Sugar and **behaviour**

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Summary

This paper describes the current state of knowledge about the potential effects of sucrose consumption on the brain and human behaviour. Scientific literature on the following issues is reviewed:

- **Brain metabolism, blood glucose and dietary sucrose**
- **Effects of sucrose intake on hyperactivity**
- **Effects of sucrose intake on cognitive performance via blood glucose**
- **Effects of sucrose on behaviour and cognitive performance via micronutrient deficiencies**
- **Effects of sucrose on serotonin synthesis in the brain**

There appears to be no scientific substantiation for any adverse effects of dietary sucrose on the brain or on human behaviour in normal healthy subjects. Only in a few children with rare hypersensitivity reactions, sucrose intake could contribute to the Attention Deficit Hyperactivity Disorder. However this cannot be the rationale to discourage sucrose intake in the general population.
There is also no evidence that habitual sucrose intake levels via balanced diets cause micronutrient deficiencies, which could negatively influence brain function and behaviour.

There is some evidence that substantial fluctuations in the blood glucose level could influence brain function in a subset of sensitive subjects. Such fluctuations may be particularly related to intake of carbohydrates with a high glycaemic index (GI). Since the GI of sucrose only has only a moderate value (68 compared to 100 for glucose), it is not likely that sucrose intake is a specific and significant factor in this regard.
Since sucrose, like all other digestible carbohydrates, stimulates insulin secretion, it will enhance the uptake of large neutral amino acids (LNAA) but not tryptophan by the muscle, which leads to an increase in the tryptophan/LNAA ratio in the blood. This contributes to the synthesis of serotonin in the brain and could have beneficial effects on mood in sensitive subjects.

1 Introduction

Dietary sucrose, produced from either sugar cane or sugar beet does not have a very positive image for many consumers. Although there is no scientific basis for rejection of moderate intake levels of sucrose, in the lay press negative prejudices on sucrose persist. Sucrose has been called ' pure, white and deadly', being a causal factor in obesity, diabetes mellitus type II, cardio vascular disease, dental caries, osteoporosis, food allergy and other chronic diseases (FAO, 1997). Sucrose intake has also been linked to behavioural disturbances such as ADHD (attention deficit hyperactivity disorder) and aggression (Bellisle, 1998; Chrit and Schaafsma, 1996). Grit and Schaafsma (1996) put forward that four major theories could explain the supposed reaction of sugar consumption on behaviour:

- Micronutrient deficiencies due to an excess of ”empty calories”
- Hypersensitivity to sucrose
- Reactive hypoglycaemia
- Serotonin synthesis in the brain

An extensive review of the literature brought the authors to the conclusion that there is no sound scientific evidence for adverse effects of dietary sugar on behaviour. However, sucrose could have beneficial effects on serotonin synthesis in the brain via its influence on insulin secretion, according to the so called Wurtman hypothesis (Wurtman, 1990; Wurtman and Wurtman, 1995).
The present paper updates and further evaluates the possible role of sucrose on behaviour. The paper starts with a general description of the metabolism of the brain and with linking blood glucose levels to brain function. Secondly, recent literature and opinions about the relation between sugar consumption and behaviour is evaluated.

2 Brain metabolism, blood glucose and dietary sucrose

The brain represent only 2 % of the body weight, but receives 15 % of the cardiac output; the brain accounts for 20 % of the oxygen consumption of the body and for 25 % of the total body glucose utilization (Magistretti et al., 2000). Nerve transmission consumes about one half of all the brains' energy.
The brain is highly dependent on glucose as a substrate for oxidation and it is only in particular conditions (starvation, diabetes, breast-fed neonates), that other substrates (e.g. ketone bodies) serve as a source of energy for the brain (Cahill, 1976).

Cognitive performance and high mental demands are associated with increased neural activity and this enhances glucose use by the brain (Benton et al., 1996). Some cognitive functions appear sensitive to short-term variations of glucose availability in certain brain areas. A glucose load or ingestion of dietary carbohydrates appeared to facilitate mental performance, particularly in situations of mental stress rather than during baseline quiet states (Bellisle, 2004). The mechanism of this beneficial effect is not entirely clear. Whether it is related to elevations of blood glucose or just to energy ingestion is unknown (Kaplan et al., 2001; Benton and Jarvis, 2007). It is possibly related to insulin-mediated enhancement of serotonin synthesis in the brain (Markus, 2006).

