Chapter 6
Umami Taste: Inborn and Experiential Effects on Taste Acceptance and Satiation During Infancy

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The sensation of taste, which has been classically delineated into the five basic taste qualities of sweet, sour, salt, bitter, and umami (Beauchamp, 2019), has attracted great interest in recent years as a major determinant of what we eat—an overlooked aspect of nutrition (Kershaw & Mattes, 2018). Taste plays a critical role as the gatekeeper of what enters the body, guarding against ingestion of dangerous substances (e.g., bitter-tasting poisons) (Glendinning, 1994) while encouraging consumption of foods important for growth and development (Kurihara, 2015; Gabriel et al., 2018), including mother's milk, readily available glucose in energy-containing plants (e.g., sweet fruits) (Beauchamp, 2016), a needed mineral (salt) (Beauchamp, 1987), and proteins (umami)—particularly the taste of the amino acid L-glutamate (Glu) and 5′-ribonucleotides (Beauchamp, 2009). In the context of feeding, these taste sensations naturally co-occur with other sensory modalities, including olfaction and chemesthesis.

This chapter focuses on umami taste in infancy. As a basic taste, the scientific investigation on umami has received perhaps the least attention in developmental studies, especially when compared to the ontogeny of sweet and salty tastes (Mennella et al., 2016a; Beauchamp & Mennella, 2009). We provide an overview of the basic biology of umami taste, from the distribution of umami taste receptors throughout the oral cavity and gastrointestinal system to its role in flavor, palatability, and food intake. We then summarize the scientific evidence on early routes of umami exposure and children's inborn and learned responses to its taste and satiating properties. We focus on the first year, when infants make the drastic transition from eating an all-liquid diet of human milk, artificial milk (infant formula), or

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both, to one containing both liquid and solid foods (Grummer-Strawn et al., 2008). This body of scientific evidence derives from a variety of precise and detailed measurements of infants' orofacial responses and well-controlled paradigms that measured their behavioral responses, intake, and satiation (Ventura & Mennella, 2017). Often the umami stimulus studied was L-glutamate, in the form of the sodium salt monosodium glutamate (MSG).

6.1 Umami Taste in the Oral Cavity and Alimentary Canal

One century after Kikunae Ikeda's description of the fifth basic taste of umami (Ikeda, 2002), scientific breakthroughs revealed its perception is mediated by activation of heterodimeric G-protein-coupled receptors (GPCRs) encoded by members of the type 1 family of taste receptor genes, *TAS1R1* and *TAS1R3* (Nelson et al., 2002; Bachmanov et al., 2016) (see Chaps. 1 and 2). In addition to the TAS1R genes, other GPCRs act as umami receptors: truncated taste versions of the metabotropic glutamate receptors (mGluRs) found in many neuronal cells, mGluR4 (Chaudhari et al., 2000a) and mGluR1 (Chaudhari et al., 2000a; Yasumatsu et al., 2015; San Gabriel et al., 2009). These umami receptors, located throughout the oral cavity and alimentary canal, are activated only by free amino acids (FAAs), not by amino acids bound in the form of proteins (Keast et al., 2021). The locations of these receptors underlie their different roles in signaling the presence of taste-reactive FAAs, which not only generate the perception of umami taste but also modulate complex digestive processes such as gastric emptying and satiety.

6.1.1 Oral Cavity and Taste Psychophysics

The T1R1 + T1R3 heterodimer receptor and mGluRs are located at the tip of taste cells distributed across the tongue (Yasumatsu et al., 2015). When activated by free L-amino acids (e.g., free Glu), 5′-ribonucleotides, or salts of glutamic acid (e.g., MSG), these receptors transmit signals to the brain. The taste of Glu is synergistically enhanced by the sodium salts of 5′-inosine monophosphate or 5′-guanosine monophosphate.

