Cognitive enhancers

Memory enhancers are often referred to as "**smart drugs**", "**study drugs**",[1] "**smart nutrients**", "**cognitive enhancers**", "**brain enhancers**" or in the scientific literature as **nootropics**.[2] They are drugs that are purported to improve human cognitive abilities.[3][4] The term covers a broad range of substances including drugs, nutrients and herbs with purported cognitive enhancing effects.

The word *nootropic* was coined in 1964 by Dr. Corneliu E. Giurgea, derived from the Greek words *noos*, or "mind," and *tropein* meaning "to bend/turn". Typically, nootropics are thought to work by altering the availability of the brain's supply of neurochemicals (neurotransmitters, enzymes, and hormones), by improving the brain's oxygen supply, or by stimulating nerve growth. However the efficacy of nootropic substances in most cases has not been conclusively determined. This is complicated by the difficulty of defining and quantifying cognition and intelligence.

Contents

Availability

Currently there are several drugs on the market that improve memory, concentration,

planning and reduce impulsive behavior. Many more are in different stages of development.[5] The most commonly used class of drug are the stimulants.[6]

These drugs are used primarily to treat people with cognitive difficulties: Alzheimer's disease, Parkinson's disease, ADHD. However, more widespread use is being recommended by some researchers.[7] These drugs have a variety of human enhancement applications as well and are marketed heavily on the World Wide Web. Nevertheless, intense marketing may not correlate with efficacy; while scientific studies support some of the claimed benefits, it is worth noting that many of the claims attributed to most nootropics have not been formally tested.

Examples

The term "drug" here is used as a legal designation, and does not indicate greater efficacy. With nootropics, the effects, effectiveness, and potency differ from substance to substance and from individual to individual. See the substance descriptions below for more detail.

Stimulants

Stimulants are often seen as *smart drugs*. Their effects are non-specific with similar results seen in children and adults with and without ADHD. One finds improved concentration and behavior in all, but only while the drug is still in the blood.[8][9][10][11] Due to their non-specific activity, stimulants have been used by writers to increase productivity,[12] as well as by the United States Air Force to improve effectiveness in combat.[13] Some scientists recommend wide spread use (of Ritalin and Adderall) by the general population to increase brain power.[6]

- Adrafinil (Olmifon) - Drug.
- Caffeine - Drug. Improves concentration, idea production, but hinders memory encoding. Large amounts produce the jitters. Caffeine is the most widely used psychoactive substance in the world, and may be susceptible to strong levels of tolerance.
- Coffee - Bean. Contains caffeine; brewed coffee is high in antioxidants.
- Nicergoline - Drug. Nicergoline is an ergoloid mesylate derivative used to treat senile dementia. It has also been found to increase mental agility and enhance clarity and perception. It increases vigilance.[14] Increases arterial flow and use of oxygen and glucose in the brain.
- Nicotine - stimulus barrier (aids in concentration). Stimulus barrier rebound effect (an unpleasant side effect).
- Cocaine - Drug. Schedule II. Increase extracellular dopamine and serotonin levels resulting in increased alertness and arousal.
- Methylphenidate (Ritalin) - aids in concentration, focus and stamina. Prescribed for ADHD.
- Dextroamphetamine - (Adderall, Dexedrine) - aids in concentration, focus and stamina. Prescribed for ADHD.
- Modafinil - (Provigil) - Drug.
- Phenibut -
- Theophylline -
- Amphetamines - aids in concentration, focus and stamina. Prescribed for ADHD.
- Carphedon (Phenotropil) -

Replenishing and increasing neurotransmitters

As the brain ages, its ability to produce and maintain youthful levels of neurotransmitters declines.[15] There are various reasons for such an insufficiency. For instance, there might be a lack of enzymes involved in the neurotransmitter synthesis. Nevertheless, in many cases, providing the brain with ample raw materials necessary to make neurotransmitters can restore them to more youthful levels and thus help maintain cognitive function at vigorous youthful levels. Furthermore, there are declines in immune and endocrine functioning.[16] Certain nootropics enhance immune and endocrine functioning.

Cholinergics

Cholinergics are substances that affect the neurotransmitter acetylcholine or the components of the nervous system that use acetylcholine. Acetylcholine facilitates memory, concentration, focus, and high-order thought processes (abstract thought, calculation, innovation, etc.). Increasing the availability of this neurotransmitter in the brain may improve these functions and increase the duration in which they may be engaged without slowing down or stopping. Oversupplying the brain with acetylcholine may have the opposite effect, temporarily reducing rather than improving mental performance. Cholinergic nootropics include acetylcholine precursors and cofactors, and acetylcholinesterase inhibitors:

Piracetam

Piracetam (Nootropil) is the original[17] and most commonly taken[18][17] nootropic supplement. It is a cholinergic agent synergistic with DMAE, Centrophenoxine, choline, Alpha-GPC and Hydergine. It increases brain cell metabolism and energy levels,[19][17] and speeds up interhemispheric flow of information (left-right brain hemisphere communication). It increases alertness,[14] improves concentration, and enhances memory. Protects neurons from hypoxia,[17] and stimulates growth of acetylcholine receptors. It has been shown through various placebo-controlled studies to stimulate arousal and a sense of motivation. It has a role in neurogenesis, and therefore in hippocampus-based learning and memory. Piracetam enhances spatial memory and spatial planning. It may also cause nerves to regenerate. Piracetam markedly decreases the formation of neuronal lipofuscin.[20] It improves posture in elderly people.[21] It is not regulated in the US. It is a pyrrolidone derivative.

Aniracetam

Aniracetam is a pyrrolidone derivative drug, analogous of piracetam, and considered more potent. Like piracetam, aniracetam protects against some memory impairing chemicals, such as diethyldithiocarbamate and clonidine.[22] Also like piracetam, aniracetam may enhance memory in aging adults by increasing levels of brain biogenic monoamines, which are beneficial to learning and memory.[15] Both racetams have possible therapeutic use in treating fetal alcohol syndrome.[23] Aniracetam increases vigilance.[14] Aniracetam has shown to positively potentiate AMPA receptors.

