Brain Mechanisms of Poor Anger Management

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Abstract

The loss of self-control is defined as a state in which impulsive aggressive behavior induced by stress cannot be restrained. The ventrolateral part of the prefrontal cortex (PFC), where projections from serotonin neurons in dorsal raphe nuclei are present, plays an important role in switching actions and controlling this impulsive aggressive behavior. Studies of the brains of individuals who have committed suicide demonstrated that serotonin secretion was deficient in the ventrolateral PFC. Since suicide is considered to be an impulsive aggressive behavior toward the self, decreased activity of serotonin neurons (5-HT-deficient brain) seems to underlie the pathologic condition of suicide. The activity of serotonin neurons is related to the arousal state because continuous activity is present during waking. Factors that further enhance the activity of serotonin neurons are the rhythmic motor exercises of walking, respiration, and mastication, in addition to sunshine. Walking in the sunshine is good for serotonin activity. However, in modern society, sitting at a personal computer and watching the display in a lifestyle that reverses day and night is common for many. Such a lifestyle carries the risk of creating the 5-HT-deficient brain. Rapid increases in the number of individuals with depressive disorder or poor anger management have recently been seen in Japan, and it seems that the 5-HT-deficient brains are involved in these symptoms. We have demonstrated with experimental data that Zen meditation, yoga, and rhythmic motor exercises such as walking are effective for preventing these conditions. There is also increasing evidence that solar irradiation and rhythmic motor exercises are important for the healthy postnatal development of brain serotonin neurons.

Key words Serotonin neurons, Prefrontal cortex, Depressive disorder, Zen meditation, Walking, Postnatal development of the brain

Introduction

Individuals who have poor impulse control represent a social problem. For example, mothers who lose self-control and abuse their infants, fathers who become angry and violent when their babies cry, elementary school children who lose control and create problems, and socially withdrawn children who lose control and kill their parents. In addition, an increasing number of people in their 30s to 50s are losing control and are being arrested for acts of violence.

Although the living environment has improved greatly and life has become more convenient, diseases of the mind are becoming more problematic. Such diseases have been increasing among people from all walks of life, regardless of age or sex, suggesting that our social environment may be responsible. Although lifestyle-related diseases such as metabolic syndrome and diabetes mellitus have been attracting a great deal of attention, it is the author's contention that poor anger management and depressive disorder also are attributable to unhealthy lifestyles. Depressive disorder is a mental condition that has recently seen an explosive increase. It is considered that one's environment can cause impairment of serotonergic neuroral system, which is related to depressive disorder, and is behind the increasing prevalence of depressive disorders (note: a brain with impaired 5-HT neurons is arbitrarily called

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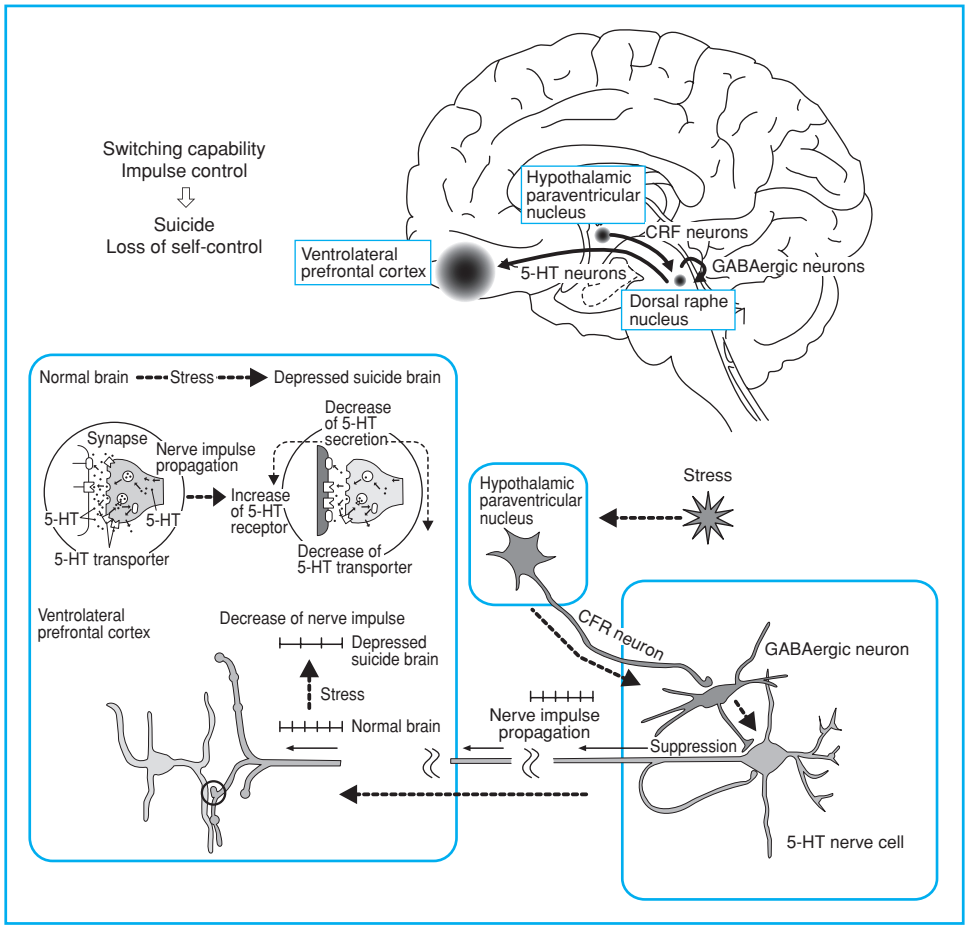

