Chapter

Roles of Glucose and Sucrose Intakes on the Brain Functions Measured by the Working Ability and Morris Maze

Akikazu Takada, Fumiko Shimizu, Yukie Ishii, M. Ogawa and Tetsuya Takao

Abstract

Sugars such as glucose or sucrose are considered hazardous foods because their intakes lead to obesity, further causing diabetes mellitus (DM), or cardiovascular diseases. However, glucose is needed for many brain functions such as memory and emotion among others. Glucose induces the secretion of insulin, which is needed for transportation of tryptophan from the blood to the brain. Serotonin, which is converted from tryptophan, is important for mood stability, control of emotion, and feeding is inhibited by serotonin in the hypothalamus. We discuss transportation of glucose from the blood to the glia cells. After glycolysis of glucose in the glia lactic acid is transported to cells such as glutaminergic neurons. After the release from neurons glutamic acid is taken up into glia cells and further to neurons again. Sucrose is degraded into glucose and fructose in the intestine thus intake of sucrose increases plasma levels of glucose. We show that intake of sucrose enhanced memory measured by Morris maze in rats and improved the working ability in humans. Roles of glucose and sucrose intakes are discussed together with the function of serotonin in feeding.

Keywords: sucrose, glucose, feeding, glucose transporter, glutaminergic neuron, Morris maze, working ability, glycolysis, astrocyte, serotonin, hypothalamus

1. Introduction

Obesity is now a global burden [1, 2]. Increase in the prevalence of obesity has lead the American Heart Association (AHA) to call for actions to prevent the consequences of this epidemic [3, 4]. Recently, the AHA reviewed many weight-loss approaches for the management and treatment of obesity [5].

Foods such as fats, carbohydrates or sugar are considered to be causes of such increase in global obesity pandemic. Intakes of carbohydrates result in increase in release of insulin which suppresses the release of fatty acids into circulation, thus storage of fat in fat cells. So carbohydrate is blamed for increase in obesity.

The German Nutrition Society published guidelines in which relationships between carbohydrate intake and prevention of nutrition-related diseases are indicated [6]. The guideline proposes that high carbohydrate intake at the expense of total fat and saturated fatty acids reduces the concentrations of total, LDL, and HDL

cholesterol. A high carbohydrate consumption at the expense of polyunsaturated fatty acids such as EPA or DHA increases total and LDL cholesterol. But reduces HDL cholesterol. Further, intake of high carbohydrate increases triglyceride concentration. High consumption of sucrose increases obesity and type2 diabetes mellitus (T2DM).

On the other hand, as stated later, glucose is needed for many brain functions such as memory, emotion, decision, motivation etc. Sucrose is degraded in the intestine and gives rise to glucose. Some studies show that sucrose intakes improve memory.

In the present review, we discuss the transportation of glucose from the blood to the brain, influences of glucose or sucrose on memory and working ability, and feeding.

2. Importance of glucose in the brain functions

It is now well known that glucose is important for a variety of brain functions. Late 20th century, the development of positron emission tomography (PET) made it possible to visualize the amount of glucose in discrete regions of the brain. For example, light stimulation increased the metabolism of cerebral glucose in the primary visual cortex [7].

The learning of a complex visuospatial motor task was shown to increase the use of glucose by the brain [8].

Summarizing data published, PET studies showed that cognitive demand increased glucose metabolism in localized regions of the brain. In PET studies radioactively labeled glucose appears in brain areas that are metabolically active within a few minutes after the injection into blood. These observations indicate that the brain relies on glucose when neurons are activated.

2.1 Transportation of glucose from blood to brain

Tsacopoulos et al. [9] indicated that capillaries of the brain are surrounded by glia cells and glucose uptaken is phosphorylated exclusively in glia cells, not in neurons.

In mammalian there is evidence that glutamate is a coupling signal between neuronal activation and glucose uptake by astrocytes [10, 11].

Astrocytes surround capillaries, which indicate that astrocytes form the first cellular barrier that glucose encounters in the brain. This suggests that astrocytes are likely sites of primary glucose uptake (**Figure 1**).

Schematic figure of the cytological relationships among capillary, astrocyte, and neuron. Processes of astrocytes surround capillaries (end-feet) and ensheath synapses. Receptors and uptake sites for neurotransmitters are on astrocytes. Astrocytes are ideally suited to sense synapse activity and to couple it with glucose uptake and its metabolism.