Other cholinergics

- Acetyl-L-carnitine (ALCAR) - Amino acid. Precursor of acetylcholine (donating the acetyl portion to the acetylcholine molecule). It is synergistic with lipoic acid.[24] Inhibits lipofuscin formation.
- Choline - precursor to acetylcholine (an essential component of the acetylcholine molecule).
  - Alpha-GPC (L-alpha glycerylphosphorylcholine, Choline alfoscerate) - most effective choline precursor, readily crosses the blood-brain barrier.
  - Citicoline - less expensive and similar in effect to Alpha GPC. Appears effective in rats.[25][26]
  - Choline bitartrate - precursor of acetylcholine, anti-depressant.
  - Choline citrate - precursor of the neurotransmitter acetylcholine, anti-depressant.
- DMAE - approved treatment for ADD/ADHD, precursor of acetylcholine, cholinergic agent, removes lipofuscin from the brain, anti-depressant.
- Galantamine - acetylcholinesterase inhibitor made from chemical synthesis or extract from plants such as Red Spider Lily (Lycoris radiata).
- Huperzine A - potent acetylcholinesterase inhibitor derived from Chinese club-moss. Recent Cochrane review concluded that it appears to have beneficial cognitive effects with limited side-effects, but more evidence is needed.[27]
- Ispronicline - recently developed selective $\alpha 4\beta 2$ partial agonist
- Lecithin - contains phosphatidylcholine, precursor of acetylcholine.
- Other pyrrolidone derivatives:
  - Etiracetam - It increases vigilance.[14]
  - Nefiracetam - Drug. Analog of piracetam, and facilitates hippocampal neurotransmission.[28]
  - Oxiracetam - Drug. Analog of piracetam, and 2 to 4 times stronger. Improves memory, concentration, and vigilance.
  - Pramiracetam - Drug. Analog of piracetam, and claimed to be 8-30 times stronger. Price is currently much higher than any of the other racetams. Limited availability from international suppliers in pill and bulk form. It is common for users to utilize the lower cost racetams by simply taking a higher dose.
  - In animal studies, nootropics such as piracetam, oxiracetam and aniracetam are known to facilitate the formation of long term memory traces and to restore object recognition in aging rats.[29] There is evidence that the beneficial effect of racetams may result from an interaction with the central glutamatergic receptor function. [29]
- Vitamin B5 - cofactor in the conversion of choline into acetylcholine, cholinergic agent, increases stamina (including mental stamina).

Excess acetylcholine is considered by many to be potentially harmful; see acetylcholinesterase inhibitor.

Acetylcholinesterase inhibitors

Acetylcholinesterase inhibitors function by inhibiting the cholinesterase enzyme which breaks down the neurotransmitter acetylcholine. They exist in the form of poisons and have been used as weapons, but they are also used to treat Alzheimer's patients. Donepezil, galantamine, and Huperzine A are notable among these.

Dopaminergics

Dopaminergics are substances that affect the neurotransmitter dopamine or the

components of the nervous system that use dopamine. Dopamine is produced in the synthesis of all catecholamine neurotransmitters, and is the rate limiting step for this synthesis. Dopaminergic nootropics include dopamine precursors and cofactors (vitamin C and vitamin B6), and dopamine reuptake inhibitors:

- Mucuna pruriens - Seed powder which contains high concentrations of levodopa (L-dopa),[30] a direct precursor of the neurotransmitter dopamine.
- Tyrosine (requires Vitamin B6 and Vitamin C) - Amino acid. Precursor to dopamine, anti-depressant, sleep reducer.
- Lazabemide - a MAO-B inhibitor and has potent membrane lipid antioxidant activity. The antioxidant effects of lazabemide are attributed to its chemical structure and direct physicochemical interactions with the membrane lipid bilayer. It is a potent antioxidant, even more powerful than selegiline (deprenyl) or vitamin E, and is used to treat Alzheimer's disease.[31]
- L-dopa - Prescription drug and dietary supplement. Precursor to the neurotransmitter dopamine, anti-depressant.
- Phenylalanine (requires Vitamin B6 and Vitamin C) - Essential amino acid. Precursor to dopamine, anti-depressant, sleep reducer.
- Selegiline - L-deprenyl is an irreversible MAO-B inhibitor, an enzyme that breaks down dopamine. Thus, it is used to treat Parkinson's disease, and has been tested as a treatment for Alzheimer's disease.[32] It protects against the genotoxin AraC, provides neuroprotection against growth factor withdrawal in PC12 cells, protects against oxidative stress in mesencephalatic neurons, and delays neuronal cell death in the hippocampus after global ischemia.[33]
- Tolcapone - Inhibits COMT (an enzyme that breaks down the neurotransmitters dopamine, epinephrine, and norepinephrine) and increases performance in tasks depending on working memory in individuals with the val/val and val/met genotype of the val158Met polymorphism of the catechol-O-methyltransferase gene, while decreasing it in presence of the met/met version. Tolcapone presents the risk of deadly side effects.
- Yohimbe - Bark. Aphrodisiac. Boosts dopamine levels, though how it does this is not yet understood. Supplements are likely to have no yohimbe in them.[34] Yohimbe poses some health risks through its side-effects: it is a neuro-paralytic which slows down breathing and induces acidosis, some symptoms of which are malaise, nausea, and vomiting. Contraindicated for users of megadoses of acidic vitamins or nutrients.
- Theanine - Found in tea. Increases serotonin and dopamine levels in the brain. Increases alpha-wave based alert relaxation.