Psychophysical studies revealed that MSG imparts a "savory" and "satisfying" sensation (Rogers & Blundell, 1990), increasing the palatability of a variety of foods, due in part to its ability to block bitter tastes (Mennella et al., 2014a). Beauchamp (2009, 2019) suggests that umami also increases palatability by functioning as a flavor enhancer (Beauchamp, 2009; Hartley et al., 2019), but the food matrix in which umami-tasting compounds are experienced is important. Although unpalatable when tasted alone or in aqueous solution, umami compounds are palatable in broth and improve the flavor of a variety of foods and flavors (Beauchamp, 2009; Yeomans et al., 2008; Yamaguchi & Takahashi, 1984), imparting a pleasant

"mouthfeel" sensation of fullness (Prescott, 2004). Glu occurs naturally in many foods, such as meats, cheeses, broths, and tomatoes, and imparts a savory taste (Gabriel et al., 2018; Ninomiya, 2003). It is notable that many cultural food traditions intended to preserve food or increase its nutritional value (e.g., extraction, curing, aging, fermentation) often increase the food's FAA, including Glu, content (Ninomiya, 2015).

6.1.2 Alimentary Canal and Feeding Behaviors

Outside of the oral cavity, T1R1 + T1R3 receptors and mGluRs are scattered widely along the lower alimentary canal, comprising the stomach (San Gabriel et al., 2007) and small intestine, where they regulate digestion, absorption, and metabolism of nutrients, especially amino acids (Keast et al., 2021). Although perception of umami taste in the mouth is a conscious sensation indicating the presence of free Glu in foods, the detection of Glu in ingested food by the gastrointestinal tract is not (Hartley et al., 2019). Instead, when umami compounds bind to receptors in the gastrointestinal system, nerves are activated, hormones are released, or both (Kondoh et al., 2009; Daly et al., 2013; Shirazi-Beechey et al., 2014). Electrophysiological studies have revealed that binding of MSG to the stomach lining, probably via stomach mGluR1, can activate the vagus nerve by releasing bioactive molecules such as serotonin (Uneyama et al., 2006), whereas molecular and physiological studies suggest that free Glu in ingested food potentiates gastric digestion and emptying of amino acid-rich foods (San Gabriel et al., 2007; Zolotarev et al., 2009). In the intestine, the binding of free Glu to T1R1 and T1R3 receptors appears to cause secretion of the hormones ghrelin and cholecystokinin, which are known to impact gastric emptying and/or satiation (Keast et al., 2021; Vancleef et al., 2015).

Brief feeding studies in healthy adults have shown that, when added to foods such as broths and vegetables, MSG imparts a "savory" and "satisfying" sensation that enhances palatability (Rogers & Blundell, 1990; McCabe & Rolls, 2007; Rolls, 2009; Carter et al., 2011). However, results on its effect on satiation (i.e., energy intake within a meal) and satiety (i.e., energy intake during a subsequent meal) in adults have not being consistent, perhaps due in part to the wide range of experimental paradigms and participant ages and health status (Keast et al., 2021) (see Chap. 4). While some studies on healthy, noninstitutionalized adults reported that, when added to a food, MSG increased satiation and reduced intake within a meal or increased sensations of fullness (Imada et al., 2014; Miyaki et al., 2016), others reported no effects (Rogers & Blundell, 1990; Luscombe-Marsh et al., 2009; Anderson et al., 2018).

6.2 Inborn Responses to Umami Taste

At birth, human infants are well equipped to convey a range of hedonic responses to tastes, odors, and complex flavors. As reviewed by Forestell and Mennella (2017), facial expressions in particular play an important adaptive role, allowing dependent infants to convey information to caretakers about the sensations they are experiencing in their oral cavity. Head turning away and displays of gaping and puckering in response to bitter and sour tastes are often recognized as signals of disgust or rejection, whereas orientation toward the food, faster sucking, and smiling are often interpreted as a signals of liking, encouraging feeding of that particular food.