There are glucose transporters (55kDA Glut1) in the inner sites and outer sites of endothelial cells, and between astrocytes and capillaries (45kDA Glut1). There are Glut 3 transporters on walls of neurons [12].

Glut 1 and Glut 3 glucose transporters are present in the walls of capillaries and neurons (**Figure 2**).

Glucose transporters, Glut1 are located in the luminal and abluminal membranes of brain endothelial cells. There are small amounts of Glut 1 located in the cytoplasm and the largest fractions of Glut1 are at the abluminal membranes. The lower content of Glut1 at the luminal membrane may be due to the comparably high glucose concentration in this membrane, which is close to the plasma concentration.

There appears to be a tight coupling between Na^+ dependent glutamate uptake by astrocytes and glucose utilization [13] (**Figure 3**).

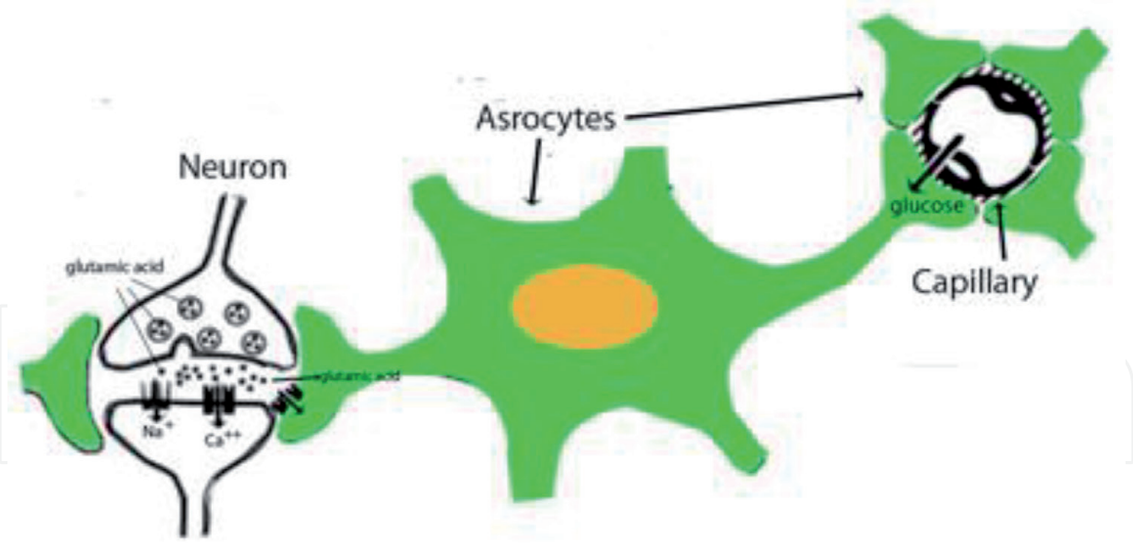

Figure 1.
Capillary, astrocyte and neuron.

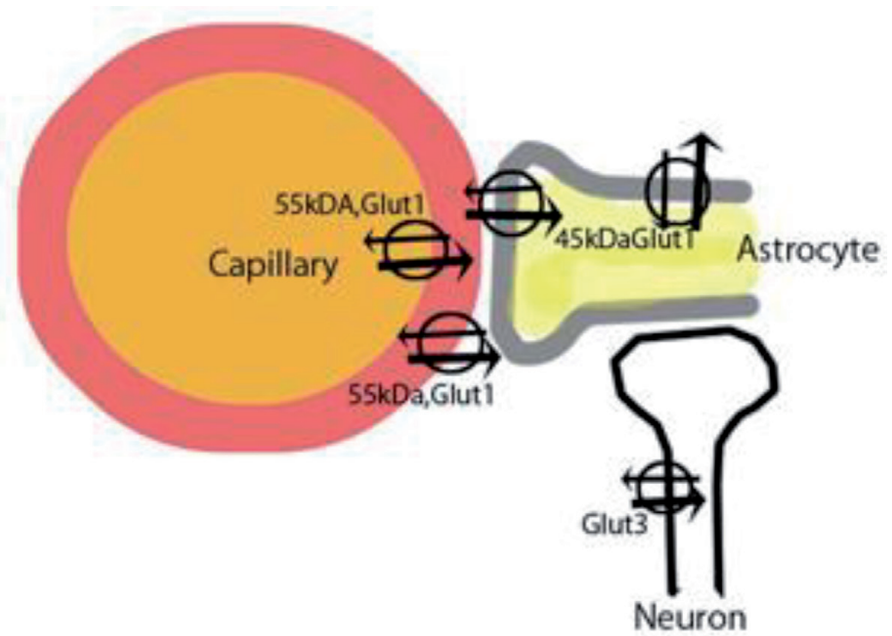

Figure 2.
Glucose transporters in the walls of capillaries and the walls of neuron.

