The Development of Taste Preferences and Health Implications

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November 11, 2015

Abstract

The gustatory system develops in utero and is influenced by the amniotic environment resulting from the mother’s diet during pregnancy. Prenatal exposure to high levels of fat and salt can predispose the offspring to have a preference for those tastants. However, the resulting preference for fatty and salty foods can exacerbate the development and progression of high-risk health conditions. This literature review investigates the factors that influence taste and taste preference development, specifically high fat and high salt diets during gestation, as well as the subsequent health risks associated with each tastant alone and in combination.
The Development of Taste Preferences and Health Implications

Introduction

The gustatory system is essential for evaluating ingested material. Taste helps organisms avoid harmful substances and seek nutritionally beneficial substances (see Yarmolinsky, Zuker, & Ruba, 2009 for review). Mammals have an innate preference for sweet tastes, which are associated with energy-rich carbohydrates and umami, which restores amino acids. Salty tastes are also preferred if the concentration is maintained below the threshold for aversion. Bitter and sour tastes are generally aversive, warning the organism of potential danger. While these preferences are likely incorporated in the organisms’ genome, preferences for certain tastes can be acquired through environmental exposure within an organism’s lifetime (Wardle & Cook, 2008). This literature review seeks to analyze the ways that taste preferences develop prenatally and how these preferences contribute to growing health problems.

Neural Pathway

Taste buds contain the neuroepithelial receptor cells of the gustatory system that transduce the stimulus into an electrochemical signal. There are approximately 2500 - 3000 taste buds found on the tongue, soft palate, epiglottis, pharynx, and larynx (Meyerhof, 2005). Taste follows a series of labeled lines in that the taste receptor and subsequent pathway for each taste is distinct and separate (Yarmolinsky et al., 2009). Salty tastes use sodium channels and sour tastes use hydrogen ions and potassium channels, both functioning through an ionotropic pathway. Sweet, umami, and bitter tastes are detected by heterodimeric G-protein coupled receptors composed of T1R receptor complexes, all functioning through a metabotropic pathway (Nelson et al., 2001). Cranial nerves VII (facial), IX (glossopharyngeal), and X (vagus) innervate the taste buds and send the electrochemical signal to the central nervous system (Northcutt, 2004).
After the signal is received by the sensory ganglia, it is relayed to the rostral nucleus of the solitary tract in the brainstem, the parabrachial nucleus, the ventral posteromedial nucleus of thalamus, and finally to the primary gustatory cortex in the insula (see Yarmolinksy et al., 2009 for review).

Taste perception relies not only on the gustatory system, but also works in combination with the olfactory system. Olfaction begins with the G-protein coupled olfactory receptors in the membranes of the olfactory sensory neuron that detect, with high specificity, the chemical odors that cross the mucus covered epithelium (see Nei, Niimura, & Nozawa, 2008 for review). The signal is then transmitted from the olfactory neurons to the ipsilateral olfactory bulb via the olfactory cranial nerve (I) forming the glomeruli at the synapse (Margot, 2009). The olfactory bulb carries the information to the primary olfactory cortex, which is subdivided into a variety of areas, each with a specific responsibility in processing different odors. The predominant subdivisions include the anterior olfactory cortex, the olfactory tubercle, the piriform cortex, the amygdala, and the entorhinal cortex. Olfaction coordinates with the gustatory system to produce flavor. For example, smelling food can increase salivation, as seen with Pavlov’s dog, and can result in the correct identification of that food and its taste qualities (Masaoka, Satoh, Akai, & Homma, 2010). Therefore, both olfaction and taste contribute to flavor and preference of food.

**Taste Development**

Prenatal development in humans is characterized by rapid growth of the organism and is critical for proper maturation as demonstrated by the adverse effects of teratogen exposure during this time. Many senses, including the gustatory and olfactory system, develop in utero. Although human cells resembling primitive taste buds congregate on the papillae around the seventh week, taste buds are not fully developed and functional until the fifteenth week of
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gestation (Bradley & Stern, 1967; Witt & Reutter, 1996). Additionally, olfactory marker proteins in olfactory receptor cells show complete maturation of the olfactory system by the twenty-eighth week of gestation (Chuah & Zheng, 1987). These findings indicate that both sensory systems that interact to produce flavor are fully mature a few months before birth, allowing enough time for the mother’s diet to influence the taste of the infant. The fetus is exposed to tastants in the womb that are ingested by the mother during pregnancy. Following consumption by the mother, food is broken down into various nutrients that are absorbed in the blood and then filtered by the placenta (Nicholson, 2013). The placenta has a selective barrier with the purpose of stopping any teratogens that may cause harm to the developing fetus. The nutrients then travel to the fetus by way of the umbilical cord, providing vitamins and minerals vital to growth. Both the early development of the olfactory and gustatory sensory systems in utero and the constant exposure to tastants during pregnancy suggest that there may be a window of opportunity for exposure to tastants during gestation to influence the offspring’s taste preferences.

A mother’s diet during pregnancy can also influence the characteristics of her amniotic fluid, exposing the fetus to different nutritional chemicals for a prolonged period of time. When amniotic fluid was analyzed from pregnant women who consumed garlic in comparison with those who did not, the fluid of the mothers who had eaten garlic was identified as having a stronger, garlic-like odor (Mennella, Johnson, & Beauchamp, 1995). The amniotic fluid was collected from the mothers after undergoing a routine amniocentesis procedure only forty-five minutes after they ingested a placebo or garlic essential oil capsule. These results set the foundation for the influence of maternal diet on infant taste preferences, demonstrating that nutrients consumed by the mother can be transmitted to the environment surrounding the fetus.
Similarly, Schaal, Marlier, and Soussignan (2000) demonstrated that three days after birth, infants would orient themselves to familiar amniotic odors. In one of their experiments, pregnant mothers were instructed to add anise flavored sweets to their diet during the last two gestational weeks of pregnancy, but to stop consumption of all anise-flavored foods a few hours before delivery. The researchers found shortly after birth that the infants whose mothers consumed anise during pregnancy oriented their head to an anise-scented swab significantly more times when compared with infants whose mothers did not ingest anise during pregnancy. Additionally, the infants of anise-consuming mothers had greater mouthing activity when an anise-scented swab was held under their nose in comparison with the infants of non-anise consuming mothers who showed neutral or even aversive responses in the form of negative facial expressions. These results extended into day four, demonstrating that the mother’s diet can influence the composition of her amniotic fluid, which then can affect the infant’s preferences postnatally. This experiment was replicated with carrots instead of anise, leading the researchers to the same conclusion (Mennella, Coren, Jagnow, & Beauchamp, 2001).

