Salud Mental 2016;39(3):175-181
ISSN: 0185-3325
DOI: 10.17711/SM.0185-3325.2016.016

Does salt addiction exist?

José Alberto Soto-Escageda,[1] Bruno Estañol-Vidal,[1] Carlos Alejandro Vidal-Victoria,[2] Anaclara Michel-Chávez,[1] Manuel Antonio Sierra-Beltran,[1] Héctor Bourges-Rodríguez[3]

Review article

ABSTRACT

Background

Salt consumption activates the brain reward system, inducing cravings and the search for salted food. Its excessive intake is associated with high blood pressure and obesity. The high quantity of salt in processed food is most likely a major cause of the global pandemic of hypertension (HT).

Objective

To review the current information on the topic of salt addiction and the health consequences this has.

Method

A search in PubMed, ScienceDirect, and EBSCOhost databases was conducted with the keywords "salt", "salt addiction", and "food addiction". Articles with information relative to the topic of interest were checked, as were references of those articles and historical and culturally complementary information.

Results

We described the historical relationship between man and salt, the physiology of salty taste perception, its role in the reward system and the health consequences of a high sodium diet.

Discussion and conclusion

There is physiological and behavioural evidence that some people may develop a true addiction to food. Among these people, salt addiction seems to be of great importance in the development of obesity, HT and other diseases. Sodium is present in high quantities in processed food as salt and monosodium glutamate (MSG), used as flavour enhancers and food preservatives, including in non-salty foods like bread and soft drinks.

Key words: Salt, salt addiction, food addiction.

RESUMEN

Antecedentes

El consumo de sal activa el sistema de recompensa cerebral, induciendo el deseo y búsqueda de alimentos salados. Su ingesta excesiva se asocia a presión arterial elevada y obesidad. La gran cantidad de sal en los alimentos procesados ha permitido que la hipertensión (HT) se instale hoy día como una pandemia.

Objetivo

Revisar la bibliografía existente en el tema de adicción a la sal y sus consecuencias en la salud.

Método

Se realizó una búsqueda en bases de datos PubMed, EBSCOhost y ScienceDirect con las palabras claves "salt", "salt addiction", "food addiction"; se revisaron los artículos que contuvieran información relativa al tema de interés así como referencias en estos mismos artículos e información histórica y cultural complementaria.

Resultados

Describimos la relación histórica entre el hombre y la sal, los mecanismos fisiológicos de percepción del sabor salado, su acción sobre el sistema de recompensa y las consecuencias en la salud de una dieta alta en sodio.

Discusión y conclusión

Existe evidencia fisiológica y comportamental de que las personas pueden desarrollar una verdadera adicción a la ingestión de alimentos. Entre estas personas la adición a la sal ¡uega un papel muy importante para el desarrollo de obesidad, hipertensión y otras enfermedades. El sodio está presente en altas cantidades en los alimentos procesados en forma de sal y glutamato monosódico (MSG), usados como conservadores o aditivos alimentarios, incluso en alimentos no salados como harinas y refrescos dulces.

Palabras clave: Sal, adicción a la sal, adicción a los alimentos.

[1] Laboratory of Clinical Neurophysiology, Department of Neurology and Psychiatry, National Institute of Medical Sciences and Nutrition Salvador Zubirán (INCMNZS), Mexico.
[2] Academic Division of Health Sciences, Juarez Autonomous University of Tabasco, Mexico.
[3] Direction of Nutrition, National Institute of Medical Sciences and Nutrition Salvador Zubirán (INCMNSZ), Mexico.

Correspondence: Dr. Bruno Estañol Vidal, Laboratory of Clinical Neurophysiology, Department of Neurology and Psychiatry, National Institute of Medical Sciences and Nutrition Salvador Zubirán (INCMNZS). Vasco de Quiroga 15, Belisario Domínguez secc. XVI, Tlalpan, 14080, Ciudad de México, México. Tel: 55 5568 - 3450. E-mail: bestanol@hotmail.com

Received first version: September 18, 2015. Second version: May 3, 2016. Accepted: May 6, 2016.