Glutamate is cotransported with Na^+, causing increase in the concentration Na^+ in astrocytes, which activate the astrocyte Na^+/K^+-ATP ace. Activation of Na^+/K^+-ATPase stimulates glycolysis. Lactate released by astrocytes is taken up by neurons and become energy source of neurons.

When summarized, glucose is degraded by glycolysis in astrocytes which generates two molecules of ATP used for uptake of K+ and glutamate from the synaptic cleft. When neurons are active, glycolysis is more active, so that transportation of glucose from the blood to astrocytes increases.

2.2 Roles of glucose in memory

It has been known long time that glucose intake improves cognitive behaviors. In elderly humans, changes in blood glucose levels following ingestion of a glucose containing drink was shown to be significantly correlated with performances in the Wechsler memory scale [14].

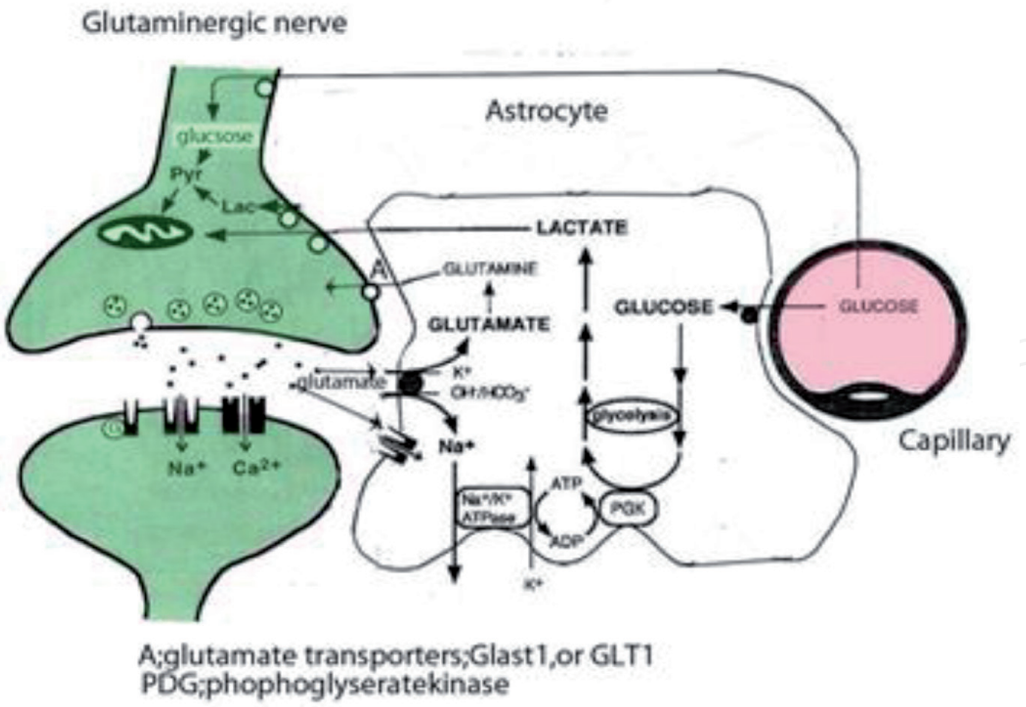

Figure 3.
Transportation of glucose from the blood to neurons.

Verbal fluency of a group of 80 females, aged 20, was measured after taking a glucose drink or placebo. The fluency was significantly higher after a glucose drink [15].

It was shown that an equilibrium starts between the level of glucose between blood and brain [16]. Such mechanism suggests that higher blood glucose levels promote better performance of brain functions.

The recall of a story was associated with blood glucose levels measured by Wechsler memory scale [17]. A positive correlation between blood glucose and forgetting was shown in young adults, thus those with higher initial blood glucose remember more.

There are various data indicating that glucose supply to the brain is necessary for maintaining good performances of brain functions.

In rats, systemic injections of glucose were shown to enhance learning and memory in many conditions. When microinjected into the specific sites of the brain, glucose levels increased and improved behavioral performances controlled by these sites [18].

Furthermore, glucose administration was shown to enhance memory in generally healthy aged rodents and humans. Glucose ingestion resulted in significant enhancement of performances on several tests including orientation, word recognition, and recall, narrative prose, and face recognition [19].

