Estrogen, serotonin, mood, and aging (DRAFT)

From the original article. Author: Ray Peat.

Here's a draft of a newsletter I'm working on, explaining a simplified approach to health--and by coincidence it explains why it's good to live in Mexico, eating tropical fruit, tortillas, chocolate atole, and chicharrones. It isn't ready for publication yet.

Effective treatments and cures for a great variety of problems--depression and aggression, inflammation and atrophy, dementia and movement disorders, shock and hypertension, reproductive disorders, immunodeficiency and tumors, etc.--are being ignored because of a failure to understand the nature of estrogen and serotonin. Commercial suppression of the facts regarding serotonin has been intricately woven into a defective view of human nature.

Not long ago, there might have seemed to be some scientific value in refining the precision of diagnoses. Many people believed that every kind of infection, every kind of cancer, all the neurological and psychiatric problems had to be distinguished from other varieties of sickness, so that a specific and effective treatment could be devised for each sharply defined medical condition.

But while medicine was multiplying the essences, biology was finding commonalities, generalities, and universals.

Several decades ago, a few ideas such as "stress" or the "general adaptation syndrome," sterile inflammation, autoimmune syndrome, and immunodeficiency syndrome started to enter the mainstream culture, and by the end of the 20th century "inflammation" was starting to be recognized as a central component of many conditions that had seemed very different from each other. "Insulin resistance" and "a diabetes-like condition" were being seen in problems that had once been seen as behavioral problems or problems of certain organs.

There are still millions of people who will try to "cure the pox by cutting out the spots," but many people are ready for a new approach, in which diseases will be treated by changing the conditions of life, and each person's restoration to health will be seen as a contribution to the more perfect understanding of life.

We are at an early stage in our understanding of the meaning of the development and evolution of organisms, so it's important to look for the basic things that give meaning to life as we experience it.

In our development we recapitulate not only primitive forms and functions, but also primitive biochemistry. In a biological crisis, those primitive functions and biochemical processes are activated, and can contribute to survival by stimulating new growth. In prolonged difficulties, such as foodless winters, they can produce adaptations such as hibernation, or the suppression of reproduction. But prolonged stress can eventually change our nature, by reducing our energetically expensive highly evolved functions and structures.

Play, imagination, curiosity, and exploration are highly evolved functions, and they require optimal functions of the highest, most human, parts of the brain. In mammals, these functions are most noticeable in youth, but when circumstances permit, they can persist strongly into maturity. Severe stress suppresses these functions, sometimes permanently. Excesses of estrogen, serotonin, and cortisol are induced by stress and are largely responsible for these sometimes adaptive, but unpleasant changes in our nature. When the stress or exaggerated exposure to those hormones occurs early in life it is teratogenic--it creates monsters. And besides the visible defects, early exposure to excessive estrogen or tryptophan (the precursor to serotonin) increases the incidence of breast and pituitary tumors later in life.

Estrogen and serotonin are very primitive regulatory substances, and both of them tend to increase the production of cortisol. Estrogen is very closely linked with the serotonin system; for example, estrogen activates the enzyme that converts tryptophan into serotonin (while progesterone inhibits the conversion), and serotonin mediates many of estrogen's actions. Estrogen and serotonin stimulate cell division, and are increased by any injury. They both decrease cells' ATP and "energy charge," and this decrease is associated with activation of the primitive mechanisms of cell division and growth. Cortisol is a catabolic hormone, that breaks down, and sometimes kills, cells that aren't immediately needed during a crisis, and this catabolism provides material from those cells to support the growth of new cells. When it causes muscles to break down, some of the tryptophan from the muscle proteins is converted into serotonin. Like melatonin, serotonin can interfere with reproduction, and its actions in the ovary and brain tend to create estrogen dominance, suppressing progesterone. Estrogen shifts tryptophan metabolism toward serotonin, away from niacin (Shibata, et al., 1997), and tends to create serotonin dominance.

These interactions mean that, once we enter the low energy state, we tend to be locked into it, unless something special happens to restore full vitality.