BACKGROUND

Salt or sodium chloride is probably the oldest spice used by man. Its extraction, distribution, and possession led to commercial trades and wars, to the point that it was known as "white gold". It is possible that primitive man found the properties of salt when he established contact with thin salt deposits left on the beach by the sea water. After that, he created his own sea water ponds that would leave small amounts of salt when water was evaporated by the sun; just as happens naturally in places far from the sea where the salt source was probably springs where briny water rose and left some salt when evaporated. In this way he could supply his own needs. These were also excellent places for hunting because different animal species gathered there with the same urge.[1]

When more advanced instruments were developed, early civilizations extracted "halite": the solid sedimented form of salt, from mines. Man also created commercial routes to distribute it to a large number of human sites where salt could be well traded for its weight in gold. In Ancient Greece and the Roman Empire, salt could be used to buy slaves, for tax payment, and as a part of the labour payment, which was called *salarium* and originated the word 'salary'.[1-3]

Ancient civilizations took advantage of salt's ability to dry out and cure food so that it could then be transported over long distances and rehydrated for consumption; this played a significant role in aiding long-distance travel and exploration.[2]

Nowadays salt is used as a meat tenderiser, agglutinating agent, and food additive to give a more attractive taste to food in general. In baking, it is used to correct flavour and control dough fermentation. In dairy products, it controls fermentation and enhances the colour, texture and flavour of preparations.

In industrial areas salt is used to produce chlorine (Cl-), caustic soda, and in the manufacture of plastic, colorants, pesticides, and drugs. It has been used in leather because of its disinfectant properties and in energy source exploration, such as oil, gas, and water treatment.

In the human body, sodium is important to maintain fluid balance and blood pressure, muscle contraction, nerve cell transmission, and most cell functions. Its consumption is so extended that it is added to other nutrients with lesser dietary distribution such as iodine, to avoid its deficiency in the general population.[1,2]

Suggested sodium intake and actual consumption

According to the World Health Organization (WHO) and other international bodies, the Tolerable Upper Intake Level (UL, the highest daily nutrient level intake that is not likely to pose a health risk) is 5 grams of salt –one teaspoon– or less than 2,300 mg of sodium per day (1 gram of salt = 390 mg of pure sodium) for the general population and less than 1,500 mg of sodium for those who have hypertension (HT), diabetes, chronic kidney disease, and for black ethnic groups.[4-7]

Table 1. Daily sodium recommended intake according to age

Age	Daily sodium intake
1–3 years old	1,000 mg
4–8 years old	1,200 mg
9–50 years old	1,500 mg
51–70 years old	1,300 mg
>71 years old	1,200 mg

Source: Dietary Guidelines for Americans 2010 USDA.

On the other hand, the Adequate Intake of sodium is smaller and depends upon age (Table 1), being higher in people between 9-50 years old (1,500mg of sodium) and declining as age increases.[8] (Adequate Intake, or AI, is the recommended daily intake of a nutrient based on the amount needed to meet the sodium needs of healthy and moderately active individuals, including sodium sweat losses in those exposed to high temperatures).

Studies like *Health Canada* and *INTERSALT* were conducted to calculate the amount of dietary sodium in different communities, and even though the salt intake percentages varied between groups, every one of them exceeded the limit for daily ingestion. On the basis of the INTERSALT study, which measured urinary excretion of sodium in 24 hours in men and women between 20-59 years old around the world, it was found that almost 50% of women had 5.9-8.8 grams of salt per day and more than 50% of men consumed 8.8-11.7 grams per day.[4,9] The Centers for Disease Control and Prevention (CDC) report an average daily sodium intake of 3,400 mg in the North American diet.[5]

Main salt sources

The proportion of salt in the diet is as follows: 12% comes naturally in food and only 11% is added by seasoning during cooking or at the table.[5,10] Therefore, more than 75% of salt comes from processed food.

In a modern diet, the major proportion of sodium comes from industrialised and processed food (instant soups, junk food, canned and frozen food, sausages, crackers, cereals, sweet beverages, salted meat, pickled foods),[10] so adding salt while cooking elevates its already high levels.

The food category with the highest sodium content (Table 2) is processed meat (with an average content of 1,100mg of sodium per 100 grams of meat)[11] but the largest amount of sodium in diet comes from food that might not even taste salty: grain-based foods (soups, pastas, breads, cakes, cookies, and crackers) from which the most daily calories are consumed, followed by meats.[12]

Table 2. Average sodium content in packaged foods

Food category	Average sodium content (mg/100 gr/mL + SD)
Processed meats	1106 ± 573
Dry cured meat	1754 ± 510
Sausages	849 ± 339
Frozen meals	681 ± 590
Frozen pizza	932 ± 577
Cheese	707 ± 795
Breads	510 ± 257
Milk	42 ± 4
Frozen fruits and vegetables	37 ± 79
Soft drinks	20 ± 35

Modified from Korošec Z, Pravst I. Nutrients 2014, 6.

