Intelligence and metabolism

From the original article in 2009. Author: Ray Peat.

Appropriate stimulation is an essential part of the developmental process. Inappropriate stimulation is a stress that deforms the process of growth. Mediators of stress, such as serotonin, can cause persistent distortions of physiology and behavior.

Education can either activate or suppress mental energy. If it is mainly obedience training, it suppresses energy. If it creates social dislocations, it disturbs mental and emotional energy.

Stress early in life can impair learning, cause aggressive or compulsive behavior, learned helplessness, shyness, alcoholism, and other problems.

Serotonin activates the glucocorticoid system, which can produce brain atrophy. Antiserotonin agents protect against brain atrophy and many other effects of stress. The brain-protecting neurosteroids, including pregnenolone and progesterone, which are increased by some kinds of stimulation, are decreased by isolation stress, and in their absence, serotonin and the glucocorticoids are relatively unopposed.

Since excess serotonin can cause thrombosis and vasospasms, and the excess cortisol resulting from hyperserotonemia can weaken blood vessels and the immune system, a person's longevity is likely to be shortened if something doesn't intervene to alter the patterns induced by stress early in life.

Baroness Blatch: "My Lords, the levels of achievement are well above the national average of our own state schools."

"This is a school which attained 75 per cent A to C passes in 1998, and 63.9 per cent in 1999. Those figures are well above national averages. There is no truancy; and there is the highest possible level of parental satisfaction with the school. When those parents are paying their money and know what they are paying for, who are we to take a different view about the philosophy of education in a private school?"

Comment during debate in House of Lords, June 30, 1999, on Chief Inspector of Schools Woodhead's threat to close Summerhill, a democratic school which had been started in 1921.

In 1927, the government inspectors had recommended that 'all educationalists' should come to Summerhill to see its 'invaluable' research, which demonstrated that students' development is better when they regulate themselves and are not required to attend lessons.

Having written about animal intelligence, and the ways in which it is similar to human intelligence, now I want those ideas to serve as a context for thinking about human intelligence without many of the usual preconceptions.

Intelligence is an interface between physiology and the environment, so it's necessary to think about each aspect in relation to the other. Things, both biochemical and social, that enhance intelligence enhance life itself, and vice versa.

Psychologists have tried to give their own definitions to words like idiot, imbecile, moron, and genius, but they have just been refining the clichés of the culture, in which "dummy" is one of the first words that kids in the U.S. learn. Many psychologists have tried to create "culture-free" tests of intelligence, making it clear that they believe in something like innate animal intelligence, though they usually call it "genetic" intelligence. Other psychometrists have transcended not only biology but even rationality, and have catalogued the ***preferences*** of people that they define as intelligent, and designed "I.Q. tests" based on the selection of things that were preferred by "intelligent people." This behavior is remarkably similar to the "psychometry" of the general culture, in which "smart" people are those who do things the "right" way.

About thirty years ago, someone found that the speed with which the iris contracts in response to a flash of light corresponds very closely to the I.Q. measured by a psychologist using a standard intelligence test. The devices used to measure reaction time in drivers' education courses also give a good indication of a person's intelligence, but so does measuring their heart rate, or taking their temperature. Colleges would probably be embarrassed to admit students on the basis of their temperature (though they commonly award scholarships on the basis of the ability to throw a ball). Colleges, to the extent that they are serious about the business of education, are interested in the student's ability to master the culture.

The way a person has learned during childhood can shape that person's manner of grasping the culture. To simply accelerate the learning of a standard curriculum will increase that person's "I.Q." on a conventional test, but the important issue is whether it is really intelligent to learn and to value the things taught in those curricula. Some educators say that their purpose is to socialize and indoctrinate the students into their discipline, others believe their purpose is to help their students to develop their minds. Both of these approaches may operate within the idea that "the culture" is something like a museum, and that students should become curators of the collection, or of some part of it. If we see the culture metaphorically as a mixture of madhouse, prison, factory, and theater, the idea of "developing the student's mind" will suggest very different methods and different attitudes toward "the curriculum"

Even sophisticated people can fall into stereotyped thinking when they write about issues of intelligence. For example, no one considers it a sign of genius when a slum kid is fluent in both Spanish and English, but when some of history's brightest people are discussed, the fact that they learned classical Greek at an early age is always mentioned. No one mentions whether they

were competent in idiomatic Spanish.