In the 1970s and 1980s, a series of pioneering studies by Steiner, Ganchrow, and colleagues revealed that, within hours after birth, newborns respond with characteristic, differential orofacial responses when small quantities of sweet-, sour-, bitter-, or umami-tasting liquids were placed on their tongue (Steiner, 1979, 1987; Ganchrow et al., 1983). Similar to infants' reactions to the taste of sugars, the facial responses to the taste of umami appear to be primarily inborn and preferred (Steiner, 1987). Newborns responded with increased sucking and mouth movements and relaxation of their face when tasting soup broth containing 0.1% and 0.5% MSG but rejected MSG when presented in water solutions. Research on older infants (2–24 months) confirmed the rejection of Glu in plain aqueous solutions (Beauchamp & Pearson, 1991) and the palatability of umami in the context of a food. Both well-nourished and malnourished 2- to 24-month-old infants preferentially ingested soup broth containing MSG relative to soup broth alone (Beauchamp & Pearson, 1991; Beauchamp et al., 1987).

This body of research highlights important aspects of the taste stimuli and methodological approaches needed to examine umami taste palatability. First, it is difficult to interpret findings when children are presented with only umami taste in plain aqueous solution (Schwartz et al., 2009). Rather, umami must be experienced in the context of other chemosensory stimuli when testing individual differences in the hedonics of umami taste in pediatric and adult populations (Beauchamp, 2009; Forestell & Mennella, 2017; Steiner, 1987). As suggested by Beauchamp (2009, 2019), umami functions as a flavor enhancer, increasing the palatability of flavors it is mixed with (Hartley et al., 2019). Second, when phenotyping orofacial taste reactivity, infants should not see the facial expression of their mothers during testing since they are sensitive to and mimic these facial expressions (Gunnar & Stone, 1984). Third, measurements of intake and acceptance should be based on infants' behavioral signaling of hunger and satiation (i.e., infant-led feeding paradigms) (Forestell & Mennella, 2017; Ventura et al., 2015) and not determined by mothers or experimenters, because they may under- or overfeed by not attending to the infant's satiation cues (Crow et al., 1980; Li et al., 2010).

6.3 Early Experiences with Umami: First Foods

Like the prenatal diet (amniotic fluid), the early postnatal diet is unique in that it is typically solely liquid based, consisting of human milk, infant formula, or both. The protein in these first foods supports infant growth, immune function, and behavioral development by supplying nitrogen and essential and semi-essential amino acids (Dewey et al., 1996). These first foods—amniotic fluid, human milk, and infant formula—as well as a variety of foods, from vegetables to meats, naturally contain FAAs, including free Glu (Yamaguchi & Ninomiya, 2000).

Infants' experiences with the taste of FAAs, and Glu in particular, can vary considerably. Table 6.1 summarizes the variation in the total FAA and free Glu content in amniotic fluid, human milk at different stages of lactation, and infant formulas from a range of studies. Although measures of FAAs in human fluids date back to the 1940s (Beach et al., 1941), we included only studies that used chromatography and spectrophotometry measures, omitting earlier ones that used microbiological

Table 6.1 Total free amino acids (FAAs) and free glutamate (Glu) content of amniotic fluid, human milk, and infant formula[a]

Sample	Concentration (μmol/L)		Selected References
	Total FAAs (number of FAA)[b]	Free Glu	
Amniotic fluid			
First and second trimesters	2036 (17)	149	Cockburn et al. (1970)
	1803 (16)	261	Lopez Ramon y Cajal et al. (2007)
	2230 (16)	149	Reid et al. (1971)
Third trimester	1070 (16)	48	Reid et al. (1971)
	1573 (16)	107	Levy and Montag (1969)
Human milk			
Colostrum	3321 (19)	1090	Zhang et al. (2013)
Transitional milk	2416 (19)	960	Zhang et al. (2013)
Mature milk	2481–2941 (19)	1175–1529	Zhang et al. (2013)
Infant formula			
Cow milk	523–864 (20)	86–109	Ventura et al. (2012a)
Soy	19,33–2450 (20)	0–11	Ventura et al. (2012a)
Partial protein hydrolysate	2329 (20)	113	Ventura et al. (2012a)
Extensive protein hydrolysate	80,375–85,445 (20)	7472–8226	Ventura et al. (2012a)