Serotonergics

Serotonergics are substances that affect the neurotransmitter serotonin or the components of the nervous system that use serotonin. Serotonergic nootropics include serotonin precursors and cofactors, and serotonin reuptake inhibitors:

- *Griffonia simplicifolia* a natural source of 5-HTP (an alternative in countries where 5-HTP not legal, freely available.)
- Tryptophan (requires Vitamin B6 and Vitamin C) - Essential amino acid. Precursor to serotonin, found in high concentration in bananas and meats, also in milk, promotes relaxed poise and sound sleep. 5-HTP is chemically related to tryptophan.
- $5HT_{2A}$ agonists such as LSD and 2C-T-7 have been shown to produce nootropic effects when used at a dose much lower than a hallucinogenic dose. (e.g. 10 μg for LSD and 1 mg 2C-T-7, 1/25 of a normal recreational dose)

- SSRIs - Class of antidepressants that increase active serotonin levels, ie, in the synaptic junction, by inhibiting its reuptake. Have also been shown to promote Neurogenesis in the hippocampus.

Anti-depression, adaptogenic (antistress), and mood stabilization

Stress, depression, and depressed mood negatively affect cognitive performance. It is reasoned that counteracting and preventing depression and stress may be an effective nootropic strategy.

Below are a list of substances purported to function as nootropics, and claimed effects:

- Beta blockers - anxiolytic [2] (http://www.economist.com/opinion/displaystory.cfm?story_id=11412603) [3] (http://articles.latimes.com/2007/dec/20/science/sci-braindoping20)
- Ashwagandha (*Withania somnifera*) - Root. Also known as Indian ginseng. Adaptogen used as a tonic to normalize body processes and reduce stress and anxiety.
- Inositol - Is a B-vitamin like substance with anti-anxiety effects. It is believed to produce its anti-anxiety effects by improving the binding of gabaergics to $GABA_A$ receptors. Inositol is a sugar, and is therefore an alternative energy source for brain and muscle tissues. It produces a sugar high without a sugar low, making it especially suited for sweetening tea (instead of sugar). It is also a membrane stabilizer which can strengthen (and therefore help protect) neurons.
- Kava kava - The roots of the Kava-Kava plant contain Kavalactones which have GABAergic properties and are used to combat anxiety.[35]
- Lemon Balm (*Melissa officinalis*) - Herb. Anti-depressant.
- Passion Flower is used to treat depression. It is commonly combined with St. John's Wort and Valerian, which work synergistically to reestablish the patients emotional balance without causing tachyphylaxia, hangovers, or addiction. [35]
- Rhodiola Rosea - Herb. Adaptogen; elevates mood, alleviates depression. Promotes mental energy and stamina, reduces fatigue. Boosts dopamine. Slows breakdown of serotonin.
- St John's Wort - Herb. The active components: hypericin and hyperforin, are clinically indicated to be effective in cases of mild to moderate depression, on par with synthetic drugs. However, St John's Wort is not suitable for the treatment of severe depression or suicidal tendencies. Side effects include gastrointestinal complaints and allergic reactions such as pruritus and phototoxicity. [35]
- Ginseng, Siberian (*Eleutherococcus senticosus*) - Root. Anti-anxiety adaptogen that normalizes physical stress and mental consequences.
- Selegiline (Deprenyl) - Along with Piracetam and Meclofenoxate, Deprenyl decreases the amount of lipofuscin pigment and ceroid pigment accumulations in the brain by improving cellular recycling activities.[36] Therefore, these nootropics may slow age-related diseases in the brain. Selegiline, an MAO-B inhibitor, is used as an antioxidant for the treatment of Alzheimer's disease. [31]
- *Sutherlandia frutescens* - Herb. Adaptogen, blood detoxifier.
- Tea - Herb. Contains theophylline and theanine. Increases alpha-wave based alert relaxation (relieves stress).
- Theanine - Amino acid. Found in tea. Increases serotonin and dopamine levels in the brain. Increases alpha-wave based alert relaxation. Also stimulates the GABAergic system.
- Tianeptine - Anxiolytic anti-depressant. It enhances working and reference memory in rats.[37]
- Vasopressin - Drug. Memory hormone produced by the pituitary gland which

improves both memory encoding and recall. Rapidly counters chronic apathy syndrome and drug-induced vasopressin depletion.
- Niacin - Mood stabilizer, with a powerful anti-anxiety effect — perhaps the best and most immediate stress reliever available (note that other forms of vitamin B do not have this effect). Side effects: gastric upset (which is easily prevented and relieved with antacids), reduced blood pressure and flushing of the skin (caused by vasodilation), and itchy sensation in the skin caused by histamine release.
- Picamilon - Crosses the blood-brain barrier and metabolizes into Niacin and GABA. The GABA might flood the brain producing an anti-anxiety effect while the Niacin is a strong vasodialator and anti-anxiolytic.
- Vitis vinifera (Grape Seed) Grape seed has antistress (adaptogenic) activity, protects against memory loss induced by scopolamine, is an antioxidant, has nootropic activities, and supports the traditional claims for the use of grape fruits and seeds in stress induced disorders. [38]

Brain function and improved oxygen supply

- Chromium- stabilises blood sugar levels promoting concentration.
- Coenzyme q-10 syn. Ubiquinone - increases oxygen transport through the mitochondria of the cells.
- Creatine - increases brain energy levels via ATP production.
- Inositol - B vitamin which synergizes with other nootropics
- Lipoic acid - synergistic with Acetyl-L-carnitine.
- Pyritinol (Enerbol) - Drug. Enhances oxygen and glucose uptake in the brain, and allows glucose to pass more easily through the blood-brain barrier. It is also a powerful anti-oxidant which scavenges hydroxyl radicals created in the very processes it is involved in.
- Vinpocetine - Vinpocetine increases blood circulation and metabolism in the brain. Animal studies have shown that vinpocetine can reduce the loss of neurons due to decreased blood flow. [17]
- Prazosin - Alpha-blocking blood pressure medication also prescribed as an anti-PTSD medication, appears to block the increase of steroid hormones known as glucocorticoids, Oregon Health & Science University and Portland Veterans Affairs Medical Center researchers have found. Elevated levels of glucocorticoids are associated with atrophy in nerve branches where impulses are transmitted, and even nerve cell death, in the hippocampus.