One of the old cultural stereotypes is that child prodigies always “burn out,” as if they were consuming a fixed amount of mental energy at an accelerated rate. (This idea of burn-out is isomorphic with the other cultural stereotypes relating aging to the “rate of living,” for example that people with slow heart beats will live longer.) Some of the men who have been considered as the world's brightest have, in fact, gone through a crisis of depression, and Terman's long-term study of bright people found that “maladjustment” did increase with I.Q., especially among women. But the facts don't support the concept of “burn-out” at all. I think the facts reveal instead a deep flaw in our ideas of education and professional knowledge.

In a world run by corporation executives, university presidents (“football is central to the university's mission”), congressmen, bankers, oilmen, and agency bureaucrats, people with the intelligence of an ant (a warm ant) might seem outlandishly intelligent. This is because the benighted self-interest of the self-appointed ruling class recognizes that objective reality is always a threat to their interests. If people, for example, realized that estrogen therapy and serotonin-active drugs and x-rays and nuclear power and atomic bomb tests were beneficial only to those whose wealth and power derive from them, the whole system would lose stability. Feigned stupidity becomes real stupidity.

But apart from ideologically institutionalized stupidity, there are real variations in the ability to learn, to remember and to apply knowledge, and to solve problems. These variations are generally metabolic differences, and so will change according to circumstances that affect metabolism. Everyday social experiences affect metabolism, stimulating and supporting some kinds of brain activity, suppressing and punishing others. All of the activities in the child's environment are educational, in one way or another.

Some of the famous prodigies of history illustrate the importance of ideology in the development of intellect. Family ideology, passing on the philosophical orientations of parents and their friends, shapes the way the children are educated.

Some of these family traditions can be traced by considering who the child's godfather was. Jeremy Bentham was John Stuart Mill's godfather, Mill was Bertrand Russell's; Ralph Waldo Emerson was William James' godfather, James was W. J. Sidis's. Willy Sidis was educated by his parents to demonstrate their theory of education, which grew out of the philosophies of Emerson and James. His father, Boris Sidis, was a pioneer in the study of hypnosis, and he believed that suggestion could mobilize the mind's “reserve energy.” Willy learned several languages and advanced mathematics at an early age. After he graduated from Harvard at the age of 16, he tried teaching math at Rice Institute, but he was displeased by the attitudes of his students and of the newspaper and magazine writers who made a profession of mocking him. He attended law school at Harvard, and would have been imprisoned as a conscientious objector if the war hadn't ended.

Antisemitism probably played a role in his sense of isolation when he was at Harvard and Rice. In 1912 Henry Goddard, a pioneer in intelligence testing (and author of ***The Kallikak Family: A Study in the Heredity of Feeble-Mindedness)***, administered intelligence tests to immigrants and determined that 83 percent of Jews and 87 percent of Russians were “feeble-minded.” By the standards of the time, it was highly inappropriate for the child of extremely poor Jewish immigrants from eastern Europe to be so bright.

Sidis hid from the press, and worked as a bookkeeper and clerk, while he studied and wrote. During his years of obscurity, he wrote books on philosophy and American history. Eventually, the journalists discovered him again, and after prolonged lawsuits against the magazines for invasion of privacy and slander, he died of a stroke at the age of 46.

Sidis is probably the culture's favorite example of the child prodigy who burns out, but people (Robert Persig, Buckminster Fuller) who have read his books have said favorable things about them. The journalists' emphasis on the fact that Sidis never held a prestigious job nicely illustrates their cliché mentality: “If you're so smart, why aren't you rich?” But throughout history, intelligent nonconformists have supported themselves as craft-workers or technicians--Socrates as a stone mason, Spinoza as a lens grinder, Blake as an engraver, Einstein as a patent examiner, for example.

In conventional schools (as in conventional society) 10,000 questions go unanswered, not only because a teacher with many students has no time to answer them, but also because most teachers wouldn't know most of the answers.