[a]Values represent normal pregnancies for amniotic fluid and term births for human milk. Data are presented as ranges of means when from more than one publication, from two stages of lactation, or from more than one brand of a given type of infant formula

[b]Total concentration based on the sum of all FAAs; numbers in parentheses indicate number of different FAAs summed

methods. Note that different studies used different numbers of FAAs to calculate total FAAs, ranging from 16 to 20 individual FAAs.

6.3.1 Amniotic Fluid

Much of the early research on amniotic fluid content aimed to help diagnose certain genetic disorders associated with aminoaciduria (Emery et al., 1970) or to identify biomarkers of inborn errors of metabolism (Reid et al., 1971) or placental dysfunction (Lopez Ramon et al., 2007). During normal pregnancies, FAA levels change dynamically in amniotic fluid (Reid et al., 1971) (see Table 6.1). In general, FAA concentrations in amniotic fluid and maternal plasma are higher during early pregnancy and lower in the third trimester and near term (Emery et al., 1970; Reid et al., 1971; Lopez Ramon et al., 2007; Athanasiadis et al., 2011; Levy & Montag, 1969; Cockburn et al., 1970). Such changes in part reflect the exchange of maternofetal fluids as the placenta and the fetus develop (Reid et al., 1971; Lopez Ramon et al., 2007). Amino acids are actively transported across the human placenta, mediated by specific transporters in plasma membranes (Jansson, 2001), and are also synthesized and metabolized through the placenta (Jansson, 2001; Cetin, 2001).

The time course and trajectory of changes in amniotic fluid during pregnancy differ among the individual FAAs (Reid et al., 1971; Guadalix et al., 1975). Overall, alanine was the most abundant amino acid in the amniotic fluid during gestation (Lopez Ramon et al., 2007). Although less abundant than alanine, free Glu is relatively abundant throughout pregnancy in humans (Table 6.1), whereas in other animals (i.e., pig), it is the most abundant FAA in both amniotic fluid and maternal plasma (Wu et al., 1995). From the perspective of early feeding and experiences, the human fetus actively swallows significant amounts of amniotic fluid, particularly during the last trimester (Underwood et al., 2005), so the varying amounts of FAAs and free Glu could result in differential exposures prior to breastfeeding.

6.3.2 Human Milk

For reasons not completely understood, the mammary tissue of many mammals produces large amounts of nonprotein nitrogenous compounds, including (protein-unbound) FAAs. Research quantifying the amino acid composition of human milk dates back to the 1940s and is a growing field of research, perhaps motivated by the need to improve the composition of infant formula, since human milk is the standard for human infant nutrition (Ballard & Morrow, 2013).

The total amino acid (both unbound and free) profile and the free Glu content of human milk at the three stages of lactation, colostrum (0–5 days), transitional milk (6–20 days), and mature milk (≥21 days), are shown in Table 6.1. Here we highlight the findings from a systematic review of 22 studies on both preterm and full-term

human milk (Zhang et al., 2013). The inclusion criteria for this meta-analysis were that the women who donated the human milk samples had to be healthy, have delivered a term infant of known age, and have to be consuming free-living diets and that the study provide adequate information for the milk samples, such as stage of lactation, method of extraction (e.g., type of pump) and storage (e.g., liquid, freeze-dried form), units of concentration, and geographic location. FAAs had to be quantified by ion exchange chromatography or an automatic amino acid analyzer and not by microbiological methods.