Purported memory enhancement and learning improvement

All of the "nergics" listed above are purported to improve memory (encoding and recall), as do all nootropics which improve general brain performance in categories such as the brain energy and oxygen supply, and nerve growth stimulation and protection. Other agents purported to have these specific benefits are mentioned in their own sections.

Other nootropics with specific effects on memory encoding and recall include:

- *Bacopa monniera* (Brahmi) - Herb. Elevates curiosity, enhances memory and concentration.[39] Brahmi also protects against amnesia inducing chemicals such as scopolamine or loss of memory due to electro convulsive shocks.[39] Improves protein synthesis in brain cell repair and new dendritic growth. It is a traditional ayurvedic medicine.
- *Brahmi rasayana* - improved learning and memory in mice.[40]
- Rosemary - Herb. Rosemary has a very old, albeit unverified, reputation for

improving memory.
- Vasopressin - Hormone, prescription drug.
- Dextroamphetamine- Adderall, Dexedrine.[41]
- Nicotine - Improves working memory and learning[42]
- *Sage* - a study of young adults found that *Salvia lavandulaefolia* improves word recall;[43] a randomized trial has found that *Salvia officinalis* improves symptoms in Alzheimer's patients[44]

Nerve growth stimulation and brain cell protection

- Ergoloid mesylates (Hydergine) - Drug. Mimics nerve growth factor (NGF), and is a powerful anti-oxidant capable of delaying brain death in cases of heart failure and stroke by several minutes with regular use. It increases vigilance.[14]
- Idebenone - stimulates nerve growth, and has same effects as Coenzyme q-10.
- Inositol - Membrane stabilizer. Strengthens neurons, making them less susceptible to damage.
- Pyritinol (Enerbol) - Drug. Powerful anti-oxidant which scavenges hydroxyl radicals.
- Rasagiline (Azilect) - Drug. Treats Parkinson's disease either as monotherapy (by itself) or in addition to levodopa therapy. Promotes increased and sustained levels of dopamine by selectively inhibiting an enzyme, monoamine oxidase-B.
- Tetrahydrocannabinol (Cannabis and THC) - Tetrahydrocannabinol, one of the main active psychoactive chemicals in the cannabis plant, has been shown to be neuroprotective.[45] It has been shown that cannabinoids closely related to THC cause cell growth, which has led some researchers to hypothesize that THC may have similar cell growth potential.[46]

Recreational drugs with purported nootropic effects

See also: Controlled substances act and Misuse of Drugs Act 1971

- Amphetamine-type stimulants (such as Adderall, Dexedrine, Desoxyn, *etc.*) are Schedule II controlled substances in the United States, and Class B drugs in the United Kingdom, with comparable legal controls in effect in most countries throughout the world. They are prescribed for attention-deficit disorders, narcolepsy, and certain cases of obesity; and are issued to counteract fatigue and to enhance performance for pilots in the armed forces of the United States of America.[47][48] These also heighten alertness, mental focus, vigilance, stamina, and sex drive. They tend to be habit-forming, and exhibit side effects with prolonged or heavy use. Personal importation of amphetamine-class drugs is prohibited in many countries, and their use for recreation or for performance enhancement without a medical prescription is likewise illegal in most countries.
- LSD - Psychedelic drug. At higher doses, sensory effects seem qualitatively different. Many psychedelic drugs are purported to produce this overwhelming effect on the mind. Aldous Huxley called this state of mind "Mind at Large". Activity in the Raphe Nuclei and Locus ceruleus increases dramatically following administration of LSD to produce extremely heightened creativity in many users. This effect on the creative process is a phenomenon that may be due to ascending traffic in the reticular activation system, which can result in stimulus overload.[49] Also produces hallucinogenic and entheogenic effects at doses as low as 30–40 μg (micrograms), with the likelihood of having a *bad trip* increasing as dose is increased if these effects are undesired. May also cause cognitive shifts, and synesthesia The drug sometimes spurs long-term or even permanent changes in a user's personality and life perspective. (*For more details, see Albert Hofmann: LSD - My Problem Child*

(http://www.maps.org/books/mpc/index.html) .)

- 4-methylaminorex
- Pemoline (Cylert)
- Psilocybin and Psilocin
- MDPV
- Mescaline
- 2C-D

Dietary nootropics

Some regular food items are rich sources of substances with alleged nootropic benefits:

- Nuts, in particular walnuts, are rich sources of alpha-linolenic acid (ALA), a type of omega-3 fatty acid. A mixture of walnuts served with dried fruit pieces is known in some regions as student food (orig. German: *Studentenfutter*) and is popularly recommended as a snack for students.
- Oily fish, such as salmon or fresh tuna (not tuna canned in oil) are also good sources of omega-3 fatty acids such as eicosapentaenoic acid and docosahexaenoic acid, whose lack in diet has been associated with increased risk of mental illnesses such as depression, anxiety, aggressive behavior, schizophrenia, or hyper-activity in children (see omega-3 fatty acids article)
- Berries containing high levels of anthocyanins have nootropic effects.[50] Blueberries, blackberries and raspberries are among those with the highest anthocyanin content.[51] These foods act through a combination of neuroprotective and neurogenesis effects. [52]