In general, young animals learn very easily, but at a certain age, behavioral rigidity sets in, making it hard to learn new things. Serotonin appears to be the factor responsible for this loss (Edagawa, et al., 2001). Aging is very much like Cushing's syndrome, a condition in which cortisol is produced excessively, without the normal stressful stimuli. Even in normal aging, there is a decrease in the ability to turn off cortisol production when it isn't needed. Serotonin, which activates all the components of the system that produces cortisol (brain, pituitary, and adrenal gland), becomes relatively dominant in old age (Weil-Fugazza, et al., 1980), and produces a steady activation of the adrenal cortex. Cortisol increases serotonin content in the brain (Neckers and Sze, 1975). Insulin resistance, muscular weakness and muscular wasting, deposition of fat on the face and trunk, reduced fertility, atrophy of brain cells and decreased mental ability, a weakened immune system, inability to sleep deeply, and anxious depression are features of Cushing's syndrome that become very common in aging.

Anti-serotonin drugs are now being successfully used in treating Cushing's disease.

Insulin resistant "diabetes" is one of the features of Cushing's disease, meaning that cells aren't able to get adequate amounts of glucose. Starvation increases the amount of serotonin in the brain, and so does diabetes, since cells are starving for glucose. Sugar is probably one of the factors, like progesterone and thyroid (T3), which decrease the formation of serotonin in the brain. This could account for the fact that eating sugar suppresses the stress reaction, as seen in the experiments of K.D. Laugero, in which sugar normalized ACTH, even in the absence of the adrenal glands (2001; Laugero, et al., 2001).

Rearing animals in isolation, or stressing them severely as in forced swimming, creates a state of chronic serotonin excess. Learned helplessness is produced when stress is inescapable, but when animals are reared in isolation, they are prone to die suddenly during stress (Rosellini, et al., 1976). These stresses, or the injection of serotonin, impair the ability to learn, and treatment with antiserotonin drugs improves learning ability. Mental retardation, autism, Down's syndrome, and uremic/dialysis dementia are associated with abnormally high levels of serotonin. On the microscopic level, stress, serotonin, and cortisol cause changes in cell structure, the reduction of branching and contacts with other cells.

Serotonin activity governs the spinal nerve systems that are responsible for locomotion in all sorts of animals--worms, fish and mammals. Activating the serotonin system causes, for example, "fictive swimming." In uremia, a prominent symptom is "periodic limb movements," or the "restless leg syndrome." Antiserotonin drugs relieve this movement disorder. Similar serotonergic processes are involved in Parkinson's disease, and are relieved by antiserotonin or pro-dopaminergic drugs. Since Parkinson's disease was found to be relieved by L-dopa 40 years ago, the role of serotonin in the disease has received little attention, but L-dopa has the ability to lower the production of serotonin (inhibiting the tryptophan hydroxylase enzyme) and to increase its decomposition. Unfortunately, it's neurotoxic in itself.

During sleep, serotonin suppresses the restorative deep slow wave sleep and the active rapid eye movement (REM) phase of sleep. During one of the intermediate phases of sleep, it increases the brain activity that corresponds to locomotion.

REM sleep involves activation of the cortex of the brain, at the same time that sensory input and motor output are inhibited.

Cholinergic nerves, from the "reticular activating system," activate the cortex, while noradrenaline and serotonin tend to decrease its activation, possibly protecting against seizure activity (Burley and Ferrendelli, 1984). The activating system is modulated by many direct or indirect inhibitory influences, including GABAergic, cholinergic, and serotonergic nerves.

Hasselmo, et al. (1997) described the inhibitory effects of norepinephrine and acetylcholine on the excited cortex in terms of limiting processes of interpretation and retrieval.

Sleep is a time of revision and reinterpretation, especially during the REM phase when the activating system is enlivening the cortex. Dreams sometimes construct the mood and the sense of possibilities for the day, and when they are very successful, we wake up with a sense of newness, and direction. I think it's accurate to say that dreams maintain the organism's coherence.

The inhibitory effects of serotonin are not limited to the reticular activating system, for example when it lowers body temperature and metabolic rate, but Kramarova, et al. (1991) show that inhibition of the reticular activation system by increased serotonin is an important part of the preparation for hibernation.

This shut-down of consciousness by stress, or by mere maturity and aging, seems to be the biological basis for a process that has been described by many writers, including Henri Bergson, Havelock Ellis, Aldous Huxley (in Doors of Perception, and Heaven and Hell), and Colin Wilson (e.g., in The Philosopher's Stone).