Hepper (1995) showed that prenatal exposure to tastants can contribute to the infant’s responsiveness to that odor. In his study, infants were presented with a garlic and a neutral cotton wool swab sometime between 15 and 28 hours after birth. The time the newborns spent facing each stimulus was recorded. Further analysis indicated that the infants who were not exposed to the garlic in utero showed a strong aversion to the garlic swab while infants who were prenatally exposed to garlic showed a slight preference for the garlic swab. Similar results have been found in other organisms as well. For example, when *Drosophila* larvae were given high levels of dietary salt, later exposure to sodium became a positive reinforcer not seen in *Drosophila* larvae on a no salt diet (Russell, Wessnitzer, Young, Armstrong, & Webb, 2011).
Normally, *Drosophila* larvae are attracted to salt until a specific concentration is reached, at which point the solution is perceived as aversive. This initial point of aversion was higher in the larvae reared on a high salt diet compared with the no salt diet control larvae. This study further demonstrates how prenatal exposure to different tastants can contribute to a learned preference for those tastes. Not only do the combinations of these findings support prenatal influence on dietary preferences, but they also show that infants can become desensitized to the aversiveness of certain foods prenatally.

**Section I: Salty Tastes**

It is important to maintain a proper balance of sodium chloride, an essential ion present at different concentrations in most foods. Salt is regulated by the kidneys, which are involved in filtration of blood plasma, reabsorption of vital nutrients, and excretion of toxic wastes (Walser, Thorpe, & Brereton 2004). Once ingested, sodium is absorbed into the blood stream where it is then filtered by the kidneys. Angiotensin and aldosterone work together to ensure that the body is retaining proper amounts of salt and water, and any excess is excreted from the body as urine. However, a diet high in sodium has been linked to hypertension and cardiovascular disease (Meneton, Jeunemaitre, de Wardener, & Macgregor, 2005) and is potentially a risk factor for cancer and osteoporosis (Strnad, 2010). Consumption of foods high in salt can cause a decrease in the ability of the kidneys to excrete salt, which can lead to a variety of health problems (Meneton et al., 2005).

For this reason, researchers are interested in the effects of maternal dietary sodium chloride intake on the offspring’s taste preference for salt. In a study by Contreras and Kosten (1983), female rats were reared on a low, medium, or high salt diet before and during pregnancy. After weaning, all offspring were then given solutions of distilled water, sodium chloride,
glucose, and potassium chloride at various concentrations in a two-bottle preference test.

Sodium concentrations were presented for two consecutive days in the following order: 0.03, 0.1, 0.2, 0.3, and 0.4 M. The same procedure was used for glucose and potassium chloride, but only 0.1 and 0.3 M concentrations were administered. On the third day before the next test solution was administered, deionized water was given to eliminate residual taste. Following this procedure, the rat pups from each dietary salt condition were examined for their maintained preference of 0.3 M sodium chloride solution for seven days. The solution preference, measured as percent intake of sodium chloride, was documented each day during the testing period. Upon analysis, the researchers found that both the male and female offspring prenatally exposed to a high salt diet had a significantly stronger preference for the sodium chloride solution when compared with the rats in other conditions. These rats chose the sodium chloride solution over water when given a choice between the two. The opposite was found for the offspring prenatally exposed to a low salt diet in that they had a significantly weaker preference for the sodium chloride solution when compared with the rats in other conditions. In regard to potassium chloride, the low-salt group showed a significant increase in preference for the salt solution in comparison with the high-salt group. These effects were non-specific in that there was also an increased preference for the glucose solution in the group exposed to high glucose diets.

Contreras and Ryan (1990) examined the perinatal effects of sodium chloride on ingestion for different dietary conditions. Rat dams were maintained on either a 0.12, 1.0, or 3.0 percent sodium chloride diet throughout pregnancy and lactation, and their offspring were given the same diet up to 30 days postpartum. Following day 30, the offspring were maintained on a diet consisting of 1.0 percent sodium chloride, and their salt and water consumption was analyzed starting on day 90 and day 150 after birth. The researchers’ first experiment conducted
on day 90 documented each offspring’s sodium chloride and water intake on a powdered 1.0 percent sodium chloride diet, a powdered 0.0 percent sodium chloride diet, and a diet with free access to water and 0.3 M sodium chloride solution. The second experiment conducted on day 150 examined the offspring’s sodium chloride and water intake following repeated sessions of acute sodium depletion achieved by a furosemide injection and 48 hours of dietary sodium deprivation. In every condition, the rats that were perinatally exposed to the 3.0 percent sodium chloride diet showed significantly greater sodium chloride consumption when compared with the rats perinatally exposed to the 1.0 or 0.12 percent sodium chloride diets.