A part of dietary sodium is also found as monosodium glutamate (MSG), which has the property of enhancing food flavour.[12,13] It is found naturally in animal products and in a lesser proportion in some vegetables. It is widely used by the food industry in soups and broths, sauces and gravies, and canned or frozen meats, poultry, vegetables, and combination dishes. MSG contains 12.3% of sodium, and as the usual MSG use is around one tenth of that of salt, MSG contributes to 7-8% of dietary sodium.[14] Its chronic consumption has been associated to β-amyloid accumulation in the brain, neuropsychiatric disorders, and neuronal loss, while acute ingestion has been related to vomiting, headache, nausea, and chest pain among other symptoms sometimes known as "Chinese restaurant syndrome", but evidence is not totally clear.[14-17]

Salt perception in the gustatory system

Through chemoreceptors located in taste buds, the tongue is responsible for perceiving flavours along with the olfactory system. The receptor for salty taste is activated by food with ionized salts, especially sodium. The *umami* ("delicious flavour" in Japanese) taste is perceived by receptors for amino acids like glutamate (in MSG) and aspartate and by nucleotides; it induces a pleasant sensation in other flavours.[18]

The chorda tympani branch of the facial nerve (cranial nerve VII, CNVII) innervates the anterior two thirds of the tongue, which is the zone with highest sensitivity to sodium because of its large amount of receptors. The glossopharyngeal nerve (cranial nerve IX, CNIX) innervates the posterior third, which is less sensitive to salt. The vagus nerve (cranial nerve X, CNX) innervates taste receptors in the epiglottis epithelium, responsible for regulating diuresis and plasma tonicity. Even though the anterior two thirds are more sensitive to salt, when NCVII is sectioned, the posterior third gets a higher sensitivity to salt perception through neuronal plasticity mechanisms, so salt consumption is always regulated.[14,19,20]

Gustatory signals pass through a totally ipsilateral pathway through the geniculate (NCVII) and inferior sensory ganglion (CNIX and CNX) to stimulate the second order neurons in the rostral portion of the solitary tract nucleus (the gustatory nucleus of the solitary tract complex) in the lower medulla. These neurons stimulate thalamic nuclei that project to the primary gustatory cortex - the inferior gyrus of the frontal lobe and anterior insula - and secondary gustatory cortex - the orbitofrontal cortex (OFC). As the sensation of flavours results from gustatory, olfactory, and somatosensory inputs, the cerebral cortex mediates the appreciation of tastes.[19]

Physiological aspects of salt addiction

Flavour information from cortical taste areas exerts strong influence on the lateral hypothalamus (LHT), which has a role in the generation of autonomic responses associated with ingestion and digestion. The taste cortex also projects directly to the amygdala and ventral striatum (nucleus accumbens, NA).[19,20]

Therefore, salt intake (as with fat, sugar or caffeine intake) induces activation of LHT that releases dopamine and glutamate in the ventral tegmental area (VTA)[21] and in turn it stimulates the NA and other limbic system structures provided with dopamine, endogenous opioids, and cannabinoid receptors. Limbic structures feed back to the medial prefrontal cortex and OFC, a pathway traditionally recognised for its role in reward, pleasure, consolidation of habits, learning, and memory[22-25] (Figure 1). These observations correlate with the lack of addictive behaviour for food when naloxone or neuroleptics (antagonists of opioid and dopamine receptors respectively) are administered.[26,27]

Substance-related obsessive thoughts and compulsion to consume are important characteristics of food and drug addictions. The activity of OFC has been implicated in impulsivity and the pathology of obsessive-compulsive disorder.[27-30]

Many authors are now using the term "food addiction"[31-33] because of the similarity of this response and the mechanisms stimulated by drugs of abuse such as amphetamines and cocaine,[34-38] which explain or support the hypothesis of an addiction produced by chronic consumption of savoury food. It seems clear that food cravings can occur in the absence of a nutritional deficit and flavour seems to be an important factor in the satisfaction of food cravings.[39] Also, it has been found that repeated consumption of a certain food when hungry –but not when satiated– produces cravings for that substance after its withdrawal,[40] suggesting that the gustatory system and learning processes are directly implicated in food addiction.[41]

Concurrently, excessive ingestion of these foods and obesity are associated with lower expression of dopami-