Bergson spoke of the "cerebral reducing valve." In Huxley's words, this "vast reducing valve" functions by "shutting out most of what we should otherwise perceive or remember at any moment, and leaving only that very small and special selection which is likely to be practically useful." But the studies of serotonin show that unfortunate conditions usually cause the brain to shut out even important and useful perceptions, interpretations, memories and associations. And James W. Prescott's study of a large body of anthropological data showed that stressful rearing practices during childhood and adolescence produced cultures that were pathologically authoritarian, cruel, and aggressive (1975).

Colin Wilson, in about 100 books written over the last 50 years, has explored these different states of consciousness, and has argued that the excitedly expectant state of consciousness of a child on Christmas morning is a model of the way the mind should function throughout life. He believes that true perception sees a world full of potential and beauty, and that it is the "practical" everyday consciousness which is deluded.

> And the chief characteristic of the opposite of affirmation-consciousness--I suppose one might call it depression-consciousness--is that when you are in it, it seems totally convincing; like a very brilliant liar, it can account for everything in its own terms.

Dostoyevky's description of these states, in Dream of an Odd Fellow (a description of how a change of consciousness prevented his suicide), in the previous century, was probably no more effective than Wilson's in causing people to take a more critical attitude toward everyday consciousness. Prescott's study suggests that this is because "depression consciousness" is built into our institutions.

Prescott's anthropological analysis shows that authoritarianism, social hierarchy, cruelty, aggression, and suicide are associated. He was fired from his US government research job when his work began showing the causes of violence and the ways it can be prevented.

The "professionals" in our culture--lawyers, physicians, police and military officers--who are often called "role models," have a high suicide rate. For more than a century, suicide rates have been increasing in many countries, and suicide is now the second or third most frequent cause of death among young people in some industrialized countries; industrialized countries have a much higher rate of suicide than poor countries. The Caribbean islands, St. Vincent and the Grenadines, have an

extremely low rate. The currently popular antidepressant drugs, which increase the action of serotonin, are strongly suspected of increasing the incidence of both suicide and aggressive violence. There are animal experiments showing that drugs of this sort can increase aggression in animals (Carlini and Lindsey, 1982), and an epidemiological study shows that violent criminals have more serotonin in their blood than normal men or non-violent criminals (Moffitt, et al., 1998). Some animal studies show that animals abused in youth become aggressors toward smaller animals, but are passively submissive toward animals of their own size or bigger (Ferris, 2000). Antiserotonin drugs inhibit aggression, and the performance of aggressive behavior increases the activity of serotonergic nerves (Vegt, et al, 2003). Other animal studies show that the destruction of serotonergic cells, either electrolytically or with a neurotoxin, decreases the anxiety resulting from stress (Andrade and Graeff, 2001).

Soon after serotonin was first synthesized, it was found to be extremely toxic to a variety of organs, but very soon, drugs derived from ergot, including LSD, were found to serve as antidotes, for example protecting the kidneys from damage by serotonin. During this time, the CIA was secretly investigating the use of LSD as a "mind control" drug. When the public started using LSD, its antagonism to serotonin became part of the popular culture, in a strange process in which the ergot drugs were said to make people violent and suicidal, and the antagonist, serotonin, began to be described as the hormone of serenity, optimism, and pleasant behavior. The development of drugs to increase serotonergic effects eventually followed. The Sandoz drug company found (or claimed) that slight modifications of the ergot drugs reduced their hallucinogenic properties, and this family of drugs has a great range of useful effects. More than 20 years ago, bromocriptine was shown to cure pituitary tumors, making most surgery for prolactinomas unnecessary, and more recently it has been used to treat infertility and Parkinson's disease. Other drugs with partial antiserotonin action have been found, in addition to the ergot alkaloids (hydergine, lergotrile, lisuride/lysenyl, metergoline, mesulergine, methylergometrine, methysergide, dihydroergocristine, dihydroergocryptine, terguride, ergometrine, ergonovine, ketanserin, dihydroergotamine, etc.), and are used to treat fibrosis, migraine, angina, intractable nausea and diarrhea (resulting from cancer chemotherapy or AIDS, for example), neurological diseases, Cushing's syndrome, acromegaly, prostatic hypertrophy, impotence or low libido, and insulin resistant diabetes, and to reduce the viscosity of blood. But they are often described as dopamine agonists, rather than as antagonists of serotonin.