The systematic review revealed that total amounts of amino acids (both unbound and free) decline during the first 4 months of lactation and remain stable thereafter (Zhang et al., 2013), a pattern that parallels the changing protein needs of growing infants (Dupont, 2003). From the data in the review (Zhang et al., 2013) and other publications, we summarized the total FAA content in human milk across lactation (Table 6.1). The pattern of individual amino acids differs over time. While most amino acids were significantly lower in mature milk than in colostrum (i.e., leucine, lysine, phenylalanine, valine, threonine, methionine, isoleucine, taurine, arginine, asparagine, tyrosine, proline) or stayed the same (i.e., histidine, glycine, serine, cysteine, alanine), the FAA glutamine and Glu increased with progressing lactation. Overall, at each stage of lactation, Glu, glutamine, taurine, and alanine were the most abundant FAAs, with Glu and glutamine accounting for about half of FAAs at each stage, a finding consistent with our own research (Baldeon et al., 2014).

To graphically depict the changes in total FAAs and free Glu during lactation, we focused on our longitudinal study on adolescent and adult mothers that measured the FAAs including free Glu content in colostrum, transitional milk, and mature milk over time (Baldeon et al., 2014). Figure 6.1 shows variation in the relative amount of FAA Glu and all other FAAs in the milk of lactating woman during the three stages of lactation. What causes this variation and whether variation in the Glu content of the maternal diet plays a role remain important areas of future research.

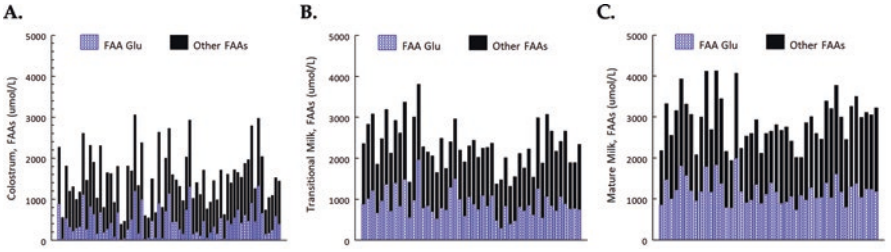

Fig. 6.1 Concentration (umol/L) of free amino acid glutamate (FAA Glu; hatched bars) and other free amino acid concentration (other FAAs; solid bars) in human colostrum (**Panel A**), transitional milk (**Panel B**), and mature milk (**Panel C**). Each bar represents an individual lactating woman (A, n = 65; B, n = 47; C, n = 45). The height of each bar represents total FAA concentration. (Data from Baldeon et al. (2014))

6.3.3 Infant Formulas

For healthy infants fed artificial milks, the four types of infant formula are currently on the market are cow milk formula (CMF), which is the most commonly consumed infant formula; soy formula; partially hydrolyzed formula; and extensive protein hydrolysate formula (EHF), a type of formula typically given to infants who have cow milk protein allergy or intolerance to intact protein (Rossen et al., 2016). Although these formulas are isocaloric and can differ in their source of carbohydrate (e.g., lactose vs. modified cornstarch), the form of the protein, the degree of hydrolysis, and in turn the concentration of FAAs are the major distinguishing factors (Ventura et al., 2012a). For example, the milk proteins (whey and casein) in hydrolysate formulas are treated with enzymes to break down their protein structure, generating FAAs, which lessens the burden of digestion and minimizes allergenicity for infants (Cook & Sarett, 1982). Thus, while infants fed any of these formulas are categorized as formula fed, they are not a homogeneous group since feeding these different formulas will lead to different exposures to proteins and FAAs, including umami-tasting compounds.

Table 6.1 presents FAA levels for the four types of infant formula. EHF had the highest levels of FAAs, averaging 120-fold higher than CMF, 39-fold higher than soy protein formula, and 36-fold higher than partially hydrolyzed formula. Compared to human milk, the concentrations of FAA and free Glu are lower in CMF but substantially higher in EHF (Baldeon et al., 2014; Ventura et al., 2012a; Agostoni et al., 2000a, 2000b). Quality control measures and manufacturing standards for infant formula minimize variations in FAA content for a given type of infant formula. For example, infants fed different brands of CMF will have a similarly low exposure to free Glu (Ventura et al., 2012a), compared to those fed breast milk, and infants fed EHF will ingest substantially higher concentrations of FAAs, experiencing different tastes (Ventura et al., 2012a). Psychophysical testing among adult sensory panels has revealed that EHF tastes less sweet, more bitter, and more savory than CMF, due in part to the differences in FAA content (Mennella & Beauchamp, 2005; Ventura et al., 2012b).