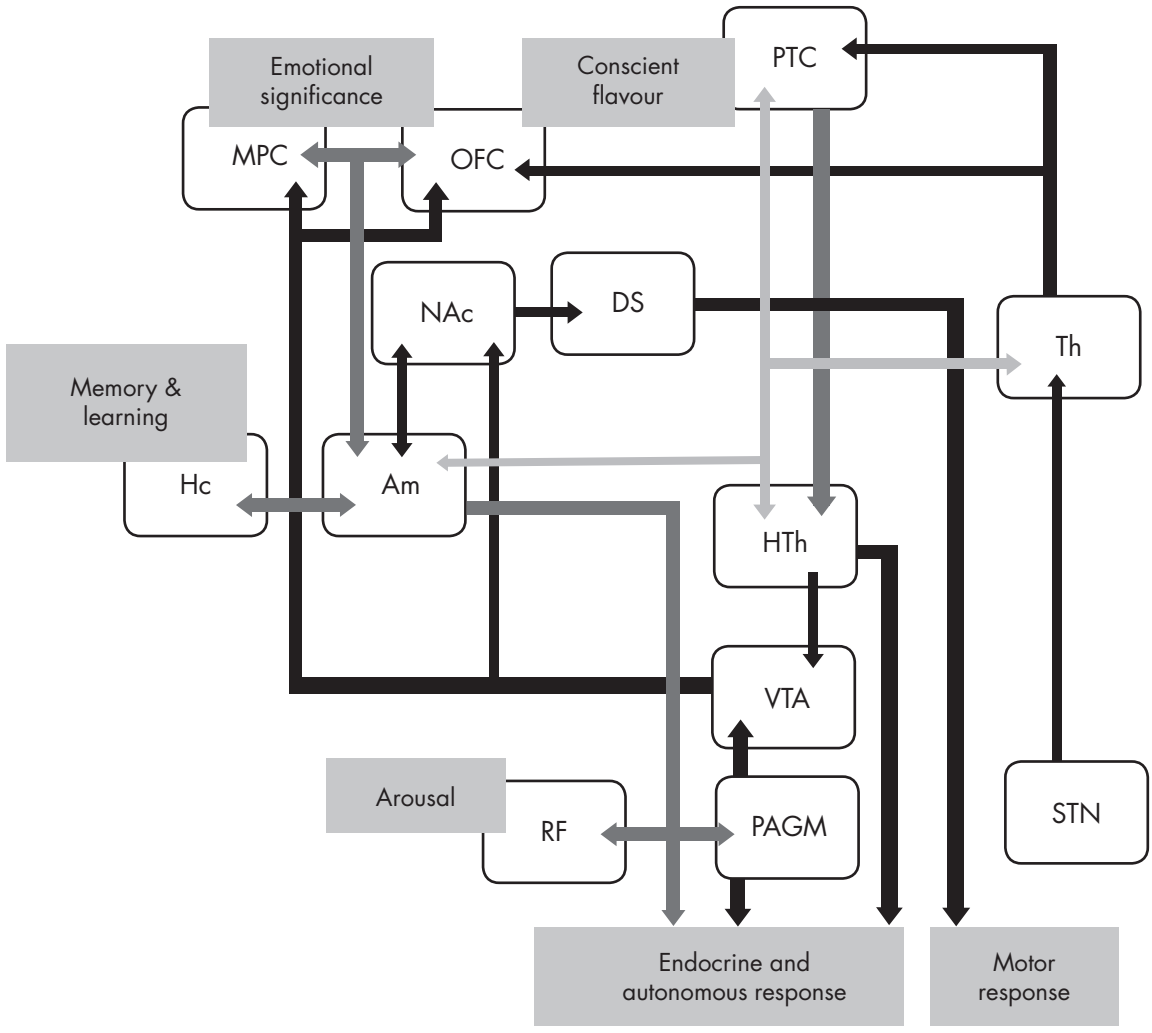

Figure 1. Taste signals from tongue get to the solitary tract nucleus (STN), it stimulates thalamus (Th) that project to primary taste cortex (PTC) and orbitofrontal cortex (OFC). PTC activates lateral nucleus of hypothalamus (Hth) to cause an autonomic response to food intake, it also activates ventral tegmental area (VTA) that releases dopamine in ventral striatum or nucleus accumbens (NAc), which connects to dorsal striatum to produce a motor response to emotions, NAc also stimulate amygdala (Am), that has reciprocal connections with medial prefrontal cortex (MPC), OFC, PFC, hippocampus (Hc), Th, Hth and stimulate inferior structures like reticular formation (RF) and periaqueductal grey matter (PAGM).

nergic D2 and opioid μ receptors,[42] consistent with a long-term reduction of sensitivity of reward centres of the brain (down regulation of receptors); this could explain the apparent tolerance due to excessive and continuous intake,[23] just like what happens with other addictive substances. The origin of this series of events is not clear; whether desensitization originates from, or is a result of over-stimulation of dopaminergic receptors, due to salt ingestion. It is evident that a greater amount of salty food is progressively needed to get the same gratifying response (tolerance),[43] therefore it turns into a vicious circle, requiring larger quantities of food. Eating more food also increments the amount of fats, carbohydrates and other nutrients that favour an increase in obesity.[44]

