA is an inhibitory neurotransmitter, piracetam does not appear to act in the same way. Piracetam has been shown in studies spanning three decades to:

- enhance memory, particularly when used in combination with choline (Bartus, Dean et al. 1981; Pragina, Voronina et al. 1990; Senin, Abate et al. 1991)
- increase attention and cognition (Gallai, Mazzotta et al. 1991)
- improve spatial learning (Canonico, Aronica et al. 1991)
- improve the use of glucose by the brain (Heiss, Hebold et al. 1988; Heiss, Szelies et al. 1991)
- improve brain circulation (Zykov 1992)
- reduce lipofuscin (age pigment) buildup in the brain (Paula-Barbosa, Brandao et al. 1991)
- act as an antioxidant (Qian, Gu et al. 1992)

One study demonstrated that piracetam facilitates learning and memory in chicks by causing increased plasma levels of corticosterone, which acts on the brain to preserve long-term memories. (Loscertales, Rose et al. 1998)

Unfortunately, piracetam has not been approved by the FDA for any use, despite it's long track record and extensive clinical use in Europe. Piracetam is not available in the US, but can be ordered from offshore pharmacies (see below).

The recommended dose of piracetam is 2400 to 4800 g a day.

Hydergine

Hydergine is a popular "smart drug" that people of all ages use to boost cognitive productivity now, and protect against brain aging in the future. The following mechanisms of action have been proposed:

- Increase blood supply to the brain (Emmenegger and Meier-Ruge 1968)
- Increase the amount of oxygen delivered to the brain (Emmenegger and Meier-Ruge 1968)
- Increase intelligence, memory, learning, and recall (Ditch, Kelly et al. 1971)
- Enhance the use of glucose by brain cells (Nagasawa, Kogure et al. 1990)
- Normalize the brain levels of serotonin (Markstein 1985)
- Enhance metabolism in brain cells (Emmenegger and Meier-Ruge 1968)

Hydergine must be obtained by physician prescription. The recommended dosage is 4 to 10 mg a day.

In 5% of people, Hydergine can induce a mild state of nausea. These people should use Sandoz brand Hydergine LC, an enteric-coated capsule that bypasses the stomach and prevents nausea. The problem with these capsules is that they only come in strengths of 1 mg. For the remaining 95% of people for whom Hydergine does not cause nausea, European suppliers sell 5 mg Hydergine tablets that make taking high doses of Hydergine convenient and very economical.

Centrophenoxine

Centrophenoxine (meclofenoxate) is widely used in Europe in combination with piracetam to improve memory and enhance mental energy. Researchers have proposed several mechanisms for Centrophenoxine, including:

- Increasing activity of free radical scavengers, especially in brain and heart tissues. (al-Zuhair, Abd el-Fattah et al. 1998)
- Providing antioxidant action, possibly due to the DMAE (dimethyl-amino-ethanol) it contains. (Zs-Nagy 1989)
- Increasing acetylcholinesterase activity in the hippocampus and brain. (Sharma and Singh 1995)
- Decreasing the deposition of the age-pigment, lipofuscin, which has been shown to cause neuronal damage. (Patro, Sharma et al. 1992)
- Inhibiting total MAO (monoamine oxidase), MAO-A and MAO-B, which have been shown to damage brain cells. (Stancheva and Alova 1988) Recall that
- Increasing the content of serotonin (5-HT), a key neurotransmitter that can be damaged by elevated MAO. (Stancheva, Petkov et al. 1988).
- Significantly increasing the fluidity of brain membranes, which can reverse the dehydration of nerve cells of older animals. (Lustyik and Nagy 1985;

Wood, Gorka et al. 1986)

One study found that Centrophenoxine significantly improved learning and retention in male albino rats when administered twice a day for 5 days. (Mosharrof, Yonkov et al. 1986)

The recommended dose of Centrophenoxine is 250 to 1000 mg a day.

Picamilon

Picamilon is a Russian drug that improves blood flow to cerebral vessels and enhances energy levels. It is a sodium salt of N-nicotinoyl-gamma-aminobutyric acid (GABA).

The recommended dose of Picamilon is 50 to 100 mg three times a day.

Pyritinol

Pyritinol has been used in Europe to enhance neuronal metabolism in order to help restore youthful cognitive function.

A randomized, double-blind crossover study of 12 healthy men who received 600 or 1,200 mg of pyritinol or placebo for 3 days showed significant improvements in the Critical Flicker Fusion and Choice Reaction Time. (Hindmarch, Coleston et al. 1990)

The recommended dose of Pyritinol is 200 mg three times a day.

Nutritional Supplements

Ginkgo Biloba

Extracts from ginkgo biloba, the "maidenhair tree", have been shown to thin the blood and improve blood flow to the brain, protect against free radicals, and improve memory. Ginkgo biloba is approved in Germany for the treatment of dementia. There are over 1,200 published studies in the scientific literature on ginkgo biloba extract. (Yoshikawa, Naito et al. 1999; DeFeudis and Drieu 2000; Diamond, Shiflett et al. 2000)

One study showed that treating rats with ginkgo biloba extract not only improved their brain function (learning and memory) but also significantly extended their lifespan. (Winter 1998)

A recent article described a 30-day randomized, double-blind, placebo-controlled clinical trial in which 61 participants were administered a battery of validated neuropsychological tests before and after treatment. Statistical analysis indicated significant improvements in speed of information processing working memory, and executive processing attributable to the ginkgo biloba extract. (Stough, Clarke et al. 2001)