2.3 Glucose and memory measured by Morris maze experiments

As stated above, glucose intakes improve brain functions. Sucrose is degraded to glucose in the intestine and glucose is transported to the blood. A few systematic studies have been carried out as to the effects of sucrose on brain function [20, 21].

Morris used the delayed matching-to-place task which is an unusual variant of the water-maze protocols [22].

2.3.1 Experimental procedures

Wistar rats aged 11 weeks were trained in water to learn the location of the platform. Rats later learned to reach the platform in 15 min. After 6–12 trials. Rats were

administered either glucose (2 g/8 ml/kg) or 8 ml/kg of water intraperitoneally. 24 hours later rats swam in Morris water maze and the ratio of stay at the platform (target) quarter to the rest of the area was measured. The distance to the target was also compared between glucose administered rats and the controls.

2.3.2 Results

Figure 4 show that the ratio of stay in the target quarter in the test was larger after glucose was given, but data are not statistically significant.

Rats were given sucrose solution (10%) or sucralose solution (0.015%) or water as a control in a drinking bottle.

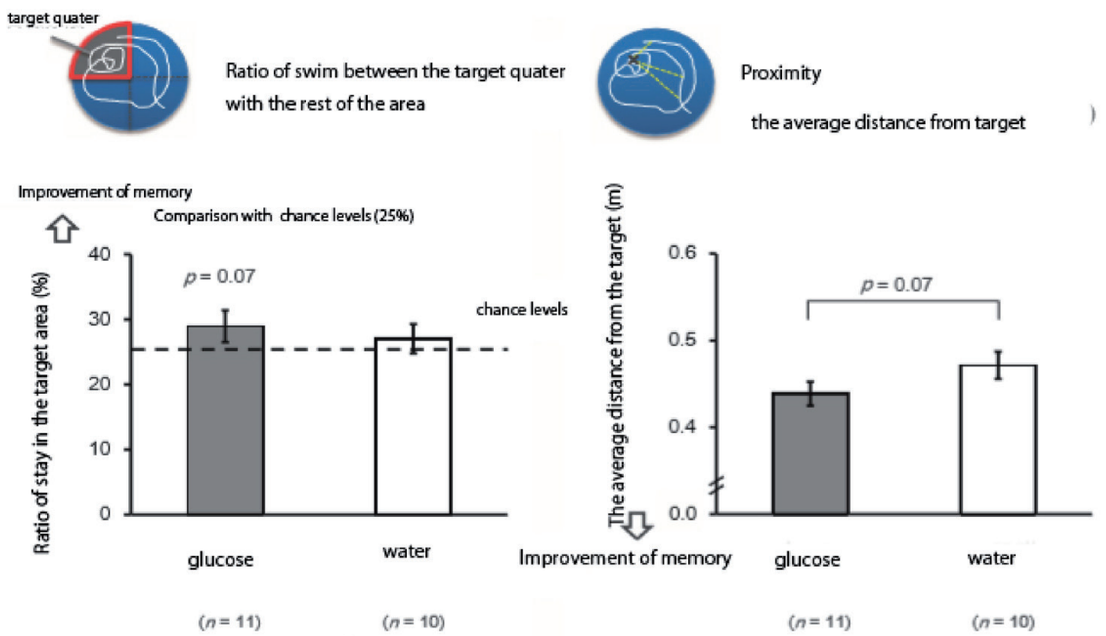

Figure 4.
Effects of glucose administration on memory [23].