Behavioural aspects of salt addiction

Although sodium intake shares neuronal networks and pathways with drugs of abuse,[36,37] it is important to classify salt as a substance of abuse through clinical features in the same way as psychoactive drugs. The *Diagnostic and Statistical Manual of Mental Disorders 5* (DSM-5) identifies substance abuse and dependence as "Substance Use Disorders" (SUDs) and points out that it is necessary to accomplish two or more of 11 criteria within a 12-month period to diagnose it. In most cases, salt consumption fulfils at least seven of these (Table 3).[43,45-47]

One of the most important SUD criterion is abstinence that dependent people present when salt is withdrawn

Table 3. Behavioural criteria for Substance Use Disorder (SUD) that compares cocaine and salt consumers according to DSM-5

Criteria	Consumer	
	Cocaine	Salt
1. Tolerance	X	X
2. Abstinence	X	X
3. Consumption in large amounts and prolonged time	X	X
4. Inability to quit or control its use	X	X
5. Excessive inversion of time to get, use or recover from its effects	X	–
6. Absence from social or recreational activities	X	–
7. To keep use even being aware of its consequences	X	X
8. Craving	X	X
9. Neglected major roles because of its use	X	X
10. Use in hazardous situations	X	–
11. Social/interpersonal problems related to use	X	–

from diet; as anorexia, anxiety, slight nausea during meal time, the need for and seeking out of the substance, etc. It is known that patients under hospital assistance present a low acceptance for food,[48] often complaining about finding it tasteless and the lack of salt in their diet.

The massive and life-long use of sodium in food and the lack of success in dietary salt restriction despite the many public health campaigns and recommendations supports its classification as a clinical addiction.[43,45,46]

Craving is the strong urge to consume a certain substance; the most frequently craved food is chocolate, followed by pizza, salty foods, ice cream, and other sweets and desserts.[49] The inability to fulfil major social roles (school, work, or home obligations) could happen due to its long-term health consequences (cardiovascular disease, chronic kidney disease, morbid obesity).[46]

Some criteria refer to significant time invested in seeking, reaching and consuming the substance; however, absence from social activities and interpersonal problems are not likely to be covered by salt addiction due to the easy access to the substance and the social acceptance of its use.[43] Use of the substance in hazardous situations is often referred to in substance intoxications, such as driving under the influence of alcohol, which is not seen in this case.[46]

Health consequences of salt addiction

A high sodium intake increases urinary calcium excretion and bone resorption markers in plasma which is associated with bone loss and a lower bone density, an effect that is more evident in those with a low calcium diet.[50,51]

Another result of high sodium ingestion is a major consumption of liquids and other nutrients such as carbohydrates and fats, leading to obesity, which is accompanied with a rise in leptin (a satiety inducer hormone) and insulin concentrations.[52,53]

Insulin and leptin resistance results in an increased salt sensitivity that predisposes a rise in BP due to high sodium intake, probably due to sympathetic and adrenal dysregulation.[54-57] Many studies have demonstrated a clear link between high salt intake and increased BP: The INTERSALT study showed a relation between salt and increase in BP, demonstrating that in subjects who ate more than 6 grams of salt per day for more than 30 years, systolic BP was 9 mmHg higher than in people with lower salt intake.[9] Another meta-analysis proved that a restriction of salt consumption to less than 6 grams decreased systolic BP in 4-7 mmHg in hypertensive patients and 2-4 mmHg in normotensive patients.[10]

Lowering dietary sodium is an important part of treatment in HT and helps to decrease the risk of cardiovascular disease such as left ventricle hypertrophy, peripheral arterial damage, cerebrovascular disease and heart failure.[5,8]

Renal function, responsible for regulating the concentration and intravascular volume of sodium, is impaired in response to large loads of sodium by the effects of angiotensin II, aldosterone, growth factors, reactive oxygen species (ROS), sympathetic hyperactivity, and direct vascular damage due to HT. This has effects throughout the kidney economy (vessels, tubules, juxtaglomerular apparatus, myocytes) impairing its autoregulatory capacity, evidenced by proteinuria, HT and renal fibrosis, becoming a positive feedback pathophysiology.[58-60] This is why high sodium diets increase the risk of developing kidney disease, and independently increases mortality rates in patients with kidney disease, and low sodium diets decrease proteinuria in patients with HT.[61,62]

Salt addiction as a public health problem

The modern world involves a faster pace of life and therefore an increase eating fast food and industrialised food. These are filled with large amounts of sodium and are directly related to an increase in obesity rates, especially in high-income countries.[11,63,64] Taking into account the addictive effect, neuronal changes, and other health consequences chronic salt consumption can produce, it can be catalogued as a pandemic.