The commercial-medical mythology of serotonin has been used to reinforce the estrogen mythology, and vice versa. It has taken more than 100 years for even part of the medical establishment to recognize that estrogen causes cancer, and although serotonin is known to be carcinogenic, the myth has almost completely blocked the investigation of the antiserotonin drugs to treat cancer, though a few studies have shown inhibition of tumor growth at doses that don't inhibit normal cell division (e.g., Tutton and Barkla, 1978). Ordinary cancer treatments inhibit the division of normal cells as well as cancer cells, producing side effects of immunosuppression, anemia, bleeding bowel, brain damage, and hair loss.

Both estrogen and serotonin cause brain damage, depression, aggression, movement disorders, extensive disturbance of the endocrine system, and mimic the problems of aging. Therapies for any of those problems should consider both of those factors, because neither excessive estrogen nor excessive serotonin can be regulated adequately without taking both systems into account.

The foods which help to optimize the function of the thyroid and the synthesis of progesterone help to prevent excessive production of serotonin, as well as of adrenaline and noradrenaline. These foods include fruits and proteins. For adults, gelatin is a protein that helps to minimize serotonin exposure, because it contains no tryptophan. Deprivation of either sugar and protein will increase serotonin, so the diet should include adequate amounts of both, maybe 100 grams of protein and 150 grams of sugar; this is sometimes called a "high protein" diet. Too much protein by itself can overstimulate insulin and cortisol production, increasing serotonin formation. Saturated fats improve assimilation of other nutrients, and tend to moderate the production of insulin and cortisol. The polyunsaturated fats shift the regulatory systems toward estrogen and serotonin, and this is probably responsible for their promotion of aggression (Hilakivi-Clarke, et al., 1996).

Soybeans don't contain very much tryptophan, but their estrogens increase tryptophan hydroxylase, the enzyme that synthesizes serotonin (Shively, et al., 2003). This could explain their toxic effects on behavior, such as increasing aggression (and decreasing friendliness) in monkeys, or increasing some cannibalistic behaviors in chickens, and increasing brain atrophy and dementia in men.

Traditional lime processed tortillas are probably helpful for controlling serotonin, since the leucine in corn tends to lower brain serotonin, and the alkaline processing converts some of the small amount of tryptophan into niacin. Chocolate is another plant protein that's rich in leucine.

The moderate hypoxia of high altitude corrects many of the hormonal imbalances that are common at sea level, and it tends to lower the amount of serotonin in the brain, by reducing the activity of tryptophan hydroxylase. Stressful exercise increases serotonin, and, if it's prolonged, will cause a chronic displacement of carbon dioxide, equivalent to hyperventilating, so physical activity should be of a non-aerobic sort.

One of the functions of the saturated fats is to act as a bowel disinfectant (especially when combined with fibrous food such as a raw carrot) reducing the amount of endotoxin that is absorbed, and so reducing the mediators of stress, especially serotonin, estrogen, cortisol, and the prostaglandins.

When we are properly nourished, we experience a positive euphoria, both waking and sleeping.

The consciousness of possibility, and the mood of exhilaration, that can sometimes be created by dreaming, are our direct experience of a metabolic and physiological process in which we are not only restored, but are reconstructed into something that never quite existed before. The things that allow us to dream properly are things that also correct our biochemistry and, on the microscopic level, our anatomy.