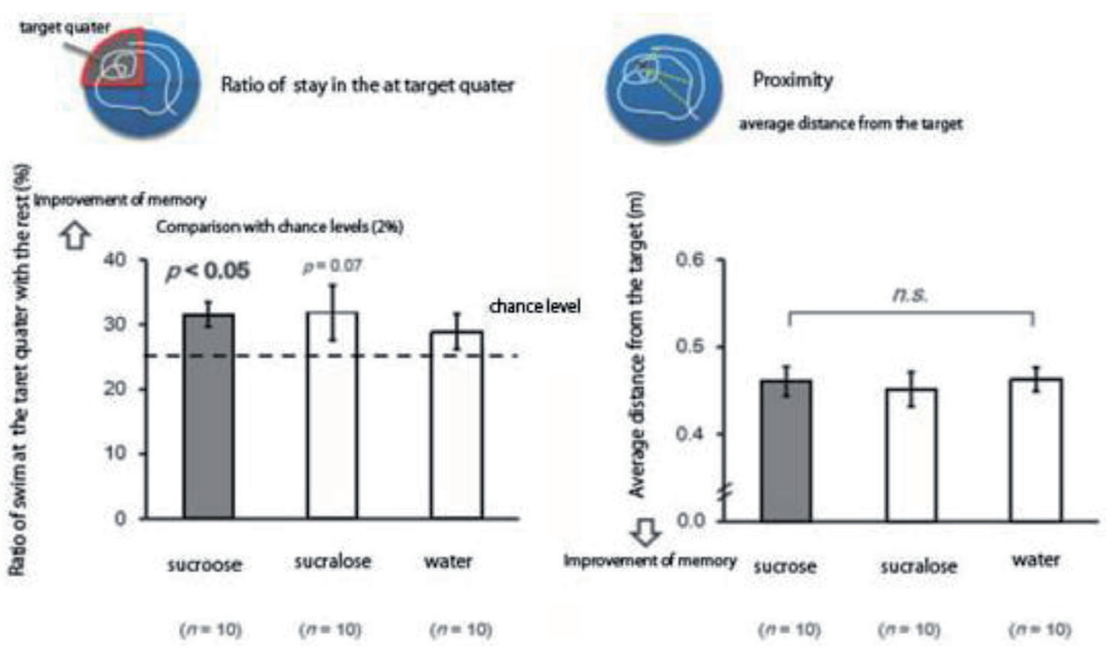

Figure 5.
Effects of sucrose administration on the improvement of memory.

Figure 5 shows that rats given sucrose stayed at the target quarter significantly more compared with rats given sucralose. There was no significant decrease about the proximity measurements between rats given sucrose and sucralose.

These results clearly show that the administration of sucrose improved memory consolidation when compared with rats given sucralose in Morris maze experiments.

3. The working ability after administration of glucose, sucrose or fructose in young women

Female college students participated in the experiments. They took Uchida-Kraaepelin tests and drank solutions containing glucose, sucrose, fructose or water as controls.

3.1 Uchida-Kraepelin tests

There are numbers of a digit lined. Two numbers lined together are added [24, 25]. The number of the higher digit is described. This procedure is repeated for 1 min. Then the addition of numbers of the second line was performed, and repeated for 15 min. The total numbers added are calculated, and the numbers are compared before and after the experiment.

The working duty of 1 min. Was repeated 15 times then drinks were taken. After blood measurements at 30 min. Tests were repeated.

Figure 6 shows that the working ability was significantly higher after the administration of sucrose, although there was a tendency for the working ability to increase after glucose or fructose administration, but not significantly.

We examined correlation coefficients between blood glucose levels and the working ability. Although there tends to be increase in the working ability with increase in blood glucose levels, but not significant.

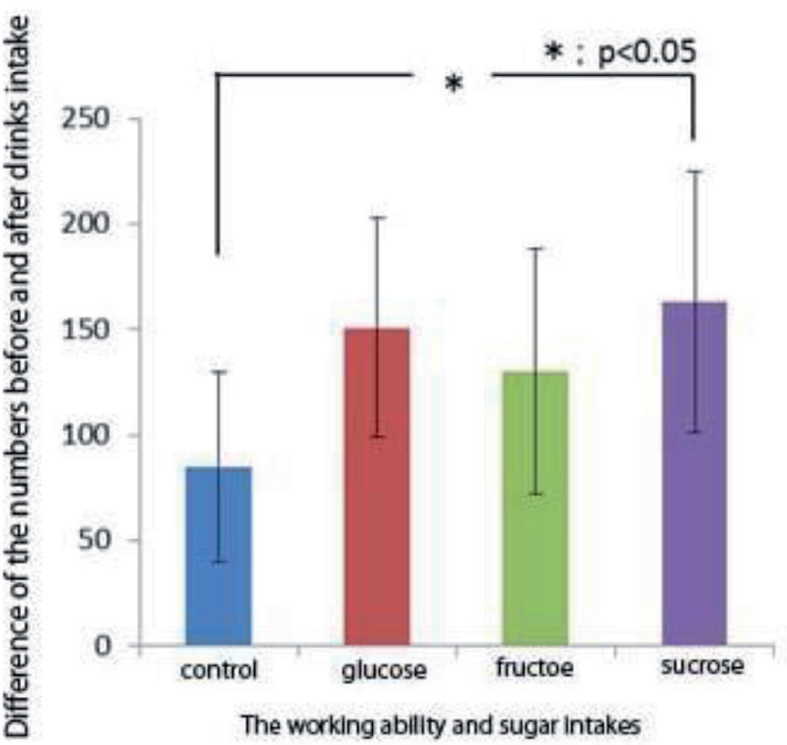

Figure 6.
Relationship between sugar administration and the working ability.