Other nootropics

- Adafenoxate - Has an anti-anxiety effect for rats[53] and possibly the same for humans.
- Moderate use of alcohol - Moderate drinking has been associated with better cognitive ability than both abstention and heavy drinking.[54][55][56][57][58]
- *Butea frondosa* - "The plant *Butea frondosa* has been indicated in the Indian system of medicine as a plant augmenting memory and as a rejuvenator. ... *B. frondosa* possesses anti-stress and weak nootropic activity."[59]
- Cabergoline (Dostinex) - An ergot derivative, is a potent dopamine receptor agonist on D2 receptors. Maybe carcinogenic.
- Cinnarizine - increases oxygen via calcium channel blockage.
- Coluracetam - It may also have potential use in prevention and treatment of ischemic retinopathy and retinal and optic nerve injury
- Desmopressin (DDAVP) - Analog of vasopressin, a neuropeptide responsible for memory.
- DHEA - Hormone created by the adrenal glands; Precursor to Estrogen and Testosterone
- Dostinex - (see Cabergoline above)
- Fasoracetam - A nootropic drug of the racetam family.
- Essential Fatty Acids- Eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are the best known. EPA in particular, has an anti-depressant function and is positively indicated in trials with autism and learning difficulties
- Fipexide (Vigilor) - It protects against some memory impairing chemicals, such as diethyldithiocarbamate and clonidine.[22]
- Gerovital H3 - Romanian anti-aging formula containing procaine hydrochloride, but which breaks down into PABA and DMAE.

- Gotu Kola - Herb and root.
- Meclofenoxate - Has an anti-anxiety effect for rats[53] and possibly the same for humans. Like Fipexide, it protects against some memory impairing chemicals, such as diethyldithiocarbamate and clonidine.[22] Like many racetams, it may treat fetal alcohol syndrome.[23]
- Nimodipine - A dihydropyridine calcium channel blocker originally developed for the treatment of high blood pressure.
- Ondansetron (Zofran) - A serotonin 5-HT3 receptor antagonist used mainly as an antiemetic to treat nausea and vomiting following chemotherapy.
- Phenytoin (Dilantin) - A neuroleptic and anti-seizure medication advocated by Jack Dreyfus for a variety of psychological conditions.
- Phosphatidylserine- In animals, PS has been shown to attenuate many neuronal effects of aging, and to restore normal memory on a variety of tasks. [17]
- Picamilon or Pikamilone - Compound of Niacin and GABA. It can pass the blood-brain barrier and increase amount of GABA in the brain.
- Pregnenolone - Hormone; Precursor to DHEA;
- Pyroglutamate - An amino acid shown to improve learning.
- Somatotropin - Growth hormone, a polypeptide containing 191 amino acids, produced by the anterior pituitary, the front section of the pituitary gland. It acts by stimulating the release of another hormone called somatomedin by the liver, thereby causing growth.
- Sulbutiamine (Arcalion) - Drug - derivative of thiamine (vitamin B1) that can cross the blood-brain barrier and work as anti-fatigue and cognitive support agent.
- Turmeric - has possible benefits in Alzheimer's disease, cancer and liver disorders. Turmeric, under the name Avea, is becoming popular to treat depression.
- MDL 26,479[60]
- Propentofylline
- Brain Toniq - a nootropic beverage that contains effective doses of Rhodiola rosea, Eleutherococcus senticosus, Choline, and DMAE.

Contentious or possibly unsafe nootropics

- Royal Jelly - Produced by bees for the Queen. Can cause fatal allergic reactions if allergic to bee products. Shown to dramatically increase nerve stem cell growth and differentiation of mice nerve cells - in vitro (petri dish).
- *Ginkgo biloba* - Patients with dementia treated with Ginkgo showed significant improvement of symptoms like memory loss, concentration difficulties, fatigue, anxiety and depressive mood.[35] As a vasodilator, it should not be taken with aspirin, for doing so could increase the risk of bleeding.[61] Ginkgo is widely used in Europe to treat subjective tinnitus, although there is as yet no hard evidence supporting this assertion.[61] Ginkgolides are extracts from the leaves of the tree. They produce a beneficial effect for Alzheimer's disease, and for amyloid-B, the toxic prion protein, which suggests they could be relevant to treating those diseases.[62]
- Arecoline

See also

Brain and neurology

- Action potential
- Neurite

- Aging and memory
- Brain
- Central nervous system (CNS)
- Dendrite
- Human brain
- Long-term potentiation
- Nervous system
- Neuron
- Neuroplasticity
- Neuroscience
- Neurotransmitter
- Sensory neuroscience
- Synapse
- Synaptic plasticity
- List of nootropics (smart drugs)

Thought and thinking (what nootropics are used for)

- Abstract thinking
- Attention
- Attitude
- Brainstorming
- Cognition
- Cognitive science
- Creative thinking
- Critical thinking
- Curiosity
- Decision
- Decision making
- Eidetic memory
- Emotions and feelings
- Emotional intelligence
- Goals and goal setting
- Idea
- Imagination
- Intelligence
- Introspection
- Lateral thinking
- Learning
- Memory
- Memory-prediction framework
- Mental calculation
- Mind's eye
- Mindset
- Mood
- Motivation
- Perception
- Personality
- Picture thinking
- Problem shaping
- Problem solving
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- Recollection (recall)
- Self-reflection
- Thought
- Visual thinking

Health

- Anxiety
- Cognitive psychology
- Clinical depression
- Confusion
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  - Prescription drug
  - Prohibition (drugs)
  - Psychoactive drug (aka psychotropic drug)
  - Psychedelic drug
- Human enhancement
  - Ergogenic aid
- Life extension
- Neurodegenerative disease
  - Alzheimer's disease
  - Parkinson's disease
- Nutrition
- Sleep disorders
- Stress
- Stress management