6.4 Effects of Early Umami Experiences on Taste Acceptance

Before tasting solid foods, infants are exposed to varying amounts of umami tastes in amniotic fluid, human milk, and the different infant formulas. Mennella, Beauchamp, and colleagues have used the differential early exposure to free Glu and umami flavors of infants feed exclusively human milk, CMF, or EHF as an experimental model system to study early flavor learning, food acceptance, satiation, growth, and the developing microbiome (Ventura & Mennella, 2017; Mennella & Trabulsi, 2012; Mennella et al., 2009, 2014b, 2022).

Forestell, Mennella, and colleagues (Mennella et al., 2009) used the striking differences in the taste and FAA content among human milk and infant formulas to understand how the earliest feeding experiences modify orofacial reactivity and intake of umami and other basic tastes both before and after the introduction of solid foods. At the time mothers decided to add cereal to their diets, 4- to 9-month-old infants who were exclusively fed human milk, CMF, or EHF were tested on six occasions, in counterbalanced order, for their acceptance of the basic tastes in a cereal matrix: sweet (0.56 M D-lactose), salty (0.1 M NaCl), bitter (0.24 M urea), savory (0.02 M MSG), and sour (0.006 M citric acid).

The type of milk infants were fed with affected their liking and acceptance of the basic tastes in a food matrix. Breastfed and EHF-fed infants were more likely than CMF-fed infants to smile (facial relaxation) while eating the Glu-flavored cereal, which likely reflects their exposure to the high concentrations of free Glu found in human milk (Baldeon et al., 2014; Agostoni et al., 2000a) and in EHF (Ventura et al., 2012a). However, breastfed infants do not all have the same flavor experiences early in life, because human milk has a great degree of individual variation in taste-reactive chemicals (for review, (Mennella, 2007; Spahn et al., 2019; Mennella et al., 2017)), including Glu (Baldeon et al., 2014) (see Fig. 6.1), and thus in the taste experiences of their infants, which presents difficulties in interpreting the results.

After weaning to table foods, as caloric intake from infant formula declined, infants' preferences for the basic tastes in cereal reflected the types of foods they had been fed: infants who ate pasta and other foods that contained cheese or tomatoes, which have naturally occurring free Glu, showed greater acceptance of the MSG-flavored cereal (Mennella et al., 2009).These findings are consistent with results from randomized feeding trials that revealed differences in food preferences in children fed EHF or CMF years after their last taste of the formula (Sausenthaler et al., 2010; Mennella & Beauchamp, 2002; Trabulsi & Mennella, 2012): the preference for umami flavors depended on the type of milk fed (Mennella & Castor, 2012; Mennella et al., 2011a). CMF and EHF differ in composition, in the profiles of volatile flavors, and in tastes other than umami, and the evidence suggests that palatability is personal, dependent on experience.

Experimental evidence demonstrates the plasticity in flavor learning during infancy. By experimentally manipulating the timing and length of exposure to EHF, Mennella, Beauchamp, and colleagues discovered a sensitive period for flavor programming during which feeding EHF renders this formula highly palatable and accepted throughout infancy (Mennella et al., 2004, 2011a). Infants introduced to EHF during the first 3.5 months accept its taste, but this acceptance diminishes in infants first introduced when they are older than 4 months (Mennella et al., 2014b; Mennella & Beauchamp, 1998). Infants exposed to EHF for at least 1 month during this sensitive period do not reject its taste when they are older: they feed EHF to satiation, prefer EHF to CMF, and do not display facial expressions of distaste while feeding, and mothers perceive their infants enjoy its taste (Ventura et al., 2015; Mennella et al., 2004, 2011a). Moreover, the flavors experienced during early breastfeeding and formula feeding "imprint" and remain preferred for a considerable time thereafter (Mennella et al., 2009, 2017; Sausenthaler et al., 2010; Schuett

et al., 1980; MacDonald et al., 1994; Owada et al., 2000; Liem & Mennella, 2002; Hepper et al., 2013). Whether variation in the umami content of the maternal diet during pregnancy and lactation results in differential exposure by their infants in amniotic fluid and human milk, respectively, is an important area for future research.

