Flavor exposure during sensitive periods of development as a key mechanism of flavor learning: implications for future research

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Sensitive periods are restricted periods of time (ie, specific ages) in development, during which there is a biological display of an extreme neural sensitivity to the storage of experience-driven sensory and probably conceptual information. A period of time is considered to be a sensitive period when the extreme neural sensitivity is not present in other time periods. Furthermore, the neural sensitivity promotes an individualized design of the shape and function of the brain that is specific to the individual’s idiosyncratic environment and which is directed to individual’s survival by safeguarding the normal development (disease-free) of sensory systems and probably of cognitive systems. The main effect of exposure to stimuli during a sensitive period concerns the imprinting effect that these experiences induce in the individual for later stages of life, in the sense that these experiences induce lasting or everlasting changes in the individual’s behavior, and in his or her underlying sensory and neural function.

The origin of study of the sensitive periods of development goes back to the discovery by the Nobel Prize-winning scientists Hubel and Wiesel of a sensitive period, in early postnatal life, for treating strabismus in cats (1). Their findings stimulated further efforts in the study of the role of stimulation in the development of the visual and auditory functions. Consequently, the existence of sensitive periods of functional development during early postnatal life within both of these sensory modalities has been rigorously documented. Indeed, it is well known that there are multiple sensitive periods for different aspects of, and within, each of these sensory modalities. For example, within the visual domain it has been consistently shown that an imbalance in binocular vision due to monocular deprivation during childhood affects visual acuity in humans and causes amblyopia in the affected eye (2). Furthermore, if children suffering from amblyopia are not operated on before they reach puberty, the risk of losing that eye increases significantly (3). Lewis and Maurer (4), in their behavioral longitudinal study, found different sensitive periods, between the ages of 6 and 14 y, for normal development as well as for damage induction and for damage recovery of different aspects of vision, such as visual acuity and peripheral vision.

The development of the human auditory system is affected by experience during sensitive periods in at least 3 ways. First, early auditory experience shapes auditory function, especially with regard to human-inherent speech perception. Kuhl (5) concluded that neonates are able to distinguish between phonemes of different languages during the first year of life and that this ability diminishes with increasing age. Second, early auditory deprivation produces an aberrant subsequent development of auditory function compared with that of normal-hearing subjects (6). Finally, early intervention by means of cochlear implantation favors the rehabilitation of auditory alterations (3), with the critical period for rehabilitation being between the ages of 4 and 6 y (7–9), whereas the opportunity of a full recovery may be lost if cochlear intervention is applied from the age of 7 onward (10).

Compared with the visual and auditory domains, potential sensitive periods of neural sensitivity to gustatory stimuli, such as human flavor learning, have been less studied, which is probably due to the lack of an experimental model to facilitate the examination of the potential existence and features of those sensitive periods. Until now, evidence has indicated that very early experiences with flavors and foods—namely, flavor and food experiences in the prenatal, early postnatal, or young childhood stages of development—induce a gustatory imprinting that is displayed in the reported preferences for sensory stimuli, such as a flavor or food in later stages of life (11–16). Preference for a given flavor and food preference status have correlated with, or have even been attributed to, early exposure to certain flavors or foods, but the specific age or ages during which that gustatory imprinting may occur have remained unknown. However, in this issue of the Journal, Mennella et al (17) present, to the best of our knowledge, the first study aimed at ascertaining the time course of a sensitive period for human acceptance learning of high sour- and bitter-tasting hydrolyzed protein hydrolysate formulas (PHFs) in terms of timing and duration. They controlled the duration of the formula-based exposure and the type of formula infants were offered during the exposure and varied the timing of the PHF-based exposure. All of the infants initially rejected the PHF, but the authors found that, in contrast to infants aged ≥3.5 mo, infants aged at least 1.5 mo but younger than 3.5 mo may learn to accept PHFs if they are exposed to this type of formula.

References

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formula for \( \geq 1 \) mo. The exposure in early infancy thus establishes a potentially long-lasting pattern of eating behavior that is based on acceptance of sour- and bitter-tasting foods, such as vegetables, whose consumption prevents future diseases. To follow on the results presented by Mennella et al (17), is this the only sensitive period available for humans to learn to accept a flavor? Although this issue requires further research, we suspect that the answer might be negative, because the study of visual and auditory learning has indicated the existence of multiple sensitive periods. Furthermore, it also remains unknown whether this is the only sensitive period available for humans to learn to accept the high sour and bitter properties of PHFs and other edibles. Again, we suspect that the answer might be negative given the available data indicating that some of the characteristics of functional plasticity, typically related to developing individuals, may be restored in mature individuals, as has been shown in the visual system of young adult rodents. Indeed, Sale et al (18) showed that exposure to enriched environments may cure amblyopia in young adulthood, even though the typical sensitive period for that recovery in early life is past. This finding implies that there may be another opportunity for amblyopia recovery in later life in cases in which recovery in early life is not possible. Transferability of this finding to the human gustatory function may reveal additional windows of opportunity for establishing healthy food intake patterns, such as in mature individuals who did not learn to accept bitter properties of healthy foods (eg, vegetables) in early life. This is of special relevance, given the evidence that a continued diet that is rich in vegetables favors longevity and a disease-free existence throughout the lifespan (19), which is probably due to the caloric restriction related to diets rich in vegetables (20).

Human acceptance, in terms of intake and preference, of the bitter taste of some healthy foods, such as vegetables, is partially genetically controlled. Specifically, genetic variation in bitter taste sensitivity, derived from the high polymorphism of the taste gene \( \text{TAS2R38} \), explains individual differences in the preference for the bitter taste. Individuals who are genetically sensitive to the bitter taste reject bitter-tasting edibles, such as glucosinolate-containing vegetables, more than do individuals who are genetically bitter insensitive (21). However, as Mennella et al (17) reported, relatively short, repeated exposures to a bitter- and sour-tasting PHF during a sensitive period may change an infant’s initial rejection into a preference for that stimulus. Thus, experience may add to genetic predisposition in controlling acceptance of bitter-tasting edibles. This result leads to the following 2 questions: Would repeated exposure to the PHF during the target sensitive period also shift the hedonic response of infants who are extremely bitter sensitive? Which specific epigenetic modifications of \( \text{TAS2R38} \), in terms of liking and as a function of the individual \( \text{TAS2R38} \) genotype, would be induced by a repeated exposure to bitter-tasting formulas during the target sensitive period? Progress in understanding the development of, and epigenetic pathways to, flavor learning may contribute to strategies for educating the gustatory sense in developing infants by indicating the optimum time for exposure to specific taste stimuli so that preferences for consumption of healthy food might be encouraged.

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REFERENCES