Fig. 1 Activation by stress of brain structures related to depressive disorder and suicide (hypothesis)

a 5-HT-deficient brain). This paper points out some of the problems related to modern life that are responsible for poor anger management, with attention focused on the 5-HT-deficient brain as a mechanism of poor anger management. Possible measures against poor anger management are also proposed in the latter half of the paper, based on the results of studies on the postnatal development of serotonin neurons in kindergarten children.

Serotonin-deficient Brain

Ventrolateral part of the prefrontal cortex (PFC) and serotonin neurons

The brain area most closely related to the phenomenon of "losing control of oneself" is the ventrolateral part of the PFC (Fig. 1). This area controls impulsive aggressive behavior and is responsible for switching actions.[1] Damage to this area causes perseveration, a characteristic that is common in autism. Damage to the area also causes the inability to change an impulsive aggressive behavior, resulting in poor anger management. If the impulsive aggressive behavior is not directed at others, but to the person himself or herself, the result may be suicide.

Although there has been little progress in the analysis of brain mechanisms of poor anger management, there have been many autopsy studies of the brains of individuals who have committed suicide.[1] According to reports of such studies, 5-HT autoreceptors (5-HT_{1A}) are increased in the dorsal raphe nucleus, where serotonin neurons that project to the PFC are distributed; this suggests diminished activity of serotonergic