6.5 Satiation, Satiety, and Growth

Relative to intact proteins, hydrolyzed proteins are absorbed and metabolized more rapidly than intact proteins (San Gabriel et al., 2007). Indeed, in feeding trials, young infants ingested more CMF to satiation than they did EHF (Ventura et al., 2012b, 2015; Hyams et al., 1995; Mennella & Beauchamp, 1996; Mennella et al., 2011b). To our knowledge, only a few experimental studies in infants have investigated the effects of MSG content on satiation (intake within a meal) and satiety (one meal's effect on intake at subsequent meal) (Ventura & Mennella, 2017; Ventura et al., 2012b).

Because Glu is the most abundant FAA in EHF (Ventura et al., 2012a), we conducted a within-subject, two-meal, 3-day study to determine whether the differences in the satiation effects of CMF and EHF were due to differences in free Glu content (Ventura & Mennella, 2017; Ventura et al., 2012b). The experimental design allowed for infants to determine the timing and duration of each meal on each testing day. In randomized order, they were fed one of three isocaloric formulas during the first meal—CMF, EHF, or CMF—plus added free Glu, in the form of MSG, to approximate levels in EHF (CMF + Glu). When infants signaled hunger several hours later, they were fed a second meal of CMF.

As shown in Fig. 6.2, the infants consumed significantly less CMF + Glu and EHF than CMF during the first formula meal, whereas intake during the second formula meal did not differ across the three testing days. Thus, adding free Glu to CMF was sufficient to induce greater satiation compared to CMF alone. That is, the infants consumed less of the two formulas higher in free glutamate (EHF, CMF + Glu) (Ventura et al., 2012b) and began displaying satiation behaviors earlier compared to feeding CMF alone (Ventura et al., 2012b, 2015), and they did not compensate at the next meal (Ventura et al., 2012b). Thus, levels of free Glu in formula affect intake, suggesting that what infants are fed may be as important as how they are fed.

As stated earlier, although isocaloric, CMF and EHF differ not only in the content of FAA Glu but also in macronutrient composition. For example, EHF contains higher concentrations of FAA and has cornstarch as the carbohydrate source, whereas CMF contains mainly intact proteins and has lactose as its carbohydrate source. Nevertheless, long-term feeding trials have consistently revealed more normative weight gain and decreased risks of diseases during childhood in infants fed EHF compared to those fed CMF. The growth trajectories of EHF-fed infants were normative and comparable to infants fed human milk (Mennella et al., 2011b), whereas infants randomized to CMF experienced accelerated weight gain during