The parents of W. J. Sidis and J. S. Mill were remarkably well educated people who, because they dissented from society's ideology, chose to spend much of their time educating their children. Whenever a question about Euclidean geometry or Greek grammar occurred to the child, it could be answered immediately. It was only natural that progress would be fast, but there were more important differences.

When questions are answered, curiosity is rewarded, and the person is enlivened. In school, when following instructions and conforming to a routine is the main business, many questions must go unanswered, and curiosity is punished by the dulling emptiness of the routine.

Some schools are worse than others. For example, slum children were given I.Q. tests when they started school, and each subsequent year, and their I.Q.s dropped with each year of school. In a stimulating environment, the reverse can happen, the I.Q. can rise each year. Since the tests aren't “culture free,” their scores reflected the material that they were being taught, but they undoubtedly also reflected the increasing boredom and despair of the children in a bad school, or the increasing liveliness of the children in the stimulating environment.

I have spoken with people in recent years who still held the idea of a fixed genetic mental potential, who believe that poor children fall behind because they are reaching their “genetic limit.” For them, the I.Q. represents an index of intrinsic quality, and is as important as distinguishing between caviar and frogs' eggs. The rat research of Marion Diamond and others at the University of California, however, showed that the structure, weight, and biochemistry of a rat's brain changes, according to the amount of environmental stimulation and opportunity for exploration. This improvement of brain structure and function is passed on to the next generation, giving it a head-start. It isn't likely that rats are more disposed than humans to benefit

from mental activity, and in the years since Diamond's research there have been many discoveries showing that brains of all sorts complexify structurally and functionally in response to stimulation.

Rats isolated in little boxes, generation after generation--the normal laboratory rats--were the standard, but now it's known that isolation is a stress that alters brain chemistry and function.

Willy Sidis and John Stuart Mill were being stimulated and allowed to develop in one direction, but they were being isolated from interaction with their peers. When Mill was twenty he went into a depression, and later he wrote that it was because he discovered that he was unable to ***feel.*** He had developed only part of his personality.

Bertrand Russell (1872-1970), orphaned at the age of four, went to live with his grandmother, who chose not to send him to school, but provided tutors. He didn't experience a sense of academic pressure, and was able to read whatever he wanted in his late grandfather's library. He didn't realize that he was unusually bright until he went to Cambridge. The unusual freedom of his childhood must have contributed to his willingness to hold unpopular opinions. In 1916 he was fined, and in 1918 imprisoned for 6 months, for opposing the war.

In 1927, Russell and his wife, Dora Black, started a school. He later wrote that, although the average student at the school was very bright, an exceptionally bright student was likely to be ostracized by the less bright students. He commented on the harm done to the brightest students by their social isolation, probably thinking about his own education in relative isolation. A psychologist (Leta Hollingworth, 1942) has made similar observations about the isolation that can be produced by a large difference of I.Q. She did a series of studies of very bright children, beginning in 1916, including working with some of them in a program she designed in a New York public school. Her empathy allowed her to discover things that weren't apparent to her contemporaries.

During this time Lewis Terman was studying bright children, and wanted to disprove some of the popular stereotypes about intelligent people, and to support his ideology of white racial superiority. In 1922 he got a large grant, and sorted out about 1500 of the brightest children from a group of 250,000 in California. He and his associates then monitored them for the rest of their lives (described in ***Genetic Studies of Genius***). His work contradicted the stereotype of bright people as being sickly or frail, but, contrary to his expectation, there was an association between maladjustment and higher I.Q.; the incidence of neurotic fatigue, anxiety, and depression increased along with the I.Q. The least bright of his group were more successful in many ways than the most bright. He didn't really confront the implications of this, though it seriously challenged his belief in a simple genetic racial superiority of physique, intellect, and character.

I.Q. testing originated in a historical setting in which its purpose was often to establish a claim of racial superiority, or to justify sterilization or “euthanasia,” or to exclude immigrants. More recently, the tests have been used to assign students to certain career paths. Because of their use by people in power to control others, the I.Q. tests have helped to create misunderstanding of the nature of intelligence. A person's “I.Q.” now has very strong associations with the ideology of schooling as a road to financial success, rather than to enrichment of a shared mental life.