Curtis, Krause, Wong, and Contreras (2004) similarly found a significant increase in total sodium chloride intake for rats perinatally exposed to 3.0 percent sodium chloride compared with those exposed to 1.0 or 0.1 percent sodium chloride following salt deprivation. The rat offspring perinatally exposed to high levels of sodium chloride also showed a decrease in water intake per unit of sodium chloride consumed. This further suggests that the rats exposed to high levels of salt in utero and during lactation may process salty tastes differently. Contreras et al. (1990) hypothesized that an increased preference for salt may be attributed to either an alteration in the neural mechanism of taste or a change in the renin-angiotensin-aldosterone system hormones that contribute to sodium retention and appetitiveness. The former may result in early development of salt-sensitive neurons within the chorda tympani and brainstem that contribute to salt preferences. The latter may be due to a change in aldosterone and angiotensin II levels, which in combination is suggested to act on the brain to increase salt intake as well as blood pressure (Shade et al., 2002). Although the mechanism is not known for certain, the findings of this study indicate that perinatal exposure to a diet high in sodium chloride can increase the offspring’s preference for salt.
Follow up studies analyzed the influence of early exposure to sodium chloride on the projection of different neurons involved with taste, specifically the chorda tympani. Pittman and Contreras (2002b) examined the responsiveness of the chorda tympani nerve to sodium chloride in the offspring of pregnant rats whose diet consisted of high (3.0 percent), intermediate (1.0 percent), or low (0.1 percent) NaCl. Their results showed that relative response amplitudes of the chorda tympani neurons to sodium chloride stimulation of the tongue were significantly lower for the group of rats reared on a low salt concentration compared with those reared on the intermediate or high concentration. This discovery was relatively specific to sodium chloride solution in that no such reduction was seen for potassium chloride and quinine hydrochloride solutions. Not only did the rats show a change in neural responsiveness dependent on maternal diet while developing in utero, but the rats raised on high concentrations of NaCl also had a significantly larger sensitivity to amiloride compared with the other two groups. Amiloride is an inhibitor of sodium channels, therefore, a larger sensitivity to this amiloride suggests that the rats exposed to a high sodium chloride diet before and after birth have more sodium channels present. These findings indicate that maternal dietary sodium levels that are present in similar concentrations in the diet of the offspring throughout adulthood can alter the development of operative, amiloride-sensitive sodium channels located on taste receptors projected by the chorda tympani nerve to the brain. Evidence for the amiloride-sensitive area of the chorda tympani as the receptor mechanism responsible for the detection of NaCl by the gustatory system is demonstrated by Contreras and Lundy (2000).

Pittman and Contreras (2002a) further investigated this change in chorda tympani responsiveness to find that the organization of chorda tympani neurons projecting to the nucleus of the solitary tract was altered depending on the diet of the offspring’s mother during
pregnancy. The subjects in both studies were exposed to similar conditions in that they were exposed to either low, intermediate, or high levels of sodium chloride in utero and after birth. Upon analysis of the afferent pattern of the chorda tympani, the volume of the dorsal terminal field in the nucleus of the solitary tract was significantly greater in the high salt group compared with the other two groups. The combination of results from the previously discussed studies indicates that an increased preference in dietary sodium exhibited by rats raised on a high salt diet may be due to a change in the first central synapse of the gustatory pathway. It is also possible that the dorsal segment of the chorda tympani has some critical function of salty taste detection and processing. Taken together, it is suggested that prenatal exposure to high sodium levels impacts the gustatory pathway, specifically chorda tympani organization and the number of functional sodium channels, which has some effect on increasing the offspring’s preference for salt.

Mangold and Hill (2007) also demonstrated that neurological changes take place during early manipulation of salt intake during gestation. Pregnant dams received either a standard diet of 0.3 percent sodium chloride or a low-sodium diet of 0.03 percent sodium chloride for nine days, between embryonic day three and embryonic day twelve, before the tongue developed. The researchers used triple-fluorescent anterograde taste nerve labeling for the chorda tympani, greater superficial petrosal, and glossopharyngeal nerves, which are all involved with relaying gustatory information to the brain. Results showed that rats exposed to the low-salt diet had larger terminal field volumes of these three nerves at adulthood, indicating that exposure to a low salt diet can restructure primary afferent projections into the gustatory brainstem. This is especially true during nucleus of the solitary tract neurogenesis. Although similar results were found in rats fed a low-sodium diet throughout development, the results are not nearly as
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The results of this study provide additional evidence for the alteration in brain organization due to prenatal exposure to tastants.

Although the subjects in these experiments are rats, it is likely that the studies analyzing prenatal salt exposure on taste preference can be applied to humans, especially given the genetic similarity between the two species. One human study investigated the influence of vomiting during pregnancy and its influence on salt preference in the offspring. While exposure to high salt during pregnancy can increase the offspring’s taste preference for sodium, an excessively low salt diet can do the same. Leshem (1998) showed that mineralofluid loss as a result of maternal vomiting during pregnancy can also increase adolescents’ preference for sodium characterized by a higher salt intake. Dietary sodium is necessary to balance electrolytes in the body, and pregnant mothers that experience mineralofluid loss are depriving their developing fetus of necessary salt. Therefore, as a way to compensate for and replenish this loss, the infants have an increased preference for sodium that extends into adolescence.

These results all indicate that there is a strong influence of prenatal diet on the offspring’s taste preference in regard to salt. Interestingly, when Midkiff and Bernstein (1983) examined the salt preference of rats in the early postweaning period, they found no evidence that the concentration of sodium chloride that the rat was exposed to during this time affected adult salt preference. It is unclear if the same results would be obtained for offspring exposed during lactation alone. Little research has been conducted on each period of development separately, while many studies examine the effects of a high or low salt diet during gestation and lactation as a whole. Studies indicate that a taste preference for salt can develop through previous exposure to the tastant, but it is difficult to differentiate whether this is influenced primarily by exposure during pregnancy, lactation, or a combination of both. Research on amniotic fluid odor
preference provides evidence for the influence of maternal diet during pregnancy alone (Schaal et al., 2000). Similarly, Leshem (1998) showed that an infant’s preference for salt could be altered if the mother experiences mineralofluid loss during pregnancy. This suggests that a main determinant of taste preference development occurs during prenatal exposure, although exposure during lactation may also contribute or even exacerbate the effect. Therefore, there is likely a sensitive period, which exists during gestation and possibly extends into lactation, when the offspring’s exposure to salt has the most extensive influence on taste.