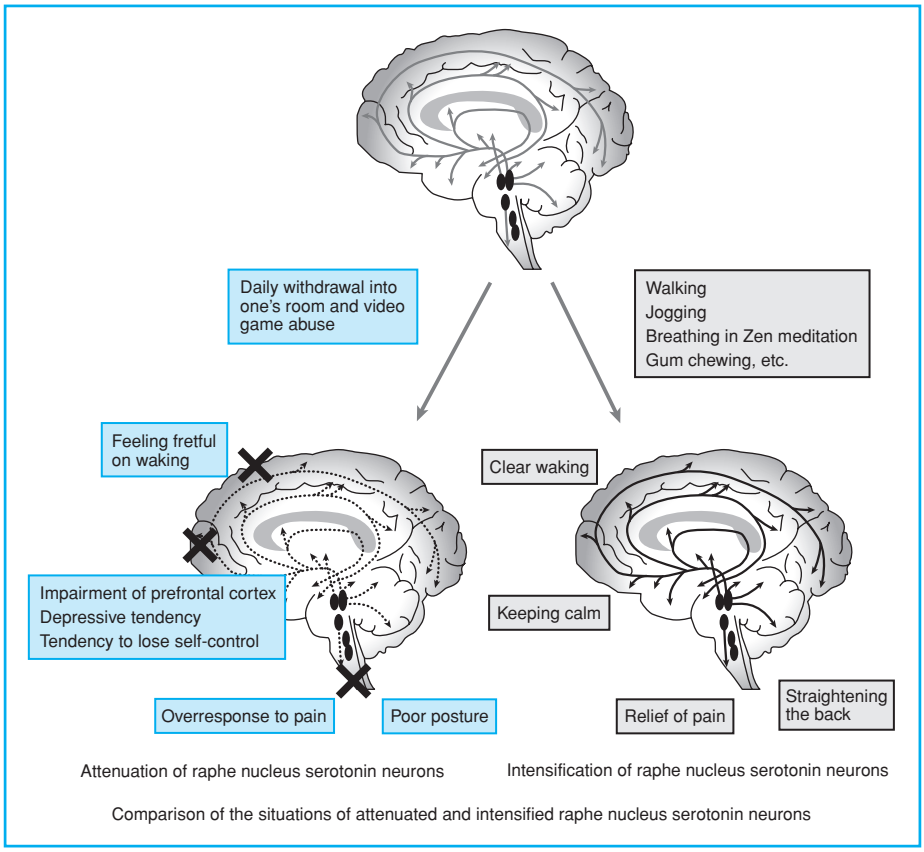

Fig. 2 Means of increasing serotonin

neuronal system. Although serotonin neurons are known to project extensively to various areas including the cerebral cortex, limbic system, diencephalon, and brainstem, a decrease in 5-HT transporters and an increase in postsynaptic 5-HT receptors are noted in the ventrolateral PFC in particular. Thus, impaired 5-HT transmission in the brains of suicides has been noted (Fig. 1).

The ventrolateral PFC is also attracting attention as an area that is activated when a person lies.[2] The act of telling a lie involves consciously inhibiting a reaction that would occur normally and substituting a different action instead. Apart from the moral issue of telling a lie, it is apparent from our daily activities that things rarely go the way we intend. We are coping with life by switching actions according to the situation at hand. In this sense, the ability to perform switching is an extremely important function in human life.

Serotonergic neuronal system enables the smooth performance of this function. If the role is not adequately exercised (as in the 5-HT-deficient brain), it seems that abnormal behaviors such as fits of rage or suicide are likely to occur.

Characteristic features of serotonergic neuronal system

Why then does typical modern life cause serotonergic neuronal system to become impaired? This can be explained by the features of serotonin neuronal activity. Animal data suggest that serotonin neurons are in the resting state while an individual is sleeping, but begin to fire continuous impulses when the person gets up in the morning. Serotonin neurons are responsible for the secretion of serotonin throughout the entire brain to facilitate the smooth performance of brain function while the person is awake. In other words, serotonin neurons are those that direct the arousal state.

The specific role of serotonin neurons is outlined as follows (Fig. 2). The reader is asked to

imagine the situation when daily activity begins upon waking up in the morning. The brain, after a night of rest, begins to work actively, causing a clear arousal level (an effect on the cerebral cortex). The autonomic nerves are stimulated, the heart beats faster, and respiration and metabolism increase, producing a standby status under sympathetic nerve dominance (an effect on the autonomic nerves). Muscles become activated; the tension of antigravity muscles and those responsible for posture increase to straighten the back and produce a clear facial expression (an effect on antigravity muscles). Mentally, the person feels less tense and anxious, and more energetic (an effect on the cerebral limbic system). Serotonin neurons exert an excitatory, modulatory effect on all these changes. Serotonin neurons are of value as a coordinator that produces a state tending toward excitation, without exerting a direct action on the muscles or the heart.

In contrast, in the 5-HT-deficient brain, the person has poor awakening, poor standby of the autonomic nerves, a loose facial expression, and weak posture. Mentally, the person feels strong tension and anxiety, and has depressive tendency, a feeling of fatigue, and loss of mental balance. These characteristics overlap with the symptoms of depressive disorders and those seen in people with poor anger management.

Rhythmic motor exercises and the information technology (IT) society

Although serotonergic neuronal system regulates the arousal state, the factor that activates serotonergic neuronal system while the person is awake consists of various rhythmic motor exercises. The serotonin neuron has a unique feature in that its firing frequency is increased by these rhythmic motor exercises. Such rhythmic motor exercises include locomotion, mastication, respiration, and other movements common in daily life. Therefore, serotonin neurons should not become weakened if an individual's life consists of ordinary physical movements.

However, diseases associated with weakened serotonergic neuronal system, such as depressive disorder and panic disorder, began to increase around the 1980s. One factor that has caused major changes in the living environment since that time is the advent of personal computers. Many people began to use personal computers, which caused prolonged periods of staring at the display while sitting at a desk. If an individual spent a great deal of time at a computer every day, the rhythmic movement of walking naturally would decrease markedly, and the person would begins to hold his or her breath unconsciously, resulting in suppression of the rhythmic movement of respiration. If the life pattern of constant inactivation of serotonin neurons continues for several months, the function of serotonin neurons attenuates, leading to the formation of a serotonin-deficient brain. If this condition is combined with negative factors such as stress and fatigue that weaken the function of serotonin neurons, the condition could rapidly develop into depression or a state of "poor anger management."