Since neurons cannot store glucose, hypoglycaemia directly affects brain function and can even lead to unconsciousness at blood glucose levels below 30 mg/100ml. Also hyperglycaemia can cause disturbances in brain function (slowed down), as has been established in diabetes mellitus type I patients (Cox et al., 2001). Brain function is optimal between blood glucose levels of 80-270 mg/100 ml. The maintenance of blood glucose within the normal range (fasting blood glucose level between 70-100 mg/100 ml; 2 hours postprandial level between 70-145 mg/100 ml) involves the hormones insulin, glucagon and cortisol. It can be concluded that rather wide ranges of blood glucose levels are associated with normal functioning of the brain.

Only in extreme situations of either hypo- or hyperglycaemia brain function is clearly disturbed. One exception to this rule may be the so called reactive hypoglycaemia. This is the popular medical term for a rare and controversial disorder, describing recurrent episodes of symptomatic hypoglycemia (blood glucose below 40 mg/100 ml) occurring 2-4 hours after a high-carbohydrate meal or oral glucose load. It is attributable to continuing action of insulin after digestion and disposal of the glucose derived from the meal. Common symptoms include irritability, tremors, flushing, increased appetite, concentration problems, nervousness, fatigue and headaches. In most cases of reactive hypoglycaemia the causes are still open to debate. Glucagon deficiency has been involved, as well as enhanced sensitivity to the normal release of the hormone epinephrine, which may cause many of the symptoms. In a recent study (Simpson et al., 2006), healthy non-obese adult women, reporting symptoms they associated with hypoglycaemia, generally did not demonstrate biochemical hypoglycaemia but did have significantly lower blood glucose levels than controls.

The effect of dietary sucrose, as compared to other carbohydrates, on the blood glucose level has been investigated in a variety of studies related to the measurement of the glycemic index (GI). The GI has been defined by FAO/WHO (FAO/WHO Expert Consultation, 1997), as the incremental area under the blood glucose response curve of a 50 grams carbohydrate portion of a test food expressed as the response to the same amount of carbohydrate from a standard food taken by the same subject. From a simple comparison of the GI's of different sugars and carbohydrate-containing foods (Table 1), it can be concluded that the GI of sucrose, contrary to the believe of many people, is moderate. Therefore it is unlikely that sucrose, as compared to other carbohydrates with a higher GI, has an adverse effect (if any) on the brain via its effect on the blood glucose concentration. The relatively low GI of sucrose is attributable to the fructose component of the sugar, which after absorption, has to be converted in the liver into glucose before it can contribute to the blood glucose level.

Table 1. GI of selected sugars and foods

Glucose (reference)	100
Fructose	19
Lactose	46
Sucrose	68
Boiled white rice	83
Maltose	105
Baked potato	85
French fries	75
French baquette	95

Source: Foster-Powel et al (2002) , International Table of Glycemic Index (GI) and Glycemic Load (GL) values.

3 Effects of sucrose intake on hyperactivity

Hyperactivity, or more specifically Attention Deficit Hyperactivity Disorder (ADHD), as defined by the American Psychiatric Association (1994), is estimated to occur in 3% of the children with the disorder being six to nine times more common in boys than girls (Schnoll et al., 2003). The affected children are described as overactive, not being able to concentrate, sit still, keep silent, and leaving one activity unfinished and go to the next. The aetiology of ADHD is complex and is thought to include genetic, environmental and possibly nutritional factors. The FAO/WHO (FAO/WHO Expert Consultation, 1997) concluded in a review that, although correlation studies and uncontrolled experiments had indicated sugar intake as a causal factor, there is little evidence from controlled experiments to support the claim that sugar intake has a significant influence on the behaviour or cognitive performance in children as popularly supposed. There could be a few children with idiosyncratic reactions or rare hypersensitivity syndromes who may respond adversely to sucrose. Idiosyncratic is a term used in psychiatry. The term refers to a personal reaction, related specifically to a unique mental condition of a person. The conclusion that sugar does not significantly influence behaviour or cognitive performance in children is based on a meta analysis (Wolraich et al., 1995) of 23 studies that have been conducted over a period of 12 years from 1982 to 1994. After this period the issue seems to have lost attention, since no new well-controlled experimental studies were published in this field after this period and a recent review on the issue (Bellisle, 2004) also dismissed sucrose intake as a causal factor of ADHD.