The literature indicates that the concentration of sodium consumed during gestation, and possibly lactation as well, can affect the offspring’s taste preference for salt. The offspring of mothers who consume high amounts of salt during pregnancy often show increased consumption of and preference for salt. Additionally, sodium deprivation in utero due to maternal mineralofluid loss can impact the infant’s preference for salt. Although the exact timing is unclear, there is likely a sensitive period during which exposure to sodium has the most profound effect on taste preference development. During this sensitive period, pregnant women should be aware of how much salt they are ingesting and more closely regulate salt intake.

For this reason, pregnant women and those who are lactating should strive to maintain the daily-recommended value of sodium ingestion to prevent potential health problems for their infants that are associated with sodium levels that deviate from this standard. It would be interesting to see if there is any effect of salt intake in the early stages of pregnancy and taste preference development, knowing that the gustatory system is not fully developed until at least fifteen weeks of gestation. Additional studies should seek to identify the timing of the sensitive period during which maternal dietary salt has the strongest influence on the infant’s taste preference and whether this period extends into lactation.
Section II: Fatty Tastes

Many processed foods commonly sold in grocery stores or restaurants in Western society are high in fats. A report by the USDA stated that foods consumed by Americans outside the home consist of 38.7 percent calories from fat, and the percent of calories consumed outside the home is as high as 37.6 percent of all calories consumed (United States Department of Agriculture, 2003). Therefore, it is not surprising that easy access to these fatty foods, especially those high in saturated fat, is contributing to the obesity epidemic as well as the development of coronary heart disease (Willett, 2012), noninsulin-dependent diabetes mellitus (Risérus, Willett, & Hu, 2009), and some forms of cancer (La Vecchia, 1992).

Recently, researchers have investigated fat as its own taste, as well as its increased palatability when paired with sugar. For example, Drewnowski and Greenwood (1983) found that hedonic preference ratings in normal rats improved with increasing concentrations of fat and that an initial increase in preference was followed by a decline with increasing concentrations of sucrose. However, when the two were combined, the hedonic preference for the sweet high-fat substance was intensified. Similarly, when free fatty acids were added to a solution consumed by rats, licking increased if the fats were added to sweet solutions and decreased if the fats were added to salty, bitter, or sour solutions (Pittman, Labban, Anderson, & O’ Connor, 2006). These results imply that fats can intensify the taste perception of flavors, possibly by depolarizing the taste receptor cells. However, when the CD36 fatty acid transporter found in lingual papillae was knocked out in rats, it resulted in an inability to detect long-chain fatty acids (Laugerette et al., 2005). These findings support fat as an additional taste with hedonic value that is detected and intensified by way of a unique and distinct mechanism.
Although there appears to be a genetic component to ingestion of fatty acids (Keller, 2012), there is also evidence that prenatal exposure can influence the offspring’s preference for foods high in fats as well as long-term neurochemistry. A study conducted by Chang, Gaysinskaya, Karatayev, and Leibowitz, (2008) examined rats in order to demonstrate this link between a maternal diet high in fats and the offspring’s increased preference for fatty acids. 

Four experimental groups were created in order to determine the direct impact of prenatal fatty acid consumption on taste preference. Each rat was exposed to either a high fat diet (HFD) consisting of 50 percent fat, a balanced diet (BD) consisting of 25 percent fat, or a combination of both during gestation and weaning. The HFD group was maintained on a HFD during the prenatal and postnatal periods, the BD group was maintained on a BD during the prenatal and postnatal periods, the HFD-BD group was maintained on a HFD prenatally and a BD postnatally, and the BD-HFD group was maintained on a BD prenatally and a HFD postnatally. Those in the HFD-BD group were cross-fostered immediately after birth with dams given a BD and never exposed to high fats. Cross-fostering was necessary because it eliminated the possibility that perinatal exposure determined the development of fatty taste preferences by only exposing the offspring to a HFD during gestation. The rats’ neuropeptide and hormone expression and serum fat levels were examined at postnatal day 15 and postnatal day 70.

The results indicated that at postnatal day 15 and postnatal day 70, the rats in the HFD and HFD-BD group showed an increase in serum triglycerides, insulin, non-esterified fatty acids, and galanin mRNA and peptides in the paraventricular nucleus. These postnatal day 15 rats additionally showed an increase in glucose and cortisone levels, an increase in encephalin and dynorphin in the paraventricular nucleus, and an increase in orexin and melanin-concentrating hormone in the perifornical lateral hypothalamus. These results were not demonstrated in the
BD group or the BD-HFD groups, indicating that the changes are strongly influenced by exposure to a HFD during gestation. An increase in orexin, galanin, encephalin, and dynorphin by means of injection has been shown to increase the consumption of high fats and is often accompanied by an increase in triglycerides and non-esterified fatty acids (Leibowitz, 2000; Zhang, Gosnell, & Kelley, 1998; Clegg, Air, Woods, & Seeley, 2002; Yun et al., 2005). Therefore, it is likely that the enhanced preference for dietary fats shown in the HFD and HFD-BD group of rats and not in the BD group can be attributed to the increase in these orexigenic peptides. There was also an increase in neurogenesis in the HFD and HFD-BD rat groups, which could impact the long-term physical and behavioral alterations, such as an increased preference for fats seen in the adult offspring.

These results suggest that prenatal, not postnatal, exposure to diets high in fatty acids increases the offspring’s preference for and consumption of fats. Consumption of foods high in fats increases circulating triglyceride levels, which in turn increases mRNA expression and peptide formation of galanin, encephalin, and orexin, possibly producing an impulse to overeat while ingesting meals high in fat (Chang, Karatayev, Davydova, & Leibowitz, 2004). Furthermore, analysis of the offspring at maturity indicates that the influence of a maternal diet high in fats extends into adulthood, potentially encouraging long-term overconsumption of fatty foods by the offspring, which can lead to the development of obesity and other related health problems. There was no significant change in the BD and BD-HFD groups, indicating that there is likely a sensitive period during gestation, but not during lactation, when exposure to fats has its greatest effects.

