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Human pheromones and food odors: epigenetic influences on the socioaffective nature of evolved behaviors

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Background: Olfactory cues directly link the environment to gene expression. Two types of olfactory cues, food odors and social odors, alter genetically predisposed hormone-mediated activity in the mammalian brain.

Methods: The honeybee is a model organism for understanding the epigenetic link from food odors and social odors to neural networks of the mammalian brain, which ultimately determine human behavior.

Results: Pertinent aspects that extend the honeybee model to human behavior include bottom-up followed by top-down gene, cell, tissue, organ, organ-system, and organism reciprocity; neurophysiological effects of food odors and of sexually dimorphic, species-specific social odors; a model of motor function required for social selection that precedes sexual selection; and hormonal effects that link current neuroscience to social science affects on the development of animal behavior.

Conclusion: As the psychological influence of food odors and social orders is examined in detail, the socioaffective nature of olfactory cues on the biologically based development of sexual preferences across all species that sexually reproduce becomes clearer.

Keywords: *behavior*; *development*; *evolution*; *odors*; *food*; *social*; *sexual*; *epigenetic*; *olfaction*; *pheromones*; *hormones*; *environment*; *animal*; *affect*; *effect*; *neuroscience*

'It is important to remember that the animal perceives erotic odors in a manner analogous to his perception of food odors.' (Bloch, 1933, p. 31)

The gene, cell, tissue, organ, organ-system pathway is a neuroscientifically established link between sensory input and behavior. Marts and Resnick (2007) stress the importance of this pathway in the context of a systems biology approach to pharmacogenomics. Naftolin (1981) stressed its importance to the understanding of sex differences. This pathway is sensitive to conditioning. Sensory input from an organism's environment activates and reactivates the pathway and causes changes in hormone secretion that *condition* hormone-driven behavior.

The evolved interaction between the environment and behavior is exemplified when sensory input epigenetically causes variations in gene expression. From the prenatal stage of mammals until death, this interaction begins with gene activation that mediates long-term effects associated with nutrition (Flagel et al., 2011; Lenroot & Giedd, 2011) and with effects of social experiences on neural networks that generate behavior (Boehm, Zou, & Buck, 2005).

Because all mammals require adequate nutrition (Fowden, Giussani, & Forhead, 2006), relevant sensory signals associated with food odors in mammals can have long-term effects on the brain and behavior (Guesry, 1998; Rosales, Reznick, & Zeisel, 2009). The link to the brain and to sexual behavior from relevant sensory signals associated with *social* experiences (Champagne, 2010; Swaney, Dubose, Curley, & Champagne, in press) can be clarified by comparing the effects of food odors associated with nutrition to the effects of social odors associated with conspecifics.

An epigenetic continuum from microbes to humans: from theory to facts

Among different bacterial species existing in similar environments, DNA uptake (Palchevskiy & Finkel,

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2009) appears to have epigenetically 'fed' interspecies methylation and speciation via conjugation (Fall et al., 2007; Finkel & Kolter, 2001; Friso & Choi, 2002). This indicates that reproduction began with an active nutrient uptake mechanism in heterospecifics and that the mechanism evolved to become symbiogenesis in the conspecifics of asexual organisms (Margulis, 1998). In yeasts, epigenetic changes driven by nutrition might then have led to the creation of novel cell types, which are required at evolutionary advent of sexual reproduction (Jin et al., 2011). These epigenetic changes probably occur across the evolutionary continuum that includes both nutrition-dependent reproduction in unicellular organisms and sexual reproduction in mammals. For example, ingested plant microRNAs influence gene expression across kingdoms (Zhang et al., 2012). In mammals, this epigenetically links what mammals eat to changes in gene expression (McNulty et al., 2011) and to new genes required for the evolutionary development of the mammalian placenta (Lynch, Leclerc, May, & Wagner, 2011) and the human brain (Zhang, Landback, Vibranovski, & Long, 2011).

A gene that codes for the mammalian olfactory receptor, OR7D4, links food odors to human hunger, dietary restraint, and adiposity (Choquette et al., 2012). OR7D4 exemplifies a direct link[1] from human social odors to their perception (Keller, Zhuang, Chi, Vosshall, & Matsunami, 2007) and to unconscious affects[2] on human behavior associated with human olfactory-visual integration (Zhou, Hou, Zhou, & Chen, 2011); human brain activation associated with sexual preferences (Savic, Heden-Blomqvist, & Berglund, 2009), human learned odor hedonics; and motor function (Boulkroune, Wang, March, Walker, & Jacob, 2007). Insect species exemplify one starting point along an evolutionary continuum from microbes to humans that epigenetically links food odors and social odors to multisensory integration and behavior.

Epigenetic effects of food odors and social odors on hormones in insects

Ants (Bonasio et al., 2010) and honeybees (Honeybee Genome Sequencing Consortium, 2006) offer emerging animal models for epigenetic effects on neural networks that are associated with food odors, food selection, social odors, and social selection[3] in mammals. In eusocial insects like the honeybee, these epigenetic effects cause a single genome to give rise to distinct castes.