References

1. ^ [1] (http://www.npr.org/templates/story/story.php?storyId=100254163)
2. ^ Pronounciation (http://cougar.eb.com/soundc11/n/nootr01m.wav)
3. ^ "Dorlands Medical Dictionary". http://web.archive.org/web/20080130031824/http://www.mercksource.com/pp/us/cns/cns_hl_dorlands.jspzQzpgzEzzSzppdocszSzuszSzcommonzSzdorlandszSzdorlandzSzdmd_n_10zPzhtm.
4. ^ Lanni C, Lenzken SC, Pascale A, *et al* (March 2008). "Cognition enhancers between treating and doping the mind". *Pharmacol. Res.* **57** (3): 196–213. doi:10.1016/j.phrs.2008.02.004. PMID 18353672.
5. ^ Sahakian B, Morein-Zamir S (December 2007). "Professor's little helper". *Nature* **450** (7173): 1157–9. doi:10.1038/4501157a. PMID 18097378.
6. ^ **a b** ""Towards responsible use of cognitive-enhancing drugs by the healthy" in *Nature: International Weekly Journal of Science*". http://www.nature.com/nature/journal/vaop/ncurrent/full/456702a.html. Retrieved on December 2008.
7. ^ "Scientists back brain drugs for healthy people - Yahoo! News". http://news.yahoo.com/s/ap/20081207/ap_on_he_me/med_brain_pills_1.
8. ^ Clayton, Paula J.; Fatemi, S. Hossein (2008). *The medical basis of psychiatry*. Totowa, NJ: Humana Press. ISBN 1-58829-917-1. http://books.google.com/books?id=RJOy1vy2RKQC&pg=PA318&dq=stimulants+improve+academic+performance&ei=H1kqSdeSJIGklQSHjq2OBA#PPA318,M1.
9. ^ "Medscape & eMedicine Log In". http://www.medscape.com/viewarticle/442882_5.
10. ^ Rapoport JL, Buchsbaum MS, Weingartner H, Zahn TP, Ludlow C, Mikkelsen EJ (August 1980). "Dextroamphetamine. Its cognitive and behavioral effects in normal and hyperactive boys and normal men". *Arch. Gen. Psychiatry* **37** (8): 933–43. PMID 7406657.
11. ^ Rapoport JL, Buchsbaum MS, Zahn TP, Weingartner H, Ludlow C, Mikkelsen EJ (February 1978). "Dextroamphetamine: cognitive and behavioral effects in normal prepubertal boys". *Science (journal)* **199** (4328): 560–3. PMID 341313. http://www.sciencemag.org/cgi/pmidlookup?view=long&pmid=341313.
12. ^ "My romance with ADHD meds. - By Joshua Foer - Slate Magazine". http://www.slate.com/id/2118315/.
13. ^ "Air force rushes to defend amphetamine use - theage.com.au". http://www.theage.com.au/articles/2003/01/17/1042520778665.html.
14. ^ **a b c d e** Saletu, B. and Grunberger, J. (1985). "Memory dysfunction and vigilance: neurophysiological and psychopharmacological aspects". *Annals of the New York Academy of Sciences* **444** (1): 406–27. doi:10.1111/j.1749-6632.1985.tb37604.x. PMID 3860093. http://www.annalsnyas.org/cgi/content/abstract/444/1/406.
15. ^ **a b** Stancheva, S.L., Petkov, V.D., Hadjiivanova, C.I., and Petkov, V.V. (1991). "Age-related changes of the effects of a group of nootropic drugs on the content of rat brain biogenic monoamines". *Gen. Pharmacol.* (Department of Experimental Pharmacology, Bulgarian Academy of Sciences, Sofia) 22 **(5): 873–7. http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=1761194&dopt=Citation.**
16. ^ Milton Hideaki Arai, Alberto JS Duarte, and Valeria Maria Natale, Disciplina de Clínica Geral do Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo, Brazil (25 August 2006). "The effects of long-term endurance training on the immune and endocrine systems of elderly men: the role of cytokines and anabolic hormones". *Immunity & Ageing* **3** (9). http://www.worldhealth.net/p/the-effects-of-long-term-endurance-training-on-the-immune-and-endocrine-systems-of-elderly-men-the-role-of-cytokines-and-anabolic-hormones-2006-10-09.html.
17. ^ **a b c d e f** McDaniel, M.A., Maier, S.F., and Einstein, G.O. (2002). "Brain-Specific Nutrients: A Memory Cure?". *Psychological Science in the Public Interest* (American Psychological Society) 3 **(1). http://www.sciencedirect.com/science?_ob=ArticleURL&_udi=B6TB0-4B0KTYF-C&_coverDate=12%2F31%2F2003&_alid=448998985&_rdoc=1&_fmt=&_orig=search&_qd=1&_cdi=5128&_sort=d&view=c&_acct=C000050221&_version=1&_urlVersion=0&_userid=10&md5=f99a155c658f3be9a94cc485fbf37262.**
18. ^ Goldman, R., Klatz, R., and Berger, L. (1999). *Brain fitness*. New York: Doubleday.
19. ^ Gabryel, B. and Trzeciak, H.I. (1994). "Nootropics: Pharmacological properties and therapeutic use". *Polish Journal of Pharmacology* **46**: 383–394. http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?