To investigate the influence of a prenatal high fat diet on hypothalamic neuron expression, Poon, Barson, Fagon, and Leibowitz (2012) analyzed whole hypothalamic tissue and
isolated hypothalamic neurons of rats at embryonic day 19 following a maternal diet high in fat or of standard chow. Examination of both whole hypothalamic tissue and isolated hypothalamic neurons revealed that, when compared with the chow feeding controls, rats exposed to a high fat diet in utero showed significant increases in encephalin and neuropeptide Y for measurements of mRNA levels, percentage of peptide expressing neurons, and peptide levels. Encephalin and neuropeptide Y have been shown to encourage feeding and contribute to obesity; therefore, if these peptides are elevated as a result of prenatal exposure, it suggests that they may contribute to overeating in the offspring after birth (Barson et al., 2009). This study by Poon et al. (2012) accounts for the prenatal exposure of fats and the impact of maternal diet on the offspring’s neurochemistry. Taken together, it is apparent that exposure to fats in utero leads to an elevated expression of hypothalamic peptides that influence feeding behavior, most likely contributing to overconsumption of and an increased taste preference for foods high in fats.

This link between circulating fats, high expression of hypothalamic peptides, and an increased preference for fatty foods has been demonstrated in additional studies. The current research supports exposure during gestation as the determining factor. Poon et al. (2012) summarized the literature on this topic as follows: the offspring of mothers who consumed a high-fat diet during pregnancy show an increase in hypothalamic peptide expression, an increase in density of peptide-expressing neurons, an increase in plasma lipids, and an increase in neurogenesis. These changes all indicate that there are neurological alterations produced in utero that may contribute to control over food intake and body weight.

A follow up study was conducted by Poon et al. (2013) to determine a possible mechanism behind the differentiation of hypothalamic orexigenic peptide-expressing neurons that occurs in response to prenatal exposure to a high fat diet. In order to do this, the researchers
studied the expression of transcription enhancer factor-1 and Yes-associated protein, which
induce cells to cease proliferating and differentiate upon inactivation or phosphorylation.
Analyses indicated that both the transcription enhancer factor-1 and Yes-associated protein
expression were suppressed in the embryos exposed to high-fat diets, which in turn led to an
increase in expression of hypothalamic encephalin neurons. This decreased expression of the
transcription enhancer factor-1 and Yes-associated protein was also found in the postnatal period
of offspring exposed to fats during gestation, suggesting that their inactivity is sustained
throughout development, leading to a prolonged increase in encephalin neurons.

High fat diets during gestation can induce epigenetic changes in the offspring as well,
causing DNA hypomethylation and changes in dopamine and opioid gene expression (Vucetic,
Kimmel, Totoki, Hollenbeck, & Reyes, 2010). The increase in dopamine and opioid gene
expression was found to be connected with the mesocorticolimbic reward system in that there
was an increase in expression of the dopamine reuptake transporter (DAT) in the ventral
tegmental area (VTA), nucleus accumbens (NAc), and the prefrontal cortex (PFC) and a
decrease in dopamine receptor 1, dopamine receptor 2, and dopamine- and cAMP- regulated
phosphoprotein-32 expression within the NAc and PFC. Together, these changes contribute to a
hypodopaminergic state characterized by an increase in dopamine reuptake. A
hypodopaminergic state is hypothesized to increase consumption of palatable food in order to
return to the body’s reward set point (Koob & Le Moal, 2008). Additionally, hypothalamic
dopamine levels stimulate the consumption of food (Meguid et al., 2000). These alterations are
therefore consistent with the results, which demonstrated that rats exposed to the high fat diet in
utero showed an increased preference for the high fat diet compared with the control. Although
not fully understood, the authors noted that not only does global DNA hypomethylation promote
fat intake, but it is often associated with adverse in utero conditions and an increased risk of developing obesity and cancer.

Ong and Muhlhausler (2011) also investigated the mesolimbic reward pathway and its relationship to prenatal fat exposure. These researchers demonstrated that consumption of “junk food” high in fats during pregnancy can alter the offspring’s food intake control manifested as an increase in fatty foods not displayed in offspring of rat dams on a control diet. The “junk food” diet administered to the rats included peanut butter, hazelnut spread, sugary cereal, cookies, lard and rat chow, processed meat, and savory snacks. The offspring exposed to high fats during gestation showed an increase in fat intake during both the juvenile and adult periods. One potential explanation for this postnatal increased intake is a higher level of opioid and dopaminergic signaling associated with the mesolimbic reward pathway displayed as young as six weeks. This increased signaling was marked by an increase in μ-opioid receptor (Mu) mRNA and a decrease in dopamine active transporter (DAT) mRNA expression in the nucleus accumbens. The researchers subsequently observed a decrease in this opioid and dopaminergic signaling following the offspring’s third month on a high sugar diet, indicating reduced sensitivity to the opioids and increased dopamine reuptake. This decreased Mu mRNA and increased DAT mRNA expression associated with desensitization furthermore intensified the rat pup’s excessive intake through the newly developed dependence on the junk food diet.

Therefore, it is important to limit high fat intake during gestation as it can cause permanent neurological alterations in the offspring that could be harmful to the fetus and contribute to many high-risk disorders. Research suggests that, as with salt, there is likely a sensitive period for fat during gestation when exposure to a high fat diet has the greatest impact on the offspring. The studies show that exposure to a high fat diet in utero is accompanied by
changes in orexigenic mRNA and peptide expression, as well as a decrease in dopamine levels and increase in dopamine reuptake. All of these changes are associated with an increase in fat consumption that may contribute to the development of health problems, especially those relating to obesity.