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4. Transportation of tryptophan to the brain and conversion to serotonin

Central serotonergic neurons play important roles in a variety of functions in animals and humans (see Review [26]).

We wanted to know if serotonin affects feeding by using injection of MAO inhibitor such as tranylcypromine (TC) intra peritoneally or by microinjection of TC into the hypothalamus.

At first, we injected TC intraperitoneally into rats and measured changes in body weights and foods intake [27].

Figure 7 shows that after the injection of TC in rats body weights decreased and amounts of food intakes decreased significantly.

Figure 8 shows that micro infusion of TC solution into the paraventricular nucleus of hypothalamus resulted in dramatic decrease of food intakes and body weight. These data suggest that serotonin inhibited feeding.

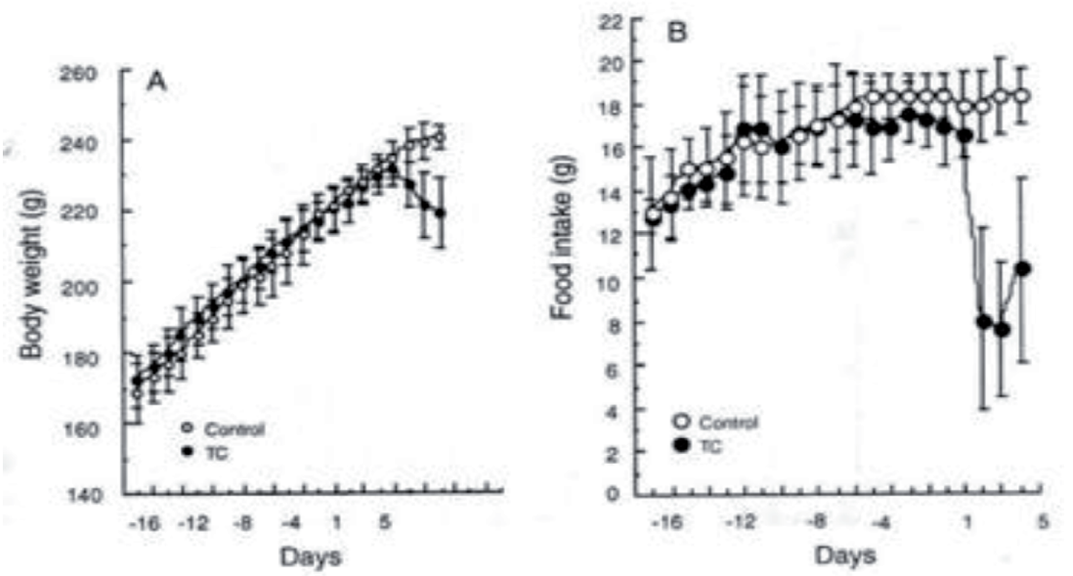

Figure 7.
Growth curves of rats administered with TC or vehicle.