If a bad school resembles, on the intellectual level, a confining rat box, the educational isolation of Mill, Russell, and Sidis was emotionally limiting, almost like solitary confinement. Once when Willy Sidis was arrested for marching in a May Day parade, his father was able to keep him from going to prison, but Willy apparently would have preferred the real prison to life with his parents.

None of these three famous intellects was known for youthful playfulness, though playfulness is a quality that's closely associated with intelligence in mammals and birds. (Russell, however, in middle age developed many new interests, such as writing short stories, and had many new loves even in old age.) Stress early in life, such as isolation, reduces the playfulness of experimental animals. Playfulness is contagious, but so is the inability to play.

In schools like Summerhill, which was founded in 1921 by A. S. Neill, students aren't required to attend classes when they would rather do something else, but at graduation they usually do better on their standardized national examinations than students who have dutifully attended classes for years. For students, as for rats, freedom and variety are good for the brain, and tedious conformity is harmful. When a school is very good, it can spread a contagion of playfulness along with an interest in learning.

An environment that fosters optimal intelligence will necessarily promote the development of emotional health, and will almost certainly foster good physical health and longevity, because no part of the physiological system can thrive at the expense of another part. And within the boundaries of life-enriching environments, there are infinite possibilities for variety.

There is a common belief in the rigidity of the adult nervous system, in analogy with feral cats or dogs, that supposedly can't be tamed if they have grown up without knowing humans. But people who have had the inclination to understand wild animals have found that, even when the animals have been captured as adults, they can become as sociable as if they had grown up in domestication. The “horse whisperer” demonstrated this sort of empathetic approach to animals. Sometimes, these people have a similar ability to communicate with people who are retarded, or autistic, or demented, but the professionalization of society has made it increasingly unlikely that people with the need for intuitive help will encounter someone who is able to give it. The closest psychology has come to professionally recognizing the importance of empathy was in Carl Rogers' work, e.g., *Client-Centered Therapy*.

Rogers showed that a sense of solidarity must exist between therapist and client for the therapy to be helpful. A similar solidarity has to exist between teacher and student, for education to be successful. If ordinary family and social contacts could occur within such an atmosphere of mutual respect, psychopathology (including learning difficulties) would be much less common.

Although three individuals don't prove an argument, I think the lives and situations of Sidis, Mill, and Russell are usefully

symbolic. Sidis, who grew up under intense pressure and social isolation and in extreme poverty, died at the age of 46. Mill, who was educated mainly by his father, in secure financial circumstances, experienced social isolation and moderate pressure, and lived about 20 years longer than Sidis did. Russell, who grew up in the highest circles of the ruling class, experienced no pressure, and only the mild kind of social isolation that wasn't exceptional for his class. He lived to be 97.

The psychopathology of social isolation has been studied in a variety of animals, and many features are similar across species, including humans. Aggression, helplessness, and reduced ability to learn are typically produced in animals by social isolation, and it's clear that certain kinds of family environment produce the same conditions in children. Schools seldom help, and often hinder, recovery from such early experiences.

"Vital exhaustion," decreased slow wave sleep, and anger, which are associated with the "type A personality" and with circulatory and heart disease, appear to have their origin in childhood experiences. Low income and financial insecurity are strongly associated with anger, sleep disturbances, and circulatory disease. In animals stressed by social isolation, similar features emerge, under the influence of decreased neurosteroids, and increased serotonin and activity of the glucocorticoid system.

The "smart drug" culture has generally been thinking pharmaceutically rather than biologically. Behind that pharmaceutical orientation there is sometimes the idea that the individual just isn't trying hard enough, or doesn't have quite the right genes to excel mentally.

Many stimulants--amphetamine and estrogen, for example--can increase alertness temporarily, but at the expense of long range damage. The first principle of stimulation should be to avoid a harmful activation of the catabolic stress hormones. Light, play, environmental variety and exploratory conversations stimulate the whole organism in an integral way, stimulating repair processes and developmental processes.