**Section III: Health Implications**

As previously discussed, diets high in salt and fat can lead to lasting problems, which is why a preference for these foods can negatively impact the health of the offspring. For example, Zinner, McGarvey, Lipsitt, and Rosner (2002) found that neonates with a preferential response to salty solutions had a higher diastolic blood pressure than those with a neutral or aversive response to the solution, even when a family history of hypertension was taken into account. The neonates’ preference for salt was analyzed by recording latency to suck, number of sucking bursts, mean sucks per burst, number of interburst intervals, and total number of sucks in the trial following the administration of microdrops of the fluid taste stimuli. These numbers were documented using a microcomputer that recorded the electrical signal converted from suction or negative pressure changes. Blood pressure was measured during a separate testing session two to four days after the infants were born to eliminate the possibility that immediate consumption of the tastants would affect the blood pressure results.

Another correlational study conducted by Málaga et al. (2005) uncovered a relationship between salt taste perception and blood pressure in normotensive human adolescent boys whose mothers had fluid loss during the first trimester of pregnancy. The adolescent participants’ taste perception was analyzed using a sensitivity test to determine sodium chloride threshold and a behavioral discrimination test to differentiate between saline solutions. Results indicated that adolescents born to mothers who experienced a high frequency of vomiting during their first
trimester showed significantly higher systolic blood pressure and lower salt sensitivity when compared with offspring of mothers who did not experience high rates of vomiting during pregnancy. As demonstrated by Leshem (1998), infants born to mothers who experience mineralofluid loss from vomiting during pregnancy have a higher preference for salt. Therefore, the negative correlation between salt sensitivity and systolic blood pressure found by Málaga et al. (2005) suggests that these offspring may consume more sodium over the course of their lifetime given their decreased sensitivity to salt, which could in turn contribute to high blood pressure.

Long-term high salt consumption can impact mechanisms within the renin-angiotensin system as well as other feedback loops. One recent study, for example, showed that a diet high in salt can lead to a disruption in the chloride ion gradient and the elimination of the baroreceptor-mediated negative feedback inhibition associated with vasopressin neurons (Choe et al., 2015). This occurs due to brain–derived neurotrophic factor-dependent activation and down regulation of potassium-chloride cotransporter 2 stemming from autocrine activation of tropomyosin-related kinase B receptors. As a result, there is greater firing from hypothalamic magnocellular neurosecretory cells, a decrease in GABAergic inhibitory signaling, and a subsequent increase in vasopressin secretion, which all contribute to elevated blood pressure.

Chronic high blood pressure, or hypertension, is one of the main contributing factors of heart disease (Beevers, Lip, & O’Brien, 2001), which is the leading cause of death worldwide (Heron, 2015). It is pertinent that, regardless of salt preference, sodium intake is regulated and monitored. This is especially important for expectant mothers during pregnancy and individuals with a history of hypertension. Consumption of a high salt diet during pregnancy can lead to an
increase in the offspring’s salt preference that extends into adulthood, contributing to future health problems.

Preference for fatty acids can also cause health problems, especially those related to obesity. Obesity is a serious and growing issue because the health risks associated with it are extensive. For example, problems related to obesity include pulmonary embolisms, coronary heart disease, hernias, cancer, pain, type two diabetes, fatigue, sleep apnea, hypothyroidism, infertility, and depression, among many others (Aronne, 2002). The increased preference for fats that can contribute to obesity may also be amplified by an impairment of proper signal functioning.

Erlanson-Albertsson (2005) showed that the feedback mechanism for appetite regulation can be altered in response to fatty foods. Normally, satiety signals are released following the intake of food, including the release of leptin by adipose tissue in proportion to fat mass. However, as discussed, prenatal exposure to fats can lead to increased expression of hypothalamic neuropeptide Y, orexin, and other neuropeptides involved with hunger. Leptin, on the other hand, in addition to insulin and cholecystokinin, is inhibited even though intracellular levels are high. Therefore, not only are the reward centers of the brain and hunger signals activated, but the satiety signals are dampened, promoting overconsumption of the palatable fatty food.

High fat consumption can also increase glucose and insulin levels. A longitudinal study of children showed that, of the children who gained weight, their fasting glucose and two hour glucose levels significantly increased compared with those who lost weight (Weiss, Shaw, Savoye, & Caprio 2009). Additionally, impaired glucose tolerance resulting from obesity was a significant contributing factor to the development of type two diabetes mellitus and metabolic
syndrome. Lee et al. (2011) also demonstrated the effects of prolonged high fat diets on insulin resistance. In this study, systemic insulin resistance was proportional to adipose tissue inflammation, with worsening glucose intolerance and systemic insulin resistance as the subjects continued to consume a high fat diet. This macrophage-mediated tissue inflammation was a major contributor to insulin resistance seen only in the obese subjects who had prolonged exposure to a high fat diet. The decrease in insulin sensitivity and the development of glucose intolerance, however, were also displayed in subjects who consumed a high fat diet for a short period of time. Long-term diets high in fat can influence sensitivity and detection of both glucose and insulin, aiding in the development of type two diabetes mellitus and hyperglycemia. Diabetes mellitus and hypertension are often comorbid, the combination of which can lead to premature atherosclerosis and an accelerated risk of cardiovascular disease (Epstein & Sowers, 1992).