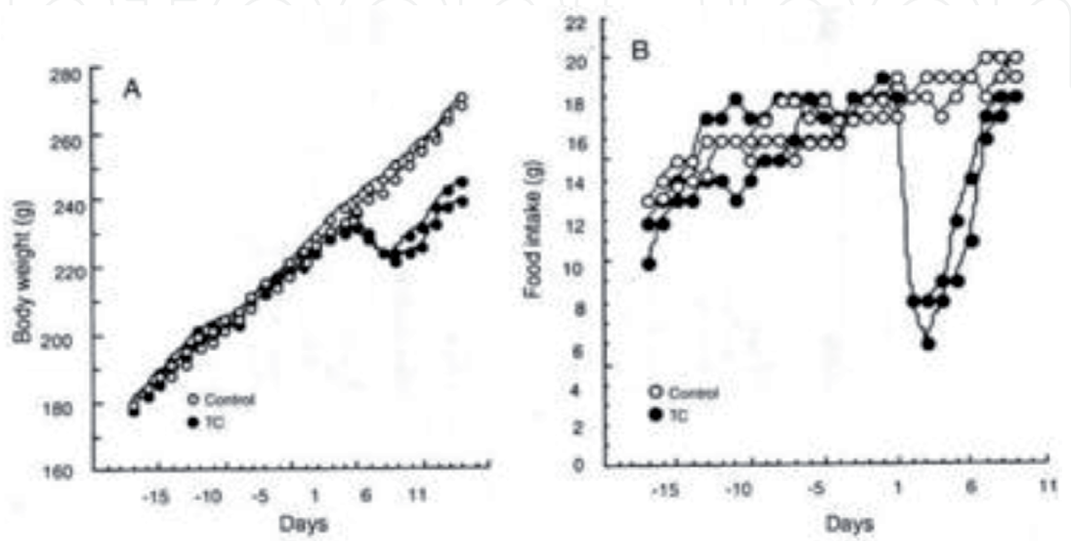

Figure 8.
Changes in body weight and amounts of food intakes after the injection of TC into hypothalamus.

5. Discussion

Obesity pandemic is a great concern for not only health professionals but lay people. Because of such concern, weight loss diets often recommended are the restriction of either carbohydrates or fats. Low fat diets were popular in late 20th century, but carbohydrate restriction became popular in recent years. The proponents of carbohydrate restriction claim that this diet decreased insulin secretion which causes elevated release of free fatty acids from adipose tissues and elevated fat oxidation and energy expenditure. The restriction of carbohydrates was reported to decrease body fat more than restriction of dietary fat [28–30].

On the other hand it is well known that glucose is needed for many brain functions. Although neurons can use lactic acid astrocytes need glucose, which is degraded by glycolysis. ATP produced during glycolysis is used for the uptake of glutamate released from activated neurons [13, 31–33].

Since the administration of glucose or sucrose improved memory functions stated above, we must pay attention to maintaining good brain function in choosing carbohydrate restricted diets.

Glucose ingestion increases blood glucose levels, further insulin levels. Burtman's group showed that insulin is needed for the transportation of tryptophan from blood to brain [34, 35].

Tryptophan is converted in the brain to serotonin, further melatonin [36].

Figure 9 shows that tryptophan absorbed from the intestine is transported to the brain in the presence of insulin. 5HT; serotonin.

Serotonin is important for many brain functions such as emotion, feeding, sleep resilience or satiety. We showed that increase in serotonin by intraperitoneal injection or by infusion into the hypothalamus of tranylcypromine resulted in inhibition of feeding (**Figures 7** and **8**).

Thus, glucose administration indirectly affects brain functions by increasing the concentration of serotonin in the brain.

Finally we should not forget the possibility of increased pleasure, thus increased motivation due to the stimulation of pleasure centers such as Nucl.Accumbens by sweet taste of sucrose as reviewed by Berridge and Kringelbach [37].

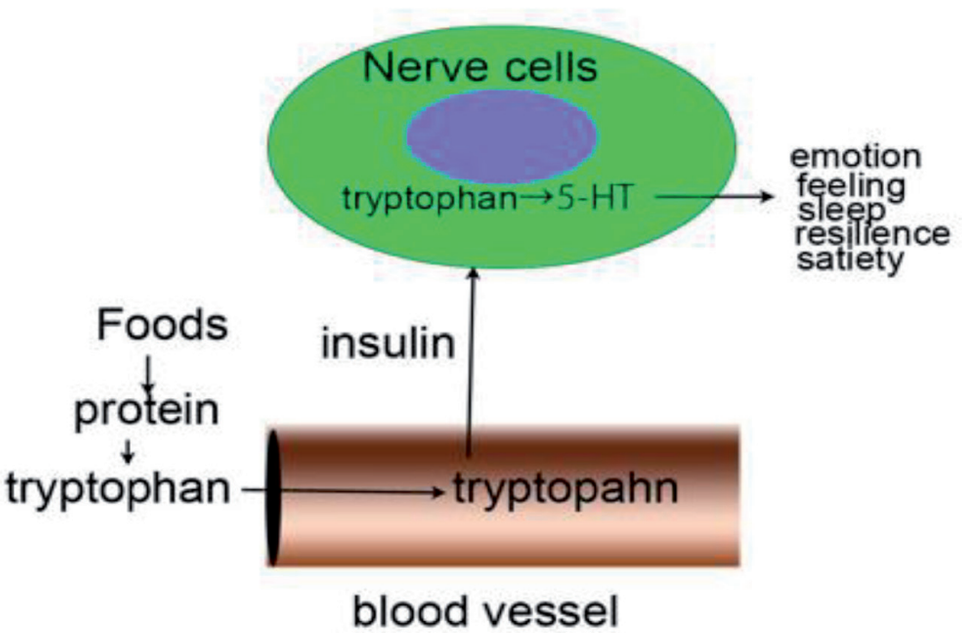

Figure 9.
Tryptophan transport from blood to brain.