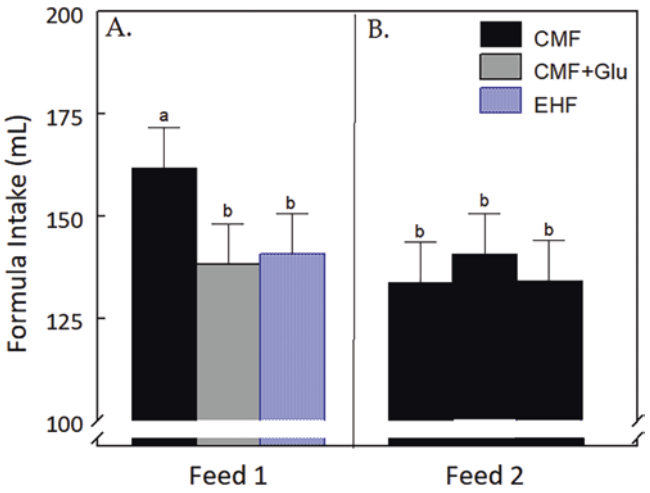

Fig. 6.2 Amount of formula (mL; mean ± SEM) ingested during three separate test sessions that occurred on three separate days. In counterbalanced order, infants were fed CMF (black bars), CMF with added Glu (CMF+ Glu; gray bars), or EHF (blue bars) during the first formula meal (A, Feed 1). Infants were fed CMF alone during the subsequent formula meal (B, Feed 2). Intake during the first formula meal, but not the second, differed across the three testing days. Different superscripts (a, b) indicate significantly different at $P < 0.05$. (Adapted with permission from Ventura et al. (2012b))

the first 4 months due to both lower energy loss and greater energy intake (Mennella et al., 2018). Two of these trials enrolled healthy infants with a family history of atopy (Roche et al., 1993; Rzehak et al., 2009) for the first 4 months (Rzehak et al., 2009) or 6 months (Roche et al., 1993), and two other trials both randomized healthy 2-week-old infants with no history of atopy to feed either EHF or CMF for 8.5 months (Mennella et al., 2011b) or 12 months (Mennella et al., 2018). In the latter trial, while within the range of typically growing infants, body weight-for-length Z scores between CMF- and EHF-fed infants remained significantly different during the first year. Because the World Health Organization standards established the growth of breastfed infants as the norm (WHO Multicentre Growth Reference Study Group, 2006), that the Z scores of infants fed EHF tracked at zero means their growth was similar to that of breastfed infants. Three other trials, each of shorter duration and with fewer subjects, did not report growth differences but did report greater satiation when infants are fed EHF than when fed CMF (Hyams et al., 1995; Vandenplas et al., 1993; Borschel et al., 2014).

Taken together, the experimental evidence reviewed herein reveals that infants respond to differences in the FAA content of their milk, in terms of intake within a meal in the short term. Whether the higher concentrations of free Glu in human milk and EHF (see Table 6.1) are the underlying mechanisms for the more normative weight gain, which is associated with lower risks of obesity in the longer term (Trabulsi et al., 2020; Zheng et al., 2018), is an important area for future research, because early rapid weight gain (Mennella et al., 2011b, 2018; Rzehak et al., 2009)

is a consistent and established risk factor for later obesity and other comorbidities (Zheng et al., 2018; Monteiro & Victora, 2005; Woo Baidal et al., 2016).

6.6 Summary

From an early age, the flavor and metabolic functions of umami taste are evident in humans. Infants are born with the capacity to detect and prefer umami taste, like they do with sweet taste, but only when it is presented in the context of a food, not in plain water, similar to findings in adults. Inherent plasticity is associated with this taste, which interacts with early experience to vary preference based on what infants are fed. Beginning with the first foods, the content of free Glu in amniotic fluid varies during pregnancy, as well as during lactation, and varies by type of infant formula. After birth, those fed human milk or protein hydrolysate formulas will have greater exposure to free Glu than those fed CMF. During early milk feedings, Glu and perhaps other FAAs can modulate satiation in the short term and growth and risks of obesity in the long term (Mennella et al., 2014b). We hypothesize that, because they are unbound, FAAs can be sensed by receptors in both the oral cavity (Chaudhari et al., 2000b) and intestinal and gastric walls (San Gabriel & Uneyama, 2013), likely conferring beneficial physiologic and metabolic effects (Ventura et al., 2012b; Mennella et al., 2011b; Burrin et al., 2008).

Experience with umami continues to evolve as children begin to eat the foods of the table. Like other flavors and tastes, these early feeding experiences "teach" children what foods are safe and what foods are eaten and preferred by their caregivers and family (Mennella et al., 2016b). In general, early experiences change not the taste quality per se but its palatability—a more labile feature of a food that drives eating behaviors and food choice (Mennella et al., 2020).

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