Another effect of a prolonged high fat diet is enteric nerve alteration found in type two diabetes patients. Stenkamp-Strahm et al. (2015) demonstrated that mice on a high fat diet had decreases in ganglionic and nerve cell body sizes and a reduction of nerve health in the duodenal myenteric plexus as well as increased nerve injury to inhibitory motor neurons. It is likely that these enteric changes affect gastrointestinal function and signaling to the brain. The researchers point out that this most likely results in impairment in glucose homeostasis, appetite regulation, and gastric emptying. The mice additionally showed characteristics of obesity and type two diabetes in as little as four weeks on a high fat diet. Consistent with other studies, Obrosova et al. (2007) also linked a high fat diet to the development of obesity, increased plasma fatty acids and insulin concentrations, and glucose intolerance. Interestingly, the researchers showed changes in nerve sensitivity in that subjects on a high fat diet had small sensory fiber neuropathy
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and a decrease in nerve conductance. Watcho, Stavniichuk, Ribnicky, Raskin, and Obrosova (2010) similarly showed that neuropathy could be induced by a high fat diet during their study of the effects of PMI-5011 as a possible treatment for this neuropathy in a prediabetic and obese mouse model.

Uetake et al. (2015) conducted a study and found that a high fat and high salt diet can induce and accelerate the progression of nonalcoholic steatohepatitis, which is characterized by fat deposits in the liver and is often associated with metabolic syndrome. Mice subjects that consumed this diet also had increased inflammation from oxidative stress, greater fatty degeneration around hepatic central veins due to fibrotic changes, and an elevated systolic blood pressure. Additionally, liver serum levels for hyaluronic acid and hepatic fibronectin expression were increased in mice on a high fat, high salt diet compared with those consuming high fat alone. Both hyaluronic acid and hepatic fibronectin were used as blood markers for the progression of hepatic fibrosis, or the accumulation of connective tissue in the liver. The increased expression indicates an increased progression of the disease. One of the most notable findings by these researchers is an increase in blood pressure, which appears to be an inevitable change associated with consumption of a high fat and high salt diet.

A study on adult Yucatan miniature swine conducted by Myrie et al. (2012) analyzed the affect of a high fat, high salt, and high sugar diet on telemetric blood pressure. The Yucatan miniature swine were used in this study due to their similarity in metabolism and nutritional requirements when compared with humans, making them an ideal model for studying cardiovascular disease. Additionally, 24 hour average hemodynamic parameters were measured using radiotelemetry, as this technology may have greater sensitivity to detection than other noninvasive, indirect techniques. Following prolonged exposure to a high fat, high sugar, and
high salt diet starting post-weaning, the miniature swine had a significant increase in blood pressure. This increase was primarily seen in the form of elevated systolic arterial pressure and an accompanied increase in pulse pressure. Diastolic arterial pressure also increased in the swine on the high sugar, high fat diet with increasing concentrations of salt. Interestingly, the increase in systolic arterial pressure was less when the swine had an acute low-salt treatment and high fat and sugar diet than those that had an acute high-salt treatment and high fat and sugar diet. As a result, the researchers concluded that a sugar and fat diet both contribute to systolic arterial pressure and pulse pressure, although salt had the greatest effect on hypertension, closely followed by the content of fat.

Shen et al. (2004) further demonstrated the effects of high fat and salt diets on hypertension by studying rats and the development of metabolic syndrome. The researchers fed rats either a control diet, a diet high in fat, or a diet high in fat and salt for six to seven months. The results showed that rats on a high fat and high salt diet developed severe visceral obesity with increases in visceral fat weight and triglyceride and free fatty acid serum levels when compared with the rats on a control diet. These rats also developed fasting hyperinsulinemia, hyperglycemia, less insulin sensitivity, greater insulin resistance, glucose intolerance, and hypertension. The significance of this study is that the researchers demonstrated the effects of a combined fatty and salty diet on health, especially the effects that contribute to the development of metabolic syndrome, type two diabetes, and cardiovascular disease. Interestingly, the development of hypertension in response to a high fat and high salt diet may be facilitated by the expression of a specific kinase. Huang et al. (2006) found that only in mice expressing the serum- and glucocorticoid-inducible kinase 1 did the addition of salt to a high fat diet increase blood pressure. The mice lacking this serum- and glucocorticoid-inducible kinase 1, which
initiates the renal epithelial sodium channel, showed resistance to hypertension. Due to the immensity of research supporting a high fat and high salt diet as an inducer of hypertension, it is possible that a prolonged, unhealthy diet can initiate an increase in blood pressure through another mechanism in cooperation with the development of a secondary disorder, such as obesity and metabolic syndrome, that allows the body to evade the protective effects of the kinase.

Most research conducted on the effects of prenatal exposure to a high fat and high salt diet analyzes each tastant separately. However, one study by Reynolds, Vickers, Harrison, Segovia, and Gray (2014) examined the effects of a diet high in both fat and salt consumed during pregnancy. The researchers studied mice offspring and found significant sex differences. The female offspring had a higher blood glucose, plasma insulin, and homeostatic model assessment-insulin resistance, while males had a high concentration of triglycerides. The high glucose and insulin levels as well as evidence for insulin resistance indicate that there is likely a dysregulation in the glucose homeostasis mechanism of mice exposed to a high fat, high salt diet in utero. Additionally, both male and female mice exposed to a high fat, high salt diet showed delayed growth at day 18 of gestation accompanied by rapid growth after weaning. Not only did the mice exposed to a high fat, high salt diet grow much quicker after weaning compared with mice exposed to either diet alone, but they also had a greater fat mass. These results indicate that prenatal exposure to both high fat and high salt may lead to the development of prediabetes characterized by insulin resistance, impaired regulation of glucose homeostasis, increased triglycerides, and increased fat mass post-weaning.

Taken together, these results indicate that high fat and high salt diets adversely affect both the nervous and endocrine systems, as well as impair critical feedback mechanisms for satiety. Not only are there changes in individuals who eat diets high in fat and high in salt for a
short period of time, but prolonged consumption can lead to lasting changes as well. These alterations can then contribute to chronic health problems, most notably those that result from obesity. As previously discussed, prenatal exposure to salt and fat increases the offspring’s preference for those tastes. Therefore, consumption of a diet high in both fat and salt during pregnancy can lead to a variety of alterations in the offspring. These alterations may promote overconsumption of fatty and salty foods in adulthood, which then may lead to additional changes in the body and brain. The combined effect of these changes can contribute to an increased risk for developing a variety of health problems that include type two diabetes, obesity, heart disease, and cancer.