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Behav Brain Res. 2003 Jun 16;142(1-2):135-42. Protective effect of 5-HT1B receptor gene deletion on the age-related decline in spatial learning abilities in mice. Buhot MC, Wolff M, Savova M, Malleret G, Hen R, Segu L. Laboratoire de Neurosciences Cognitives, CNRS UMR 5106, Universite de Bordeaux 1, Avenue des Facultes, 33405 Talence Cedex, France. Buhot@neurocog.u-bordeaux.fr We previously observed that 5 months old serotonin 1B receptor knockout (5-HT1BKO) mice exhibited a facilitation of learning in a long-term spatial memory task in a water maze. In this study, we attempted to assess whether this effect might persist during aging. We compared the performances of young-adult (3 months old) and aged (22 months old) 5-HT1BKO and wild type (WT) mice in the same task. Young-adult and aged KO mice exhibited facilitated acquisition of the reference memory task as compared to their respective WT controls. Generally, the performance of aged KO was similar to that of young-adult WT on the parameters defining performance and motor (swim speed) aspects of the task. During probe trials, all mice presented a spatial selectivity, which was, however, less pronounced in aged than in young-adult WT. No such age-related effect was observed in KO mice. In a massed spatial learning task, aged KO and WT mice globally exhibited the same level of performance. Nevertheless, young-adult and aged KO mice were superior to their WT controls as concerns the working memory component of the task. The data suggest that 5-HT1BKO mice are more resistant than WT to age-related memory decline as concerns both reference/long-term and working/short-term spatial memory.

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Exp Physiol. 2000 Mar;85 Spec No:85S-90S. Adolescent stress and neural plasticity in hamsters: a vasopressin-serotonin model of inappropriate aggressive behaviour. Ferris CF. Psychiatry Department, University of Massachusetts Medical Center, Worcester 01655, USA. Cferris@banyan.ummed.edu Animal studies show that arginine vasopressin facilitates aggression, while serotonin (5-HT) inhibits aggression by blocking the activity of the vasopressin system. Clinical studies report that subjects with a history of 'fighting and assault' show a significant positive correlation between cerebrospinal fluid concentrations of vasopressin and aggression in the presence of a hyporeactive 5-HT system. Thus, in animals and humans, a hyporeactive 5-HT system may result in enhanced vasopressin activity and increased aggression. Can the stress of emotional and physical insult, i.e. threat and attack, during adolescence affect the development of the vasopressin and 5-HT systems and alter normal aggressive behaviour in early adulthood? Adolescent male golden hamsters were weaned at postnatal day 25, and stressed for 2 weeks by daily 1 h bouts of threat and attack by adult hamsters. Male littermates were run in a parallel stress study using daily 1 h trials of isolation in a novel environment. During early adulthood, on postnatal day 45, 3 days after the cessation of stress trials, animals were tested for aggression in a resident: intruder model. The results show a context-dependent change in aggression. Animals with a history of abuse show exaggerated attack behaviour toward smaller males compared to littermates with a history of isolation stress. Conversely, when confronted by males of equal size, animals with a history of abuse show diminished aggression and increased submission compared to controls. It was determined that the density of vasopressin fibres and neurones in the hypothalamus is lower in abused animals compared to controls. In contrast, the number of 5-HT terminals within the hypothalamus is higher in abused animals compared to controls. These results provide evidence in an animal model that stress in the form of threat and attack during adolescence can alter the balance between vasopressin and 5-HT in the brain, resulting in inappropriate aggressive behaviour in early adulthood.

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Cancer Center, Georgetown University Medical Center, Washington, DC 20007, USA. The present study investigated whether dietary fat increases aggressive behavior in male mice and rats. High fat consumption may elevate circulating estrogen levels and estrogens, in turn, are associated with various non-reproductive behaviors, such as male aggression. The animals were assigned to two groups including those consuming a diet high in polyunsaturated fats (43% calories from fat) and those consuming a low-fat diet (16% calories from fat). Each male animal was housed with two females for three weeks. The male mice and rats were then confronted with an intruder kept on a medium-fat feed. The latency to first aggressive encounter was significantly shorter among the male animals kept on a high-fat diet than those males kept on a low-fat diet. Furthermore, the time spent exhibiting aggression was longer in the high-fat groups. Serum levels of estradiol (E2) were elevated by 2-fold in the male animals consuming a high-fat diet, when compared with the male animals kept on a low-fat diet. These findings suggest that dietary fat can increase aggressive behavior in male mice and rats, possibly by elevating circulating E2 levels.

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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 Laboratory of Neuroendocrinology, Rockefeller University, New York, NY 10021, USA. 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.