An article published in the journal *Psychopharmacology* described a double-blind, placebo controlled, 14-week, trial of 60 mg of a standardized extract of ginkgo biloba and 100 mg of a standardized extract of Panax ginseng. Two hundred and fifty-six healthy middle-aged volunteers successfully completed the study. The ginkgo/ginseng combination was found to significantly improve an Index of Memory Quality. This effect represented an average improvement of 7.5% and reflected improvements to a number of different aspects of memory,

including working and long-term memory. This enhancement to memory was seen throughout the 12-week dosing period. (Wesnes, Ward et al. 2000)

Another article published in the same journal described another experiment with the same ginkgo and ginseng combination on 20 healthy young people. Compared with the placebo, Ginkgo significantly improved cognitive function, particularly the "speed of attention" factor. (Kennedy, Scholey et al. 2000)

A 6-week, double-blind, fixed-dose, placebo-controlled, parallel-group examined the efficacy of 180 mg of ginkgo biloba extract daily on the cognitive functioning of cognitively intact participants between the ages of 55 and 86 years. Participants who received the ginkgo biloba extract exhibited significantly more improvement on a task assessing speed of processing abilities (i.e., Stroop Color and Word Test color-naming task) by the end of treatment as compared to participants who received placebo. Trends favoring improved performances in the ginkgo biloba group were also demonstrated in three of the four remaining tasks that involved a timed, speed of processing component, although they did not reach statistical significance. (Mix and Crews 2000)

The recommended dose of ginkgo biloba extract is 120 mg per day.

Acetyl-L-carnitine

Acetyl-L-Carnitine is the biologically active amino acid involved in the transport of fatty acids into the cell's mitochondria for the purpose of producing energy. It has been shown to improve mood, memory, and cognition.

A recently published article reported on research that showed that acetyl-L-carnitine modulated the use of glucose in the brain of rats. (Aureli, Di Cocco et al. 1998) It was also shown to improve learning and memory processes in studies conducted with laboratory animals. (Bossoni G 1986)

The recommended dose of acetyl-L-carnitine is 1,000 to 2,000 mg a day.

DHA

Docosahexaenoic acid (DHA) is a long chain omega-3 fatty acid that is present in high concentrations in the central nervous system. Fish oil contains both EPA (eicosapentaeonic acid) and DHA.

A recent study evaluated the changes in learning associated with a diet deficient in omega-3 fatty acids. Rats were fed a diet deficient in omega-3 fatty acids for two generations. The second generation omega-3-deficient group had 81% less brain DHA (82% less in the olfactory bulb) and made significantly more errors in a series of olfactory-cued, 2-odor discrimination tasks when compared to the group fed adequate amounts of omega-3 fatty acids. (Greiner, Moriguchi et al. 1999; Greiner, Moriguchi et al. 2001) Another study found that the second and third generation of rats fed a diet deficient in omega-3 fatty acids took longer to escape from a Morris water maze. (Moriguchi, Greiner et al. 2000)

DHA can be found in Life Extension's Super Max EPA (1,000 mg per tablespoon), Mega EPA (300 mg per softgel). The recommended doses are 2 softgels daily of Mega EPA or 1 tablespoon

daily of Super Max EPA.

Choline

Choline is part of the neurotransmitter acetylcholine which is used to send messages between cells.

One study found that cytidine (5') diphosphocholine (CDP-choline) had effects on learning and memory similar to meclofenoxate and piracetam. (Petkov, Mosharrof et al. 1992)

Choline, lecithin, and phosphatidylcholine are best taken early in the day to maximize improvement in brain productivity throughout the day. Suggested dosage ranges are 2,500 to 10,000 mg a day of choline or 10,000 to 15,000 mg a day of lecithin, and/or 1,200 to 6,000 mg a day of phosphatidylcholine.

Pregnenolone and DHEA

Pregnenolone and DHEA improve brain cell activity and enhance memory. (Pregnenolone is converted into DHEA in the body.) Together, pregnenolone and DHEA help to maintain the brain cells' ability to store and retrieve information in short-term memory.

DHEA is the most plentiful steroid hormone in the human body, but its exact function is unknown. What is known is that its concentration plummets with age: its daily production drops from 30 mg at age 20 to less than 6 mg at age 80. DHEA is naturally synthesized in abundance in young people from pregnenolone in the brain and the adrenal glands. It is known to affect the excitability of neurons in the hippocampus, the part of the brain responsible for memory. Current findings suggest that DHEA enhances memory by facilitating the induction of neural plasticity, the condition that permits the neurons (nerve cells of the brain) to change in order to record new memories.

Pregnenolone, pregnenolone sulfate and DHEA were shown to improve memory retention in tests on laboratory animals. (Flood, E. et al. 1992)

The suggested supplementation range for pregnenolone is 50 to 150 mg a day in three equal doses. The recommended dosage for DHEA is 25 to 50 mg a day. Women usually need less DHEA than men.

Recommendations

Innovative Drugs

Take one or a combination of the following drugs:

Piracetam (2,400 to 4,800 mg a day)

Hydergine (4 to 10 mg a day)

Centrophenoxine (250 to 1,000 mg a day)

Picamilon (50 to 100 mg three times a day)

Pyritinol (200 mg three times a day)

Supplements

The following supplements were described in this protocol:

Ginkgo biloba extract (120 mg a day)

Acetyl-L-carnitine (1,000 to 2,000 mg a day)

Choline (250 mg a day)

DHA (500-1000 mg a day)

In addition, the following supplements were covered in the Age-Associated Mental Decline Protocol:

Coenzyme Q10 (100 to 200 mg a day)

Hormones, including DHEA, Pregnenolone, Testosterone, Estrogen and Melatonin.

Antioxidants

B vitamins, including methylcobalamin

Vinpocetine (15 mg a day)

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