Discussion

Many studies have provided evidence for the influence of prenatal and perinatal exposure to diets high in fats and salts on taste preferences that persist into adulthood. There is evidence that the gustatory system becomes fully developed in utero, potentially providing a window of opportunity in the early stages of development for the formation of taste preferences. While the studies provided focused primarily on the development of taste preferences resulting from environmental exposure, there may be a genetic component to this development that is generally unexplored.

Ferrell, Lanou, and Gray (1986) investigated the development of salt preferences in salt-sensitive and salt-resistant weaning rats. The rats were separated by genotype and subsequently split into groups that were given either a low salt (0.4 percent sodium chloride) or high salt (8.0 percent sodium chloride) diet for four weeks. Following this four-week treatment, all the rats were switched to the low salt diet until examination using a two-bottle preference test containing salt and water solutions. The salt-sensitive rats reared on a high salt diet consumed significantly
more water and salt than the salt-resistant rats on the high salt diet, although both groups drank
significantly more than the rats on the low salt diet. The rat’s preference for salt initially
increased with concentration until about 0.18 M, at which point the solution became more
aversive as concentration of salt continued to increase. These results indicate that salt preference
is not only influenced by environmental factors, but that genetics may play a role as well. This
raises the question of how much genetic composition and how much behavior and diet affect the
development of taste preferences.

As previously described, Shen et al. (2004) found that only mice with the serum- and
glucocorticoid-inducible kinase 1 showed an increase in blood pressure when reared on a high
salt and high fat diet. These findings suggest that there may be a genetic component, such as the
expression or repression of specific genes, that can contribute to the development of health
related symptoms and that exposure to high fat and salt may act on an already established
predisposition. This theory that additional factors apart from diet alone may be necessary to
induce hypertension is supported by Morrison et al. (2007), who found a difference between
obese and lean rats on the same diet. The development of obesity is multifactorial, shown to be
influenced by both genetic alterations (Rojas, Aguirre, Velasco, & Bermúdez, 2013) and the
environment (Epstein, Wing, Penner, & Kress, 1985). The obese rats on a moderately high fat
diet with the addition of salt were more likely to develop diet-induced hypertension, decreased
nitric oxide metabolite excretion, and decreased nitric oxide synthase when compared with lean
rats that were given the same diet. These results may be due to an increase in salt-sensitivity of
blood pressure with an impairment of nitric oxide production as seen in the obese rats. Whether
this salt-sensitivity is a result of the obesity or is a co-inherited genetic predisposition with
obesity is unclear. It is important to note that the rats were given a “moderately” high fat diet
that may not have met the threshold to cause high fat diet-induced obesity in the lean rats when diet-induced obesity may be a major factor in the development of hypertension.

As indicated by these studies, diets high in both fat and salt have a synergistic effect on the development and progression of high-risk health disorders, such as obesity, hypertension, inflammation, and diabetes mellitus (Uetake et al., 2015; Myrie et al., 2012; Shen et al, 2004). Many of these conditions are even key risk factors for cardiovascular disease, the current leading cause of death (Heron, 2015). Myrie et al. (2012) demonstrated that the greatest increase in blood pressure in Yucatan miniature swine occurred when their diets were high in fat, sugar, and salt. Although blood pressure increased with consumption of high salt or high fat diets alone, the effect was amplified when combined. Unfortunately, most processed foods sold in convenience stores are characteristic of these combination diets. Bayol, Farrington, and Strickland (2007) studied the effects of exposure to the “junk food” diet in rats during pregnancy and lactation by using biscuits, marshmallows, cheese, jam doughnuts, chocolate chip muffins, butter flapjacks, potato crisps, and caramel/chocolate bars as a model for high fat, sugar, and salt diets. The researchers found that rats exposed to this “junk food” diet perinatally showed a preference for the fatty, sugary, and salty foods in comparison with their respective controls. These researchers also indicated that rats perinatally exposed to the “junk food” diet, or the cafeteria diet, demonstrated increased adiposity and impaired skeletal muscle development in comparison with the controls (Bayol, Simbi, & Strickland, 2005). Additionally, these rats developed metabolic disorders, which are typically associated with insulin resistance.

Although the researchers used animal models in their studies, it is likely that their results can be applied to humans as well given the genetic similarities. The results suggest that infants exposed to a “junk food” diet during gestation and lactation will develop a preference for those
foods, promoting increased consumption of this diet in childhood. Additionally, as indicated by its name, foods high in fat, sugar, and salt are often distributed in school cafeterias. This can become a problem as it may hinder proper skeletal development and contribute to the development of insulin-resistant diabetes and obesity as demonstrated in the rats. Instead, school cafeterias and vending machines should be replaced with healthy, low fat, low salt, and low sugar options.

It is extremely important to decrease daily consumption of fat and salt, especially during pregnancy and lactation. Perinatal exposure to fat and salt can increase the offspring’s preference for these tastants through a variety of mechanisms that promote further consumption of these foods. This positive feedback loop encouraging overconsumption of unhealthy foods can then result in the development of childhood obesity, which often leads to an increase in cardiovascular morbidity and mortality (Baker, Olsen, & Sørensen, 2007). Other health problems associated with high intake of fats and salts include diabetes, cancer, hypertension, glucose impairment, and undesirable nerve alterations. While genetics appear to influence the development of some of these diseases, diet plays a critical role in its progression. For this reason, people should monitor their diets, especially pregnant and nursing mothers during their infant’s perinatal period of development. One of the best ways to minimize unhealthy eating is to advocate, potentially through education or interventions, for low salt, low fat, and low sugar diets in order to remain healthy and prevent disease development.
References


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