Sunlight and reversal of day and night

Another factor that activates the function of serotonin neurons is solar irradiation (sunlight). Over the past 10 years or so, convenience stores and family restaurants shifted to 24-hour operations, allowing anyone to lead a life in which day and night are reversed. As a result, some people began to stay awake during the night and go to bed in the morning. However, a human being is a diurnal animal that is genetically organized to have brain and autonomic functions suitable for daytime activity. Humans are not nocturnal animals like rats. If people disregard this fact and live a life that conflicts with our diurnal nature, various mental and physical complaints eventually will appear.

The activation of serotonin nerves by sunlight is easy to understand when the mechanism of winter depression (seasonal affective disorder) is considered. The point is that the light in this case is not ordinary electric light but sunlight; there is a large difference in illumination between the two types of light. High illumination phototherapy is applied to actual clinical cases.

Serotonergic neuronal system and stress

Factors that aggressively attenuate serotonergic neuronal system are stress and fatigue. It is a clinically well-known fact that stress induces depressive disorder. It has been established that the endocrine system, including the hypothalamus-pituitary-adrenal axis, is involved in the response to stress. Stress-related hormones such as cortisol and ACTH do not exert a direct inhibitory effect on serotonin neurons in the raphe nucleus. However, a neural circuit that directly inhibits

serotonin neurons from the stress center of the hypothalamic paraventricular nucleus has recently been found[3] and has attracted much attention. More specifically, it has been demonstrated in animal experiments that there is a neural circuit in which corticotropin-releasing factor (CRF) neurons within the hypothalamic paraventricular nucleus directly project to the dorsal raphe nucleus and inhibit serotonin neurons via gamma-aminobutyric acid GABAergic neurons present in the dorsal raphe nucleus (Fig. 1). Therefore, if stress continues, serotonin neurons will be greatly inhibited.

Meanwhile, the question remains as to whether today's society truly is under enormous stress. Since World War II, the Japanese people have enjoyed about 60 years peace. The living environment is convenient and comfortable, and the intensity of stress should not be compared to that of people living in countries undergoing warfare.

In the author's opinion, the locus of the problem is stress in the human brain rather than events in the environment. The recent explosive increase in the incidences of depressive disorders and poor anger management is considered to be attributable to individual's weakened tolerance to stress. The real problem seems to be that the aforementioned unhealthy lifestyles are producing serotonin-deficient brains.

Evaluation of the Activity of Serotonergic Neuronal System in Humans

We have investigated possible methods of activating the function of serotonergic neuronal system, and have proposed various means including conscious abdominal breathing in Zen meditation or yoga, rhythmic walking and other motor exercises (jogging, bicycle ergometer exercise, squats, etc.), rhythmic masticatory movement (gum chewing), and truncal rhythmic movement (hula dancing).[4–6] We have shown that these rhythmic motor exercises activate serotonergic neuronal system and cause high-frequency alpha waves in electroencephalogram (EEG) to occur, providing an analgesic effect and exerting a facilitatory effect on antigravity muscles. In addition, psychologic tests have demonstrated that the rhythmic motor exercises also relieve tension and anxiety, improve depressed mood, and elevate the vigor activity index (Fig. 2).

It has already been shown in animal experiments that elevation of the brain serotonin concentration due to activated serotonin neurons results in the release of serotonin into peripheral blood via serotonin transporters present in vascular endothelial cells of the blood-brain barrier.[7] Therefore, when serotonin secretion is increased in an extensive area of the brain after the activation of brain serotonergic system, the secreted serotonin is released into peripheral blood via serotonin transporters in vascular endothelial cells. This enables us to evaluate serotonin activity using peripheral blood or urine samples.

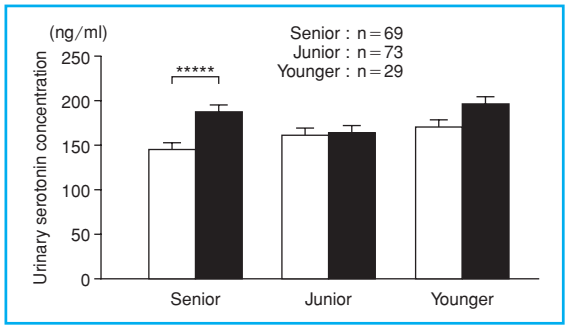

Fig. 3 Changes in mean urinary serotonin (5-HT) concentrations in senior, junior, and younger kindergarten children before and after a rhythmic exercise program (REP)

White columns and black columns denote mean urinary 5-HT concentrations before and after REP, respectively.