4 Effects of sucrose intake on cognitive performance via blood glucose

As indicated in section 2, the blood glucose level may have an influence on cognitive performance. Particular attention has been given to the effects of diet on behaviour and cognition in children (Bellisle, 2004). Measurement of cognitive performance includes score assessment in a multidimensional set of abilities, using validated tests for issues like memory (short-term, long-term, visual, spatial, verbal declarative, semantic, strategic), attention and psycho-motor coordination. According to Bellisle (2004), the basic message that seems to emerge from the extensive research on blood glucose and brain function is that the brain is sensitive to short-term fluctuations of the glucose supply. It might therefore be beneficial to maintain glycaemia at adequate levels between meals to optimize cognition. According to Benton et al (2003), low-glycaemic-index foods that minimize glycaemia fluctuations could facilitate mental performance in the hours that follow ingestion. This hypothesis is supported by a study in diabetes mellitus type II patients, showing that consumption of a low-GI 50 g carbohydrate meal relative to a high-GI carbohydrate meal resulted in better cognitive performance in the postprandial period, particularly in those individuals who experience the greatest diet-induced elevations in blood glucose levels (Papanikolaou et al., 2006; Greenwood et al., 2003). Children may display a higher sensitivity to glucose supply than adults, because their brain consumes substantially more glucose relative to the rest of their body.

It can be concluded that maintenance of adequate levels of blood glucose between meals without large fluctuations in the blood glucose level optimize cognition. Therefore carbohydrates with a low GI should be preferred over those with a high GI. Since sucrose has a moderate GI, a negative effect of sucrose intake on cognition is unlikely.

5 Effects of sucrose on behaviour and cognitive performance via micronutrient deficiencies

It is well-established that micronutrient deficiencies (particularly B-vitamins) can have adverse effects on brain function or cognition (and probably on behaviour as well). Excessive intake of sucrose may dilute the micronutrient content of the diet and this could explain why sucrose is linked to reduced cognition or behavioural disturbances. Bellisle (2004) reviewed the available research on diet, behaviour and cognition in children and concluded that supplementation of certain nutrients does not induce cognitive performance per se, but rather may reverse in certain individuals, the adverse effects of a poor nutritional status. The author indicates that a number of well-designed studies suggest a potential role of certain nutrients, or elements of the eating pattern, in cognitive functioning in children and adolescents. It has been revealed that the clearest effects of nutritional manipulations on cognitive efficiency and behaviour are obtained in young people with a poor nutritional status. This evaluation confirms that corrective nutritional interventions can only reverse the negative impact of inadequate diets and is in harmony with earlier observations by Schoenthaler and Bier, (1999 and 2000) and Schoenthaler et al, (2000). Their conclusion was that there is no evidence that healthy well-fed

young and older persons can benefit intellectually from acute micronutrient supplementation or that this supplementation can reduce their anti-social behaviour.

Whereas in theory, a high intake level of sucrose in low-energy diets, (for instance via sweets, soft drinks, desserts and snacks) is expected to reduce the nutrient density of the diet and thus the intake of micronutrients, food consumption surveys in the Netherlands have not revealed that sugar intake is a serious concern when it comes to the nutrient supply (Hulshof et al., 2006). In fact in the recently released new dietary guidelines for the Netherlands (Netherlands Health Council, 2006), it is stated that it is possible to reach an adequate intake of nutrients within a wide range of the amount of added sugars (saccharose, fructose and glucose). In the Dutch situation, intake levels of added sugars up to 20 % of energy intake (current average level: approx. 15 % of energy) are not to be associated with an unfavourable intake of essential nutrients. Nevertheless in persons with a relatively low energy requirement such as children until the age of 9 years and elderly subjects, reduction of the intake of added sugars can be desirable, although data are lacking to substantiate an upper limit of 10-15 % of the energy in low energy diets (< 8 MJ), as done in the Nordic countries (Nordic Nutrition Recommendations, 2004) . In the US some critics were raised against the US suggested Dietary Reference Intake levels for added sugars with a maximum of 25 % of energy intake (Kranz et al., 2005;). Although the majority of pre school children in the US had intake levels of added sugar below 25 % of energy, the increase of added sugar was paralleled by a decrease of nutrient and food group intake and an increase of the number of children with intakes below the Dietary References Intake values.