Excessive salt intake contributes to 10% of cardiovascular disease, it is one of the main causes of increased BP and causes more deaths than other food-related factors, compared to high trans-fat consumption, alcohol ingestion, and low intake of fruits and vegetables.[65-67] It is also common for young people to prefer salty food, resulting in a major development of HT and other conditions at an early age which, when coupled with the global tendency of greater life expectancy, translates as an important problem for international economy and health professionals.[41,68,69]

Due to its relation to addictive behaviour, obesity, HT and other conditions, governments around the world and global organisations should give the population clear and practical recommendations about sodium consumption and closely regulate the food industry about salt and monosodium glutamate use, distribution and labelling.[69]

DISCUSSION AND CONCLUSION

There is certainly a need to go into depth about the mechanisms implied in reward pathways that may turn food into addictive substances and methods to effectively stop or revert them.

Currently an important number of researchers consider excessive sodium consumption an addiction.[31-33] It is important to assume that salt is categorically an addictive substance just as psychotropic drugs, as they share cerebral pathways that perpetuate their excessive consumption. Salt intake implicates more than just a preference for salty taste but further studies must be conducted in the future to clinically define the precise concept of salt addiction.

The large number of patients with obesity, cardiovascular disease, and renal substitutive treatment is an important warning, because if these diseases do not get appropriate treatment and control, they will continue causing incapacity and death all around the world.

Accomplishing dietary sodium recommendations is a challenge: the population at large is exposed to large amounts of salt and people ignore the amount of sodium in their diet, because most of it is previously added during processing and hidden in non-salty foods like breads, desserts and soft drinks.

Funding

None.

Conflicts of interests

No author of this paper has a conflict of interest, including specific financial interest, relationships and/or affiliations relevant to the subject matter included in this article.

REFERENCES

1. Eskew GL. Salt, the fifth element - the story of a basic American industry. Chicago: JG Ferguson and Associates; 1948; pp7-13.
2. Arsenau, N, Rose C, Azullay A, Meyer R. Explorers, traders tracking the cultural and social impacts of the global commodity trade & immigrants. Hemispheres: University of Texas; 2008; pp133-137.
3. Kass L. The hungry soul: eating and the perfecting of our nature. Chicago: University of Chicago Press; 1994; p123.
4. World Health Organization. Reducing salt intake in populations: Report of a WHO forum and technical meeting. Geneva, Switzerland. World Health Organization; 2007.
5. U.S. Department of Agriculture and U.S. Department of Health and Human Services. Dietary Guidelines for Americans, 2010. 7th Edition, Washington, DC: U.S. Government Printing Office; 201; pp21-23.
6. Institute of Medicine. Strategies to reduce sodium intake in the United States. Washington, DC: National Academies Press; 2010.
7. Dasgupta K, Quinn RR, Zarnke KB, Rabi DM et al. The 2014 Canadian Hypertension Education Program Recommendations for Blood Pressure Measurement, Diagnosis, Assessment of Risk, Prevention, and Treatment of Hypertension. Can J Cardiol 2014;30:485-501.
8. Borghi C, Tartagni E. The older patient with hypertension: care and cure. Ther Adv Chronic Dis 2013;3(5):231-236.
9. INTERSALT Cooperative Research Group. Intersalt: an international study of electrolyte excretion and blood pressure. Results for 24 h urinary sodium and potassium excretion. BMJ 1988;297:319–328.
10. He FJ, Marrero NM, MacGregor GA. Salt intake is related to soft drink consumption in children and adolescents: A link to obesity? Hypertension 2008;52:629-634.
11. Korošec Z, Pravst I. Assessing the average sodium content of prepacked foods with nutrition declarations: The importance of sales data. Nutrients 2014;6:3501-3515.
12. Center for Disease Control and Prevention (CDC). Sodium intake among adults — United States, 2005−2006. MMWR 2010;59(24):742-745.
13. Livingstone VH. Current clinical findings on monosodium glutamate. Can Fam Physician 1981;27:1150-1152.
14. Yoshi-Hisa S. Flavor enhancers. In: Branen AL, Davidson PM, Salminen S, Thorngate JH (eds.). Food additives. 2da ed. New York: Marcel Dekker, Inc; 2002; pp423-445.
15. Dief AE, Kamha ES, Baraka AM, Elshorbagy AK. Monosodium glutamate neurotoxicity increases beta amyloid in the rat hippocampus: a potential role for cyclic AMP protein kinase. Neurotoxicology 2014;42:76-82.
16. Quines CB, Rosa SG, Da Rocha JT. Monosodium glutamate, a food additive, induces depressive-like and anxiogenic-like behaviors in young Rats. Life Sci 2014;107(1-2):27-31.
17. Schaumberg HH, Byck R, Gertsl R et al. Monosodium L-glutamate: Its pharmacological role in Chinese Restaurant Syndrome. Science 1969;163:826-828.
18. Chandrashekar J, Hoon MA, Ryba NJ et al. The receptors and cells for mammalian taste. Nature 2006;444:288-294.
19. Noback CR, Strominger NL, Demarest RJ, Ruggiero DA (eds.). The human nervous system, structure and function. Sixth ed., New Jersey: Humana Press Inc; 2005; pp262-265.
20. Purves D, Augustine GJ, Fitzpatrick D et al (eds.). Neuroscience. Fifth edition: Sinauer Associates; 2012.
21. You ZB, Chen YQ, Wise RA. Dopamine and glutamate release in the nucleus accumbens and ventral tegmental area of rat following lateral hypothalamic self stimulation. Neuroscience 2001;107(4):629-639.
22. Wise RA. Roles for nigrostriatal—not just mesocorticolimbic—dopamine in reward and addiction. Trends Neurosci 2009;32(10):517–524.
23. Volkow ND, Fowler JS, Wang GJ. The addicted human brain: insights from imaging studies. J Clin Invest 2003;111(10):1444-1451.
24. Gearhardt AN, Corbin WR, Brownell KD. Preliminary validation of the Yale Food Addiction Scale. Appetite 2009;52:430-436.
25. Michel-Chávez A, Estañol-Vidal B, Sentíes-Madrid H et al. Reward and aversion systems of the brain as a funcional unit. Basic mechanisms and functions. Salud Ment 2015;38(4):299-305.
26. Drewnowski A, Krahn DD, Demitrack MA, Nairn K et al. Naloxone, an opiate blocker, reduces the consumption of sweet high-fat foods in obese and lean female binge eaters. American J Clinical Nutrition 1995;61:1206–1212.
27. Schultz W. Predictive reward signal of dopamine neuron. J Neurophysiol 1998;80(1):1-27.
28. Shi Z, Yuan B, Wittert GA, Pan X et al. Monosodium glutamate intake, dietary patterns and asthma in Chinese adults. PLOS ONE 2012;7(12):1-6.
29. Volkow ND, Fowler JS. Addiction, a disease of compulsion and drive:

involvement of the orbitofrontal cortex. Cereb Cortex 2000;100:318–325.
30. Baylis LL, Rolls ET, Baylis GC. Afferent connections of the caudolateral orbitofrontal cortex taste area of the primate. Neuroscience 1995;64:801–812.
31. Innamorati M, Imperatori C, Manzoni GM et al. Psychometric properties of the Italian Yale Food Addiction Scale in overweight and obese patients. Eat Weight Disord 2015;20(1):119-127.
32. Schulte EM, Joyner MA, Potenza MN, Grilo CM, Hearhardt AN. Current considerations regarding food addiction. Curr Psychiatry Rep 2015;17(4):563.
33. Volkow ND, Wang GJ, Fowler JS, Tomasi D et al. Food and drug reward: overlapping circuits in human obesity and addiction. Curr Top Behav Neurosci 2012;11:1-24.
34. Parylak SL, Koob GF, Zorrilla EP. The dark side of food addiction. Physiology Behavior 2011;104:149-156.
35. Urban NB, Martínez D. Neurobiology of Addiction. Insight from Neurochemical Imaging. Psychiatr Clin N Am 2012;35:521–541.
36. Grace AA. The tonic/phasic model of dopamine system regulation and its implications for understanding alcohol and psychostimulant craving. Addiction 2000;95(2):119–128.
37. Liedtke WB, McKinley MJ, Walker LL, Zang H et al. Relation of addiction genes to hypothalamic gene changes subserving genesis and gratification of classic instinct, sodium appetite. PNAS 2011;108(30):12509-12514.
38. Corsica JA, Pelchat LM. Food addiction: true or false? Curr Opin Gastroenterol 2010;26:165-169.
39. Michener W, Rozin P. Pharmacological versus sensory factors in the satiation of chocolate craving. Physiol Behav 1994;56:419–422.
40. Pelchat ML. Of human bondage: Food craving, obsession, compulsion, and addiction. Physiology Behavior 2002;76:347–352.
41. Harris G, Booth DA. Infants' preference for salt in food: its dependence upon recent dietary experience. J Reprod Infant Psychol 1987;5:97–104.
42. Colantuoni C, Schwenker J, McCarthy J, Rada P et al. Excessive sugar intake alters binding to dopamine and mu-opioid receptors in the brain. Neuroreport 2001;12(16):3549–3552.
43. Tekol Y. Salt addiction: A different kind of drug addiction. Medical Hypotheses 2006;67:1233-1234.
44. Horstmann A, Villringer A. The brain's role in human obesity. E-Neuroforum 2013;4:79-84.
45. Ifland JR, Preuss HG, Marcus MT, Rourke KM et al. Refined food addiction: A classic substance use disorder. Medical Hypotheses 2009;72:518-526.
46. Meule A, Gearhardt AN. Food Addiction in the light of DSM-5. Nutrients 2014;6(9):3653-3671.
47. Hasin DS, O'Brien CP, Auriacombe M et al. DSM-5 Criteria for substance use disorder: Recommendations and rationale. Am J Psychiatry 2013;170(8):834-851.
48. Sousa AA, Gloria MS, Cardoso TS. Aceitação. Revista Nutrição 2011;24(2):287-294.
49. Weingarten HP, Elston D. Food cravings in a college population. Appetite 1991;17(3):167-175.
50. Bedford JL, Barr SI. Higher urinary sodium, a proxy for intake, is associated with increased calcium excretion and lower hip bone density in healthy young women with lower calcium intakes. Nutrients 2011;3(11):951-961.
51. Dawson-Hughes B, Fowler SE, Dalsky G, Gallagher C. Sodium excretion influences calcium homeostasis in elderly men and women. J Nutr 1996;126(9):2107-2112.