Measurement of Urinary Serotonin in Kindergarten Children

Effect of a rhythmic exercise program

During the recent two years, urinary serotonin concentrations were measured in kindergarten children in relation to rhythmic motor exercises, solar irradiation, and fatigue, which was implemented as one of the Programs for Promoting Educational Reform by the Ministry of Education, Culture, Sports, Science and Technology. As a result, it was apparent that the implementation of rhythmic movements activated serotonin neurons in kindergarten children aged 3–6 years (Fig. 3).

Effect of solar irradiation

To determine the effect of solar irradiation, urinary serotonin concentrations measured at rest in winter, spring, and summer were compared, and a significant increase in the concentration was

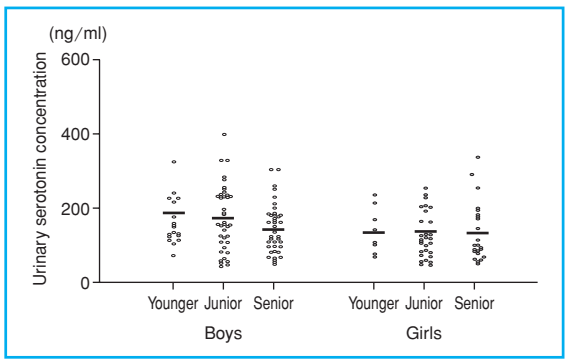

Fig. 4 Distribution of urinary 5-HT concentrations in kindergarten children at rest in relation to age (younger, junior, senior) and sex

found in summer. When the effect of rhythmic motor exercises in winter was examined in relation to the presence or absence of sunshine, urinary serotonin concentrations were found to be higher in the presence of sunshine. However, there was no combined effect of sunshine and rhythmic motor exercises in summer. Moreover, when rhythmic motor exercises were performed under strong sunshine in summer, there was no substantial increase in the activity of serotonin neurons. Although there is no established explanation for this finding, additional activation by rhythmic movements may not be available under a situation in which serotonin neurons have been fully activated by sunshine.

Effect of fatigue

To determine the inhibitory effect of fatigue on the function of serotonin neurons, changes in urinary serotonin concentrations created by rhythmic motor exercises were examined before and after a day when the children went on an excursion. Rhythmic motor exercises caused a decrease in serotonin concentrations on the day after the excursion, suggesting that fatigue inhibited the function of serotonin neurons. This inhibitory effect of excursion-induced fatigue was found to disappear on the following day.

Postnatal development of brain serotonergic system

When mean urinary serotonin concentrations at rest (in the morning) were compared between age groups, values were highest in younger children (3–4 years of age). Slightly lower values were obtained in children 4–5 years of age, and the lowest values were noted in older children 5–6 years of age (Fig. 4). Urinary serotonin concentrations in the senior children were similar to those obtained in adults. These results are compatible for findings that brain serotonin concentrations are higher in infancy than in adulthood, and decrease to reach a stable level during the course of postnatal development. When viewed from another angle, it is presumed that the ages from 3–6 years after birth are critical period for postnatal development of serotonin neurons.

A comparison of urinary serotonin concentrations in boys and girls showed that there was a gradual decrease in serotonin concentrations in boys from 3–6 years after birth toward an adult level, whereas serotonin concentrations in girls decreased to an adult level earlier, at the age of 3–4 years. Thus, there may be gender differences in the postnatal development of brain serotonergic system.

Countermeasures and Issues to Solve

As mentioned previously, the time from birth to age 6 is considered to be an extremely important period for the postnatal development of brain serotonergic system. Two activators are effective for the healthy development of brain serotonergic system in children aged 3–6 years. During that time rhythmic movements and solar irradiation clearly activate serotonin neurons. Thus, it is important to promote the healthy postnatal development of brain serotonergic system by incorporating these two factors in the daily activities of kindergarten children.

In contrast, lifestyles characterized by withdrawal at home, lack of exposure to sunlight, and staying up late at night are negative factors against the development of brain serotonergic system. It is possible that such lifestyles contribute to the development of poor anger management and depressive tendencies.

Finally, it should be noted that grooming is a third factor in activating serotonin neurons. Carrying a baby on the back or in the arms is regarded as a grooming action between mothers and children, and these actions lead to the activation of brain serotonergic system in both mothers and children. Information on the development of brain serotonergic system prior to the age of three years is awaited from future studies.

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