It can be concluded that there is no evidence that added sugar consumption at levels up to at least 20 % of energy intake causes micronutrient deficiencies. Habitual intake levels cannot be held responsible for adverse effects on cognition and behaviour.

6 Effects of sucrose on serotonin synthesis in the brain

The neurotransmitter serotonin is involved in brain functioning. Decreased serotonergic activity is associated with depression and various mood disorders. In the nerve cells of the brain the essential amino acid tryptophan is converted into serotonin. To enter into the brain, tryptophan has to be transported from the blood to the brain. Therefore it has to pass the brain capillary endothelial wall, called the blood-brain barrier, and the brain cell plasma membrane. The transport through the blood brain barrier is transcellular and is mediated by a carrier. Tryptophan competes with the so called large neutral amino acids (LNAA: valin, leucin, isoleucin, phenylalanine and tyrosin) for this carrier and the ratio tryptophan/LNAA in the blood is a critical parameter for the availability of tryptophan for the brain to synthesize serotonin. A carbohydrate-rich meal stimulates insulin secretion, resulting in an enhanced uptake of LNAA by the muscles. Since tryptophan is the only large neutral amino acid that is bound to albumin (50-85%), it cannot be taken up by muscle with the same rate as the other LNAA. This results in an increase of the plasma tryptophan/LNAA ratio and increased availability of tryptophan to serotonin synthesis (Fernstrom and Wurtman, 1971). Depression is known to show a seasonal variation and this lead to the concept of SAD (Seasonal Affective Disorder; Rosenthal et al., 1984). The most abundant clinical features of SAD are depressive mood, lack of energy, hyposomnia, carbohydrate craving and weight gain. The decrease of light during winter time is believed to cause a drop in brain serotonin levels in individuals susceptible to developing SAD. Melatonin, the hormone that induces sleepiness, is produced out of serotonin in the pineal gland. The enzymes involved in this conversion (N-acetyl transferase and hydroxyl indole-othomethyl transferase) show an increased activity during dark periods and a decreased activity during the day (Wurtman and Moskowitz, 1977). Exposure of the retina to bright light results, via the suprachiasmatic nucleus, in the inhibition of conversion of serotonin to melatonin in the pineal gland. Lack of light could result in lowered serotonergic functioning in people susceptible to SAD. It is therefore not surprising that SAD is often successfully treated with light therapy (Winton et al., 1989; Swedo et al., 1997) and with the use of selective serotonin reuptake inhibitors (Partonen and Lonnqvist, 1996), both treatments resulting increased serotonergic functioning.

Improved serotonergic functioning, stress reduction and enhancement of mood could also be obtained by modulating food intake in such a way that the tryptophan/LNAA ratio in blood increases. This can be achieved by: (1) an increase in the intake of tryptophan; (2) a decrease in the intake of LNAA; (3) an increase of carbohydrate intake to stimulate insulin and (4) a combination of two or more of these measures (Markus et al., 2000a and 2000b). In a recent study by the same group of scientists (Markus et al., 2006) it was shown that dietary manipulation (increased intake of tryptophan via the tryptophan-rich milk protein alpha-

lactalbumin) in 28 subjects with mild sleep complaints caused a 130% increase in the plasma Trp/LNAA ratio after an evening meal in a controlled study. The increased Trp/LNAA ratio in plasma was associated with improvement of memory functions after sleeping in healthy subjects. This beneficial effect was explained by improved sleep.
It can be concluded that stimulation of insulin secretion by sucrose intake could help to increase the availability of tryptophan for serotonin synthesis in the brain, leading to improvement of serotonergic functioning in subjects where this functioning is reduced.

7 Discussion

Any possible effects of dietary sucrose on brain function and behaviour could occur via different mechanisms: (1) directly via effects on the blood glucose level, (2) indirectly via micronutrient deficiencies and (3) indirectly via insulin secretion and increased serotonin synthesis.