52. Grimes CA, Wright JD, Liu K et al. Dietary sodium intake is associated with total fluid and sugar-sweetened beverage consumption in US children and adolescents aged 2–18 y: NHANES 2005–2008. Am J Clin Nutr 2013;98(1):189-196.
53. Fonseca-Alaniz MH, Brito LC, Borges-Silva CN et al. High dietary sodium intake increases white adipose tissue mass and plasma leptin in rats. Obesity 2007;15(9):2200-2208.
54. Ogawa Y, Masuzaki H, Aizawa M, Yura S et al. Blood pressure elevation in transgenic mice over expressing leptin, the obese gene product. J Hypertens 1998;16:7.
55. Radin MJ, Holycross BJ, Hoepf TM, McCune SA. Increased salt sensitivity secondary to leptin resistance in SHHF rats is mediated by endothelin. Mol Cell Biochem 2003;242(1-2):57-63.
56. Stocker SD, Madden CJ, Sved AF. Excess dietary salt intake alters the excitability of central sympathetic networks. Physiol Behav 2010;100(5):519-524.
57. Fujita T. Mechanism of salt sensitive hypertension: focus on adrenal and sympathetic nervous systems. J Am Soc Nephrol 2014;25(6):1148-1155.
58. Meneton P, Jeunemaitre X, De Wardener HE, MacGregor GA. Links between dietary salt intake, renal salt handling, blood pressure, and cardiovascular diseases. Physiol Rev 2005;85: 679-715.
59. Castrop H. Blunted renal autoregulation during high salt intake: Advantageous or deleterious? Am J Physiol Renal Physiol 2014;307(3):273-274.
60. Habibi J, Hayden MR, Ferrario CM, Sowers JR et al. Salt loading promotes kidney injury via fibrosis in young female Ren2 rats. Cardiorenal Med 2014;4:43-52.
61. Mc Causland FR, Sushrut SW, Brunelli SM. Increased dietary sodium is independently associated with greater mortality among prevalent hemodialysis patients. Kidney Int 2012;82(2):204-211.
62. Swift PA, Markandu ND, Sagnella GA, He FJ et al. Modest Salt reduction reduces blood pressure and urine protein excretion in black hypertensives: A randomized control trial. Hypertension 2005;46:308-312.
63. De Vogli R, Kouvonen A, Gimenoc D. The influence of market deregulation on fast food consumption and body mass index: a cross-national time series analysis. Bull World Health Organ 2014;92(2):99–107.
64. Brown IJ, Tzoulaki I, Candeias V, Elliot P. Salt intakes around the world: implications for public health. Int J Epidemiol 2009;38:791–813.
65. Mendis S, Puska P, Norrving B (eds.). Global atlas on cardiovascular disease prevention and control. Geneva: World Health Organization; 2014; p32.
66. Dennis B, Stamler J, Buzzard M et al. INTERMAP: the dietary data-process and quality control. J Hum Hypertens 2003;17:609-622.
67. Lawes CM, Vander-Hoorn S, Rodgers A. Global burden of blood-pressure-related disease, 2001. Lancet 2008;371:1513–1518.
68. Desor JA, Greene LS, Maller O. Preference for sweet and salty in 9 to 15 year old and adult humans. Science 1975;190(4215):686-687.
69. Charlton K, Webster J, Kowal P. To legislate or not to legislate? A comparison of the UK and South African approaches to the development and implementation of salt reduction programs. Nutrients 2014;6(9):3672-3695.