Any chemical support for intelligence should take into account the mind-damaging stresses that our culture can impose, and provide defense against those. In darkness and isolation, for example, the stress hormones increase, and the brain-protective steroids decrease. The memory improvement that results from taking pregnenolone or thyroid (which is needed for synthesizing pregnenolone from cholesterol) is the result of turning off the dulling and brain-dissolving stress hormones, allowing normal responsiveness to be restored.

If we know that rats nurtured in freedom, in an interesting environment, grow more intelligent, then it would seem obvious that we should experiment with similar approaches for children--if we are really interested in fostering intelligence. And since violence and mental dullness are created by the same social stresses, even the desire to reduce school violence might force the society to make some improvements that will, as a side effect, foster intelligence.

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John Holt, from an interview in *Mother Earth News,* July/August, 1980**:** "I suggested that we simply provide young people with schools where there are a lot of interesting things to look at and work with . . . but that we let the chidlren learn in their own wqys. If they have questions, answer the questions. If they want to know where to look for something, show them where to look."

John Holt, from the introduction to his book, *Teach Your Own,* (New York: Dell, 1981)**:** "The children in the classroom, despite their rich backgrounds and high I.Q.'s, were with few exceptions frightened, timid, evasive, and self-protecting. The infants at home were bold adventurers."

"It soon became clear to me that children are by nature and from birth very curious about the world around them, and very energetic, resourceful, and competent in exploring it, finding out about it, and mastering. In short, much more eager to learn, and much better at learning, than most adults. Babies are not blobs, but true scientists. Why not then make schools into places in which children would be allowed, encouraged, and (if and when they asked) helped to explore and make sense of the world around them (in time and space) in ways that most interested them?"

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Pharmacol Biochem Behav 1976 Jul;5(1):55-61. **The role of serotonergic pathways in isolation-induced aggression in mice.** Malick JB, Barnett A Male mice that became aggressive following four weeks of social isolation were treated with seven known serotonin receptor antagonists. All of the **antiserotonergic drugs selectively antagonized the fighting behavior of the isolated mice; the antiaggressive activity was selective since, at antifighting doses, none of the drugs either significantly altered spontaneous motor activity** or impaired inclined-screen performance. **Antagonism of 5-HTP-induced head-twitch was used as an in vivo measure of antiserotonergic activity and a statistically significant correlation existed between potency as an antiserotonergic and potency as an antiaggressive.** PCPA, a serotonin depletor, also significantly **antagonized isolation-induced aggression** for at least 24 hr postdrug administration. The interrelationship between cholinergic and serotonergic mechanisms in the mediation of isolation aggression was investigated. The involvement of serotonergic systems in isolation-induced aggression is discussed.

Probl Endokrinol (Mosk) 1979 May-Jun;25(3):49-52 **[Role of serotonin receptors of the medial-basal hypothalamus in the mechanisms of negative feedback of the hypophyseal-testicular complex].** Naumenko EV, Shishkina GT. "Administration of serotonin into the lateral ventricle of the brain of male rats, against the background of complete isolation of the medial-basal hypothalamus was accompanied by the block of the compensatory elevation of the blood testosterone level following unilateral castration."

Encephale 1994 Sep-Oct;20(5):521-5. **[Can a serotonin uptake agonist be an authentic antidepressant? Results of a multicenter, multinational therapeutic trial].** Kamoun A, Delalleau B, Ozun M The classical biochemical hypothesis of depression posits a functional deficit in central neurotransmitter systems particularly serotonin (5-HT) and noradrenaline. The major role suggested for 5-HT in this theory led to the development of a large number of compounds which selectively inhibit 5-HT uptake. Numerous clinical trials have demonstrated the antidepressant efficacy of such types of serotoninergic agents, supporting 5-HT deficit as the main origin of depression. **Therefore, everything seemed clear: depression was caused by 5-HT deficit. Tianeptine is clearly active in classical animal models predictive of antidepressant activity, and is also active in behavioral screening tests: it antagonizes isolation induced aggression in mice and behavioral despair in rats.** Biochemical studies have revealed that in contrast to classical tricyclic antidepressant, **tianeptine stimulates 5-HT uptake** in vivo in the rat brain. This somewhat surprising property was observed in the cortex and the hippocampus following both acute and chronic administrations. This increase in 5-HT uptake has also been confirmed in rat platelets after acute and **chronic administrations. Moreover, in humans, a study in depressed patients demonstrated that tianeptine significantly increased platelet 5-HT uptake after a single administration as well as after 10 and 28 days of treatment. The antidepressant activity of tianeptine has been evaluated in controlled studies versus reference antidepressants. Another study aiming to compare the antidepressant efficacy of tianeptine versus placebo and versus imiporamine is** presented. 186 depressed patients were included in this trial. They presented with either Major Depression, single episode (24.6%) or Major Depression recurrent (66.8%) or Bipolar Disorder (depressed) (8.6%).