Regarding the first mechanism, brain function is dependent on the supply of glucose as a substrate for the metabolism of the brain cells. Therefore, indeed a rationale exist for a link between the blood glucose level and the brain function. Although existing data indicate that brain functions normally within a wide range of blood glucose concentrations, it is possible that small changes in the blood glucose level over time are associated with an influence on brain function. Carbohydrate intake can cause changes in the blood glucose level, but sucrose with its modest Glycaemic Index, does not have an outstanding position among other dietary carbohydrates in this regard and any specific effect of sucrose on brain function and behaviour via effects on the blood glucose level is highly unlikely.

Regarding the second mechanism, there is no doubt that excessive intake of sucrose, particularly in low-energy diets, can dilute the nutrient content of the diet to such an extent that nutrient deficiencies develop, some of which could influence adversely cognitive functions and behaviour. On the other hand, moderate sucrose intake levels, up to 20 % of energy intake are not known to cause such micronutrient deficiencies and thus cannot be held responsible for adverse effects on behaviour, via this route.

Regarding the third mechanism, there is convincing evidence that stimulation of insulin secretion through carbohydrate intake may result in an increased transport of tryptophan over the blood-brain barrier and to an enhanced production of the neurotransmitter serotonin. In sensitive subjects this can have a beneficial effects on mood, sleep and cognitive functions. Such effects are not specific for a particular carbohydrate type and thus not for sucrose.

8 Conclusion

There is no scientific substantiation for adverse effects of sucrose intake on the brain or on human behaviour. There is evidence that dietary carbohydrates, via their effect on the blood glucose concentration and plasma insulin levels, can influence brain function either in a positive way (cognition and mood) or in a negative way (reactive hypoglycaemia). These effects are not specific for sucrose and also attributable to other simple or complex carbohydrates in the diet.

9 References

Bellisle F (2004), Effects of diet on behaviour and cognition in children. British Journal of Nutrition 92, Supplement 2; S227-S232.

Bellisle F, Blundell JE, Dye L, Fantino M, Fern E, Fletcher RJ, Lamber J, Roberfroid M, Specter S, Westerhöfer J and Westertep-Plantenga MS (1998), Functional food science and behaviour and psychological functions. British Journal of Nutrition 80: S173-S193.

Benton D, Ruffin MP, Lassel T, Nabb S, Messaoudi M, Vinoy S, desor D and Lang V (2003). The delivery rate of dietary carbohydrates affects cognitive performance in both rats and humans. Psychopharmacology (Berl) 166: 86-90.

Benton D & Jarvis M (2007), The role of breakfast and a mid-morning snack on the ability of children to concentrate at school. Physiology and Behavior 90: 382-385.

Cahill GFJ (1976), Starvation in man. Clinical Endocrinoly and Metabolism 5: 397-415.

Cox DJ (2001), Too much blood sugar slows brain function in Type 1 diabetes patients. Presented at the annual meeting of the American Diabetes Association.

FAO (1997), Is sugar “pure white and deadly?” From the proceedings of the Fiji/FAO 1997 Acia Pacific, prepared by the Nutrition Programme Service, Food and Nutrition Division of FAO. http://www.fao.org.

FAO/WHO Expert consultation (1997). Carbohydrates in human nutrition: report of a joint FAO/WHO Expert Consultation, Rome 14-18 April 1997. Rome, Food and Agriculture Organization.

Fernstrom JD and Wurtman RJ (1971), Brain serotonin content: increase following ingestion of a carbohydrate diet. Science 174: 1023-1025.

Foster-Powell K, Holt SH and Brand Miller JC (2002), International table of glycemic index and glycemic load values. American Journal of Clinical Nutrition 76: 5-56.

Greenwood CE, Kaplan RJ, Hebblethwaite S and Jekins DJ (2003), Carbohydrate-induced memory impairment in adults with type 2 diabetes. Diabetes Care 26: 1961-1966.

Grit CTF and Schaafsma G (1996), Sugar consumption and behaviour, a critical review of the literature. TNO-report V96180.

Health Council of the Netherlands (2006). Guidelines for a healthy diet 2006. Health Council of the Netherlands, 2006; publication no 2006/21.