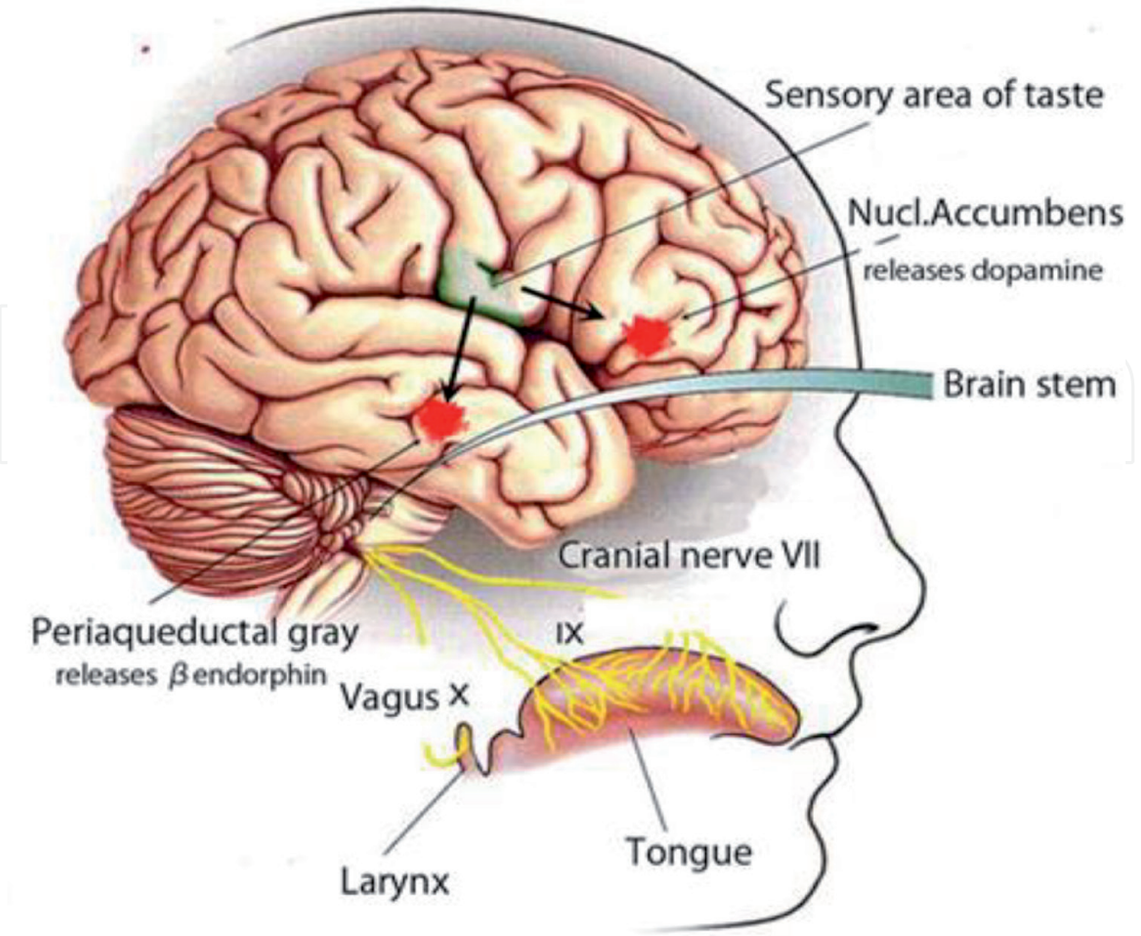

Figure 10.
Brain areas related to the stimulations by taking palatable foods.

Figure 10 shows a schematic representation of brain areas stimulated by palatable foods such as sucrose.

Sucrose applied to the taste buds on the tongue stimulates afferent fibers of cranial nerves such as IX or VII, which send informations of the taste to sensory areas of the brain. The stimulations of the taste area further activate Nucl.Accumbens, releasing dopamine and the periaqueductal gray in the midbrain, releasing βendorphin. Such stimulation may enhance the motivation [38, 39].

6. Conclusion

Since brain needs glucose for variety of functions, attention must be paid to glucose when various diets related to glucose administration are discussed.

Conflicts of interest

There is no conflict of interest for any author.

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