cmd=Retrieve&db=PubMed&list_uids=7894524&dopt=Citation.
20. ^ Paula-Barbosa, M.M., Brandao, F., Pinho, M.C., Andrade, J.P., Madeira, M.D., and Cadete-Leite, A. (1991-10-01). "The effects of piracetam on lipofuscin of the rat cerebellar and hippocampal neurons after long-term alcohol treatment and withdrawal: a quantitative study". *Alcohol Clin. Exp. Res.* **15** (5): 834–8. doi:10.1111/j.1530-0277.1991.tb00610.x.
21. ^ Riedel, W.J., Peters, M.L., Van Boxtel, M.P.J., and O'Hanlon, J.F. (1998-12-04). "The influence of piracetam on actual driving behaviour of elderly subjects". *Human Psychopharmacology: Clinical & Experimental* **13** (S2): S108–14. doi:10.1002/(SICI)1099-1077(1998110)13:2 <S108::AID-HUP55>3.0.CO;2-R (inactive 2008-06-21). http://www3.interscience.wiley.com/cgi-bin/abstract/4292/ABSTRACT?CRETRY=1&SRETRY=0.
22. ^ **a b c** Genkova-Papasova, M. and Lazarova-Bakurova, M. (1988). "Influence of nootropic drugs on the memory-impairing effect of diethyldithiocarbamate and clonidine in "step down" passive avoidance in albino rats". *Acta Physiol. Pharmacol. Bulg.* (Institute of Physiology, Bulgarian Academy of Sciences) 14 **(4): 36–41. http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=2854355&dopt=Citation.**
23. ^ **a b** Vaglenova, J. and Petkov, V.V. (February 2001). "Can nootropic drugs be effective against the impact of ethanol teratogenicity on cognitive performance?". *European Neuropsychopharmacology* **11** (1): 33–8. doi:10.1016/S0924-977X(00)00129-2. http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11226810&dopt=Citation.
24. ^ Liu J, Killilea DW, Ames BN. "Age-associated mitochondrial oxidative decay: improvement of carnitine acetyltransferase substrate-binding affinity and activity in brain by feeding old rats acetyl-L- carnitine and/or R-alpha -lipoic acid." Proc Natl Acad Sci U S A. 2002 February 19; 99(4): 1876–1881.
25. ^ http://www.pubmedcentral.nih.gov/articlerender.fcgi?tool=pmcentrez&artid=548494
26. ^ Changes in brain striatum dopamine and acetylcholine receptors induced by chronic CDP-choline treatment of aging mice. (http://www.pubmedcentral.nih.gov/articlerender.fcgi?tool=pmcentrez&artid=1908237)
27. ^ PMID 18425924
28. ^ Nomura, T. and Nishizaki, T. (2000-07-07). "Nefiracetam facilitates hippocampal neurotransmission by a mechanism independent of the piracetam and aniracetam action". *Brain Res.* (Department of Physiology, Kobe University School of Medicine. Kobe, Japan) 870 **(1–2): 157–62. http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10869513&dopt=Citation.**
29. ^ **a b** Zdenek Hlinak and Ivan Krejci (18 July 2000). "Oxiracetam prevents the MK-801 induced amnesia for the elevated plus-maze in mice". *Behavioral Brain Research* **117**: 147–151. doi:10.1016/S0166-4328(00)00298-9.
30. ^ Medical Toxicology (http://books.google.com/books?id=qDf3AO8nILoC)
31. ^ **a b** R. Preston Mason, Edwin G. Olmstead Jr., and Robert F. Jacob (2000). "Antioxidant Activity of the Monoamine Oxidase B Inhibitor Lazabemide". *Biochemical Pharmacology* **60**: 709–716. doi:10.1016/S0006-2952(00)00374-9.
32. ^ Selegiline in the treatment of Alzheimer's disease: a long-term randomized placebo-controlled trial. Czech and Slovak Senile Dementia of Alzheimer Type Study Group. (http://www.pubmedcentral.nih.gov/articlerender.fcgi?tool=pmcentrez&artid=1189014)
33. ^ Tiina Suuronen, Petri Kolehmainen, and Antero Salminen, Department of Neuroscience and Neurology, University of Kuopio, Finland. (2000). "Protective Effect of L-Deprenyl against Apoptosis Induced by Okadaic Adic in Cultured Neuronal Cells". *Biochemical Pharmacology* **59**: 1589–1595. doi:10.1016/S0006-2952(00)00282-3. http://www.ihop-net.org/UniPub/iHOP/pm/8443936.html?pmid=10799657.
34. ^ An evidence-based approach to dietary supplements for ED (Part 2 of 2) (http://www.modernmedicine.com/modernmedicine/article/articleDetail.jsp?id=112017)
35. ^ **a b c d** Susanne Kienzle-Horn (2002). "Herbal medicines for neurological diseases" (PDF). *Current Opinion in Investigational Drugs* **3** (5): 763–767. http://www.biomedcentral.com/content/pdf/cd-451283.pdf.
36. ^ Riga, D. and Riga, S. (1995). "Brain lipofuscinolysis and ceroidolysis--to be or not to be". *Gerontology* (Institute of Neurology and Psychiatry, Bucharest, Romania) 41 **(S2): 271–81. http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=8821338&dopt=Abstract.**
37. ^ "Tianeptine (Stablon, Coaxil) : an unusual antidepressant". Tianeptine.com. http://www.tianeptine.com/profile.html. Retrieved on 2008-11-14.