Hulshof KFAM, Blader HF en ter Doest D (2006), Suikers in de Nederlandse voeding. TNO Kwaliteit van Leven, Zeist, rapport nr. V6834.

Kaplan RJ, Greenwood CE, Winocur G and Wolever TMS (2001), Dietary protein, carbohydrate, and fat enhance memory performance in the healthy elderly. American Journal of Clinical Nutrition 74: 687-693.

Kranz S, Smiciklas-Wright H, Siega-Riz AM and Mitchell D (2005), Adverse effects of high added sugar consumption on dietary intake in American preschoolers. Journal of Pediatrics 146: 105-111.

Magistretti PJ, Pellerin L and Martin J-L (2000), Brain Energy Metabolism. http://www.acnp.org.

Markus CB, Jonkman LM, Lammers JHCM and Deutz NEP (2006), Evening dietary tryptophan improves post-sleep bahavioral measures of memory function in healthy subjects. Current Topics in Nutraceutical Research 4: 79-111.

Markus CR, Klopping-Ketelaars WI, Pasman W, Klarenbeek B and Berg H van den (2000a), Dose-dependent effect of alphalactalbumin with different doses of glucose on the plasma Trp/LNAA ratio. Nutritional Neuroscience 3: 345-355

Markus CR, Olivier B, Panhuysen G, Gugten J van de, Alles M, Westenberg H, Fekkes D, koppeschaar H, and DeHaan EHF (2000b), The bovine protein alpha-lactalbumin increases the plasma Trp/LNAA, and in vulnerable subjects it raises brain serotonin activity, reduces cortisol and improves mood under stress. American Journal of Clinical Nutrition 71: 1536-1544.

Papanikolaou Y, Palner H, Binn MA, jenkin DJ and Greenwood CE (2006), Better cognitive performance following a low-glycaemic-index compared to a high-glycaemic index carbohydrate meal in adults with type 2 diabetes. Diabetolica 49: 855-862.

Partonen L and Lonnqvist J (1996), Moclobemide and fluoxetine in treatment of seasonal affective disorder. Journal of Affective Disorders 41: 93-99.

Rosenthal NE, Sack DA, Gillin JC et al. (1984), Seasonal Affective Disorder: a description of the syndrome and preliminary findings with light therapy. Archives of General Psychiatry 41: 72-80.

Schoenthaler SJ and Bier ID (1999), Vitamin-mineral intake and intelligence: a macrolevel analysis of randomized controlled trials. Journal of Alternative and Complemetary Medicine 5: 125-134.

Schoenthaler SJ and Bier ID (2000), The effect of vitamin-mineral supplementation on juvenile delinquency among American schoolchildren: a randomized double-blind placebo-controlled trial. Journal of Alternative and Complementary Medicine 6: 7-17.

Schoenthaler SJ, Bier ID, Young K, Nichols D and Janssens S (2000), The effect of vitamin-mineral supplementation on the intelligence of American schoolchildren: a randomized, double-blind placebo-controlled trial. Journal of Alternative and Complementary Medicine 6: 19-29.

Simpson EJ, Holdsworth M and Macdonald IA (2006), Ambulatory blood glucose measurements, dietary composition and physical activity levels in otherwise healthy women reporting symptoms that they attribute to hypoglycaemia. British Journal of Nutrition 95: 1127-1133.

Winton F, Corn T, Huson LW, Franey C, Arendt J and Checkly SA (1989), Effects of light treatment upon mood and melatonin in patients with seasonal affective disorder. Psychology and Medicine 19: 585-590.

Wolraich ML, Lindgren SD, Stumbo PJ, Stegink LD, Appelbaum MI and Kiritsy MV (1994), Effects of diets high in sucrose or aspartame on the behaviour and cognitive performance of children. Niw England Journal of Medicine 330: 301-307.

Wurtman JD and Moskowitz MA (1971), The pineal organ. New England Journal of Medicine 296: 1329-1333 and 1383-1386.

Wurtman JJ (1990), Carbohydrate craving; relationship between carbohydrate intake and disorders of mood. Drugs 39, Suppl 3: 49-52.

Wurtman RJ and Wurtman JJ (1995), Brain serotonin, carbohydrate-craving, obesity and depression. Obesity Research 3, suppl. 4: 477S-480S.