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Biol Psychiatry. 1998 Mar 15;43(6):446-57. Whole blood serotonin relates to violence in an epidemiological study. Moffitt TE, Brammer GL, Caspi A, Fawcett JP, Raleigh M, Yuwiler A, Silva P. Institute of Psychiatry, London, United Kingdom. BACKGROUND: Clinical and animal studies suggest that brain serotonergic systems may regulate aggressive behavior; however, the serotonin/violence hypothesis has not been assessed at the epidemiological level. For study of an epidemiological sample we examined blood serotonin, because certain physiological and behavioral findings suggested that it might serve as an analog marker for serotonergic function. METHODS: Whole blood serotonin was measured in a representative birth cohort of 781 21-year-old women (47%) and men (53%). Violence was measured using cumulative court conviction records and participants' self-reports. Potential intervening factors addressed were: gender, age, diurnal variation, diet, psychiatric medications, illicit drug history, season of phlebotomy, plasma tryptophan, platelet count, body mass, suicide attempts, psychiatric diagnoses, alcohol, tobacco, socioeconomic status, IQ, and overall criminal offending. RESULTS: Whole blood serotonin related to violence among men but not women. Violent men's mean blood serotonin level was 0.48 SD above the male population norm and 0.56 SD above the mean of nonviolent men. The finding was specific to violence, as opposed to general crime, and it was robust across two different methods of measuring violence. Together, the intervening variables accounted for 25% of the relation between blood serotonin and violence. CONCLUSIONS: To our knowledge, this is the first demonstration that an index of serotonergic function is related to violence in the general population.

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the PCPA-MAOI treatment avoids the prostate carcinogenic risk of testosterone administration in aging males, and seems to have euphorizing effects stronger than those expected only from MAOI therapy. Because of the several side effects of PCPA-MAOI testosterone, the present experiments should be interpreted very cautiously.

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Eur J Pharmacol 1995 Dec 29;294(2-3):721-726. Chronic forced swim stress of rats increases frontal cortical 5-HT2 receptors and the wet-dog shakes they mediate, but not frontal cortical beta-adrenoceptors. Takao K, Nagatani T, Kitamura Y, Kawasaki K, Hayakawa H, Yamawaki S Department of Psychiatry and Neurosciences, Hiroshima University School of Medicine, Japan. We studied the effects of chronic forced swim stress on 5-HT2 receptors and beta-adrenoceptors in the rat frontal cortex. The number of 5-HT2 receptors was increased immediately after the last chronic stress, but not after an acute stress. In vivo, the number of wet-dog shakes induced by a 5-HT2 receptor agonist, (+/-)-1-(2,5-dimethoxy-4-iodophenyl)-2-aminopropane (DOI), was increased 24 h after the last chronic stress. However, the concentrations of 5-HT and 5-hydroxyindole acetic acid (5-HIAA), measured by high pressure liquid chromatography (HPLC), were not altered by this stress. Binding sites for [3H]CGP-12177, i.e., beta-adrenoceptor sites, were unchanged after both the acute and the chronic stress. These results suggest that, in the rat, the chronic forced swim stress increases the number of frontal cortical 5-HT2 receptors and the number of wet-dog shakes mediated by these receptors, while the number of frontal cortical beta-adrenoceptors is not increased by this treatment.

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Behav Neurosci. 2003 Aug;117(4):667-74. Activation of serotonergic neurotransmission during the performance of aggressive behavior in rats. van der Vegt BJ, Lieuwes N, van de Wall EH, Kato K, Moya-Albiol L, Martinez-Sanchis S, de Boer SF, Koolhaas JM. Department of Animal Physiology, University of Groningen, Biological Centre, Haren, The Netherlands. B.j.van.der.vegt@biol.rug.nl High aggression is often linked to lowered serotonin (5-HT) neurotransmission. Although this may hold for high aggression as a trait characteristic of an individual, serotonergic activity is probably increased during performance of aggressive behavior. To test this hypothesis, first, the 5-HT1A agonist alnespirone and gamma aminobutyric acid-A agonist muscimol were administered into the dorsal raphe nucleus. These treatments, which inhibit 5-HT neuronal activity, were shown to decrease performance of aggressive behavior. Second, after a resident-intruder test, the activation of 5-HT neurons (measured by c-fos expression) was increased in high-aggressive rats, compared with low-aggressive rats or control rats that were not subjected to a social confrontation. Results show that performance of aggressive behavior increases 5-HT neuronal activity and that preventing this activation inhibits expression of aggressive behavior. J Cardiovasc Pharmacol.

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