Psychopharmacology (Berl) 1998 Oct;139(3):255-60. **Ca2+ dependency of serotonin and dopamine release from CNS slices of chronically isolated rats.** Jaffe EH. "We have used chronic isolated housing as an animal model of depression." "The following questions were addressed: first, if there is a change in the depolarization dependent release of DA and 5-HT from these CNS structures, and second, if the release is through the classical exocytotic mechanism. **A significant increase in KCl stimulated release of 5-HT was observed in chronically isolated animals when compared to controls.** 5-HT release was completely abolished from controls or isolated animals, when slices were incubated with Krebs containing zero Ca2+/10 mM Mg2+, the inorganic Ca2+ channel blockers, Cd2+ or Ni2+ and the calmodulin inhibitor, trifluoperazine." **"The basal release of DA and 5-HT was similar in control and isolated animals and was not affected by the Ca2+ channel antagonists. The results suggest that extracellular Ca2+-dependent release of 5-HT and, to a lesser degree, of DA, is increased in this chronic animal model of depression in** several CNS structures."

Gen Pharmacol 1994 Oct;25(6):1257-1262. **Serotonin-induced decrease in brain ATP, stimulation of brain anaerobic glycolysis and elevation of plasma hemoglobin; the protective action of calmodulin antagonists.** Koren-Schwartzer N, Chen-Zion M, Ben-Porat H, Beitner R Department of Life Sciences, Bar-Ilan University, Ramat Gan, Israel. **1. Injection of serotonin (5-hydroxytryptamine) to rats, induced a dramatic fall in brain ATP level, accompanied by an increase in P(i). Concomitant to these changes, the activity of cytosolic phosphofructokinase, the rate-limiting enzyme of glycolysis, was significantly enhanced. Stimulation of anaerobic glycolysis was also reflected by a marked increase in lactate content in brain. 2. Brain glucose** 1,6-bisphosphate level was decreased, whereas fructose 2,6-bisphosphate was unaffected by serotonin. 3. All these serotonin-induced changes in brain, which are characteristic for cerebral ischemia, were prevented by treatment with the calmodulin (CaM) antagonists, trifluoperazine or thioridazine. 4**.. Injection of serotonin also induced a marked elevation of plasma hemoglobin, reflecting lysed erythrocytes,** which was also prevented by treatment with the CaM antagonists. 5. **The present results suggest that CaM antagonists may be effective drugs in treatment of many pathological conditions and diseases in which plasma serotonin levels are known to increase.**

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J Neural Transm 1998;105(8-9):975-86. **Role of tryptophan in the elevated serotonin-turnover in hepatic encephalopathy.** Herneth AM, Steindl P, Ferenci P, Roth E, Hortnagl H. "The increase of the brain levels of 5-hydroxyindoleacetic acid (5-HIAA) in hepatic encephalopathy (HE) suggests an increased turnover of serotonin (5-HT)." "These results provide further evidence for the role of tryptophan in the elevation of brain 5-HT metabolism and for a potential role of BCAA in the treatment of HE."

Tugai VA; Kurs'kii MD; Fedoriv OM. **[Effect of serotonin on Ca2+ transport in mitochondria conjugated with the respiratory chain].** Ukrainskii Biokhimicheskii Zhurnal, 1973 Jul-Aug, 45(4):408-12.

Kurskii MD; Tugai VA; Fedoriv AN. **[Effect of serotonin and calcium on separate components of respiratory chain of mitochondria in some rabbit tissues].** Ukrainskii Biokhimicheskii Zhurnal, 1970, 42(5):584-8.