38. ^ Sreemantula et al. (19 January 2005). "Adaptogenic and nootropic activities of aqueous extract of Vitis vinifera (grape seed): an experimental study in rat model". *BMC Complementary and Alternative Medicine* **5** (1): 1. doi:10.1186/1472-6882-5-1.
39. ^ **a b** Singh, H.K. and Dhawan, B.N. (1997). "Neuropsychopharmacological effects of the Ayurvedic nootropic *Bacopa monniera* Linn. (Brahmi)". *Indian Journal of Pharmacology* **29** (5): 359–65. http://ijp-online.com/article.asp?issn=0253-7613;year=1997;volume=29;issue=5;spage=359;epage=365;aulast=Singh;type=0.
40. ^ Brahmi rasayana Improves Learning and Memory in Mice (http://www.pubmedcentral.nih.gov/articlerender.fcgi?tool=pmcentrez&artid=1375237&rendertype=abstract)
41. ^ Rapoport, J.L., Buchsbaum, M.S., Zahn, T.P., Weingartner, H., Ludlow, C., and Mikkelsen, E.J. (1978). "Dextroamphetamine: cognitive and behavioral effects in normal prepubertal boys". *Science* **199** (4328): 560–3. doi:10.1126/science.341313. PMID 341313.
42. ^ Edward D. Levin, F. Joseph McClernon and Amir H. Rezvani1. "Nicotinic effects on cognitive function: behavioral characterization, pharmacological specification, and anatomic localization". *Psychopharmacology* **184**: http://www.springerlink.com/content/y41lg2qj24xvvh31/.
43. ^ PMID 12895685
44. ^ PMID 12605619
45. ^ Journal of Neuroscience http://www.jneurosci.org/cgi/content/full/21/17/6475
46. ^ New Scientist http://www.newscientist.com/article.ns?id=dn8155
47. ^ D. BROWN *et al.*, "Performance Maintenance During Continuous Flight Operations - A Guide for Flight Surgeons" (http://navymedicine.med.navy.mil/Files/Media/directives/6410.pdf) ; NAVMED-P6410, 1st. Ed., January 1, 2000; (US) Naval Strike and Air Warfare Center; pp. 4, 10–18, 38, 55.
48. ^ CHOATE *et al.*, "Amphetamine's prescribed use defended by Air Force, M.D." (http://www.globalsecurity.org/org/news/2006/060926-usaf-amphetamines.htm) ; Abilene Reporter News, September 26, 2006. (republished by GlobalSecurity.Org at "http://www.globalsecurity.org/org/news/2006/060926-usaf-amphetamines.htm", accessed February 27, 2008)
49. ^ Bacon, et al., "The Effect of LSD on the Human Brain" (http://www.cem.msu.edu/~cem181h/projects/96/lsd/drug.html) , 1996. Retrieved October 16, 2007
50. ^ Berries & Memory. www.oneirics.com (http://www.oneirics.com/articleberry.html) . Accessed 8/24/08
51. ^ Wu X, Beecher G, Holden J, Haytowitz D, Gebhardt S, Prior R. Concentrations of Anthocyanins in Common Foods in the United States and Estimation of Normal Consumption. J. Agric. Food Chem. 2006, 54, 4069-4075
52. ^ McGuire S, Sortwll C, Shukitt-Hale B, Joseph J, Hejna M, Collier T. Dietary supplementation with blueberry extract improves survival of transplanted dopamine neurons. Nutr Neurosci. 2006; 9 (5-6):251-8
53. ^ **a b** Petkov, V.D., Getova, D., and Mosharrof, A.H. (1987). "A study of nootropic drugs for anti-anxiety action". *Acta Physiol. Pharmacol. Bulg.* (Institute of Physiology, Bulgarian Academy of Sciences, Sofia) 13 **(4): 25–30. http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=2896427&dopt=Citation.**
54. ^ Britton, A., Singh-Manoux, A., Marmot, M. Alcohol consumption and cognitive function in the Whitehall II Study. American Journal of Epidemiology,2004 Aug 1;160(3):240-7.
55. ^ Launer LJ, Feskens EJ, Kalmijn S, Kromhout D Smoking, drinking, and thinking. The Zutphen Elderly Study American Journal of Epidemiology 1996 Feb 1;143(3):219-27
56. ^ Galanis, DJ; Joseph C, Masaki KH, Petrovitch H, Ross GW, White L A longitudinal study of drinking and cognitive performance in elderly Japanese American men: the Honolulu-Asia Aging Study American Journal of Public Health Vol 90, Issue 8 1254-1259
57. ^ Dufouil, Carole; Ducimetière, Pierre; Ducimetière, Pierre Sex Differences in the Association between Alcohol Consumption and Cognitive Performance American Journal of Epidemiology Vol. 146, No. 5: 405-412
58. ^ Rodgers, B., et al. Non-linear relationships between cognitive function and alcohol consumption in young, middle-aged and older adults: The PATH Through Life Project. Addiction, 2005, 100(9), 1280-1290; Anstey, K. J., et al. Lower cognitive test scores observed in alcohol are associated with demographic, personality, and biological factors: The PATH Through Life Project. Addiction, 2005, 100(9), 1291-1301.
59. ^ Soman, I., Mengi, S.A., and Kasture, S.B. (2004). "Effect of leaves of *Butea frondosa* on stress,

anxiety, and cognition in rats". *Pharmacology, Biochemistry & Behavior* (C.U. Shah College of Pharmacy, SNDT University Santacruz, Mumbai, Maharashtra, India) 79 **(1): 11–6. http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=15388278&dopt=Citation.**

60. ^ MDL 26,479: a potential cognition enhancer with benzodiazepine inverse agonist-like properties. (http://www.pubmedcentral.nih.gov/articlerender.fcgi?tool=pmcentrez&artid=1907590)
61. ^ **a b** Paul F Smith & Cynthia L Darlington Department of Pharmacology and Toxicology, School of Medical Sciences, University of Otago, Dunedin, New Zealand (2005). "Drug treatments for subjective tinnitus: Serendipitous discovery versus rational drug design". *Current Opinion in Investigational Drugs* **6** (7): 712–716. http://www.biomedcentral.com/1472-4472/id/cd-608223/abstract/.
62. ^ Clive Bate, Mario Salmona, and Alun Williams (11 May 2004). "Ginkgolide B inhibits the neurotoxicity of prions or amyloid-B_{I-42}". *Journal of Neuroinflammation* **1** (4): 4. doi:10.1186/1742-2094-1-4. http://www.jneuroinflammation.com/content/1/1/4.

External links

- Greely H, Sahakian B, Harris J, *et al* (December 2008). "Towards responsible use of cognitive-enhancing drugs by the healthy". *Nature* **456** (7223): 702–5. doi:10.1038/456702a. PMID 19060880. http://www.nature.com/nature/journal/vaop/ncurrent/full/456702a.html.
- Business Week Online - "I Can't Remember" (http://www.businessweek.com/@@*TTz0oUQYsI6ogEA/magazine/content/03_35/b3847001_mz001.htm) September 1, 2003 at Business Week
- List of Nootropic drugs (http://www.erowid.org/smarts/smarts.shtml) at Erowid

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