Watanabe Y; Shibata S; Kobayashi B. **Serotonin-induced swelling of rat liver mitochondria.** Endocrinologia Japonica, 1969 Feb, 16(1):133-47.

Mahler DJ; Humoller FL. **The influence of serotonin on oxidative metabolism of brain mitochondria.** Proceedings of the Society for Experimental Biology and Medicine, 1968 Apr, 127(4):1074-9.

Eur J Pharmacol 1994 Aug 11;261(1-2):25-32. **The effect of alpha 2-adrenoceptor antagonists in isolated globally ischemic rat hearts.** Sargent CA, Dzwonczyk S, Grover G.J. "The alpha 2-adrenoceptor antagonist, yohimbine, has been reported to protect hypoxic myocardium. Yohimbine has several other activities, including 5-HT receptor antagonism, at the concentrations at which protection was found." "Pretreatment with yohimbine (1-10 microM) caused a concentration-dependent increase in reperfusion left ventricular developed pressure and a reduction in end diastolic pressure and lactate dehydrogenase release. The structurally similar compound rauwolscine (10 microM) also protected the ischemic myocardium. In contrast, idozoxan (0.3-10 microM) or tolazoline (10 microM) had no protective effects. The **cardioprotective effects of yohimbine were partially reversed by 30 microM 5-HT. These results indicate that the mechanism for the cardioprotective activity of yohimbine may involve 5-HT receptor antagonistic activity."**

Zubovskaia AM. **[Effect of serotonin on some pathways of oxidative metabolism in the mitochondria of rabbit heart muscle].** Voprosy Meditsinskoi Khimii, 1968 Mar-Apr, 14(2):152-7.

Warashina Y. **[On the effect of serotonin on phosphorylation of rat liver mitochondria**]. Hoppe-Seylers Zeitschrift fur Physiologische Chemie, 1967 Feb, 348(2):139-48.

Eur Neuropsychopharmacol 1997 Oct;7 Suppl 3:S323-S328. **Prevention of stress-induced morphological and cognitive consequences**.. McEwen BS, Conrad CD, Kuroda Y, Frankfurt M, Magarinos AM, McKittrick C. Atrophy and dysfunction of the human hippocampus is a feature of aging in some individuals, and this dysfunction predicts later dementia. There is reason to believe that adrenal glucocorticoids may contribute to these changes, since the elevations of glucocorticoids in Cushing's syndrome and during normal aging are associated with atrophy of the entire hippocampal formation in humans and are linked to deficits in short-term verbal memory. We have developed a model of stress-induced atrophy of the hippocampus of rats at the cellular level, and we have been investigating underlying mechanisms in search of agents that will block the atrophy. Repeated restraint stress in rats for 3 weeks causes changes in the hippocampal formation that include suppression of 5-HT1A receptor binding and atrophy of dendrites of CA3 pyramidal neurons, as well as impairment of initial learning of a radial arm maze task. **Because serotonin is released by stressors and may play a role in the actions of stress on nerve cells, we investigated the actions of agents that facilitate or inhibit serotonin reuptake.** Tianeptine is known to enhance serotonin uptake, and we compared it with fluoxetine, an inhibitor of 5-HT reuptake, as well as with desipramine. **Tianeptine treatment (10 mg/kg/day) prevented the stress-induced atrophy of dendrites of CA3 pycamidal neurons,** whereas neither fluoxetine (10 mg/kg/day) nor desipramine (10 mg/kg/day) had any effect. **Tianeptine treatment also prevented the stress-induced impairment of radial maze learning.** Because **corticosterone- and stress-induced atrophy of CA3 dendrites is also blocked by phenytoin, an inhibitor of excitatory amino acid release and actions, these results suggest that serotonin released by stress or corticosterone may interact pre- or post-synaptically with glutamate released by stress or corticosterone, and that the final common path may involve interactive effects between serotonin and glutamate receptors on the dendrites of CA3 neurons innervated by mossy fibers from the dentate gyrus. We discuss the implications of these findings for treating cognitive impairments and the risk for dementia in the elderly.**