Honeybee castes (workers, nurses, and queens) are behaviorally differentiated during their development by hormone-mediated programs of gene expression (Evans & Wheeler, 2001). During their development, as well as throughout their adult life, these castes display dramatic physiological, morphological, and behavioral differences.

In honeybees, the genetically predisposed production of the queen's social odors is influenced by what she eats. Her social odors influence transitional stages of larvae. They also influence adults within the hive and outside the hive. Fertile queens, males, and non-reproductive workers with phenotypically distinct brain neuroanatomy and behavior develop from the same genome due to the epigenetic influences of the queen's diet and her social odors, which have far-reaching effects on every organism in the hive (Honeybee Genome Sequencing Consortium, 2006; Lyko et al., 2010).

Although the queen eats only 'royal jelly', other bees gather the food that sustains the hive by responding to the ongoing and ever-changing influences of plant odors and by responding to social odors. Finding nutritious food is a function of hormone-driven individuals learning to also avoid eating toxic food (Wright, 2011). The behavior of bees can be predicted to change with changes in their food supply and with changes in the social odors in their environment.

Epigenetic effects of food odors and social odors on hormones in mammals

The epigenetic effects of food odors and social odors associated (1) with hormones, diet, and nutrition (Wright, 2011) and (2) with the differentiation of hormone-mediated brain neuroanatomy and behavior in the honeybee model (Honeybee Genome Sequencing Consortium, 2006; Lyko et al., 2010) provide a biological basis for extending an animal model of epigenetic effects on hormones and behavior from insects to humans because the molecular biology of cause and effect crosses species boundaries and is exhibited in hormone-mediated affects on behavior.

In mammals, the chemical signals in food odors and social odors also cause hormone-mediated changes in behavior (Le Magnen, 1982, 1998). Food odors associated with nutrition affect the genetically predisposed hormone-mediated development of the brain and food preferences. Social odors, which are associated with conspecifics, affect the genetically predisposed hormone-mediated development of the brain and social preferences.

Social odors: pheromones cause changes in hormones

During interactions among mammalian conspecifics that have variable genotypes and hormone-dependent

[1]This 'direct link' is between the ligand: androstadienone, and the OR7D4 receptor.
[2]'Effect(s)' and 'affect(s)'. In context, sensory input effects hormones that affect behavior. An effect of sensory input on hormones can result in behavioral affects/affects on behavior.
[3]Social selection refers to an organism's ability to interact with other organisms in different social situations (d'Ettorre & Moore, 2008).

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phenotypes, social selection ensures ongoing and repeated exposure to social odors, just as it does in eusocial insects. Social odors, which are commonly known as pheromones[4] in all species (Kohl & Francoeur, 1995/2002; van den Hurk, 2007; van den Hurk, 2011), are species-specific chemical signals that directly register information about the variable genotypes and hormone-dependent phenotypes of conspecifics into the brains of mammals.

In order to directly register information about others in the brain and to link that information to mammalian behavior, electrophysiological activity, gene activation, and the initiation of a hormone response from neurons in the brain (i.e. a neuroendocrine response) are required. Pheromones act on olfactory receptors to elicit electrical activity in neurons (Pick et al., 2009), and the electrophysiological translation of mammalian pheromones from chemical signals to electrical signals allows them to physiologically cause gene activation (Loebrich & Nedivi, 2009). More specifically, Boehm et al. (2005) found that mammalian pheromones cause gene activation in neurons of the brain. These neurons are cells that collectively initiate change in the secretion of gonadotropin releasing hormone (GnRH) from tissue in the brain. The change in GnRH secretion (Stowers & Logan, 2010) is the neuroendocrine response that directly links information about the genotype and hormone-dependent phenotype of one mammal to the brain and behavior of other mammals via the required gene, cell, tissue, organ, organ-system pathway.

The evolved neuroendocrine potential in mammals causes changes in their behavior

The direct electrophysiological effect of pheromones on gene activation and on the neuronal activation of the brain's GnRH-secreting neurons (Boehm et al., 2005), both predicts and defines the role that pheromones play in the hormone-mediated development of mammalian social behavior. Predictably, the interactions among many different neuronal systems allow a neuroendocrine potential for the release of GnRH to build until the right stimulus is experientially present or experimentally applied (Grumbach & Styne, 1992)[5]. The stimulus results in the rapid activation of GnRH-modulated physiological systems (Hofmann, 2010). Gene activation and expression in GnRH neurons (Boehm et al., 2005) is a marker of neuronal activity that shows that these neurons are directly involved in the transmission of signals to other neurons (West & Greenberg, 2011), which process other sensory input associated with odors and pheromones. The effect of pheromones on the expression of early genes in GnRH neurons and on GnRH secretion from these neurons helps to explain the affects of pheromones on behavior because GnRH-secreting nerve cells '... control a wide variety of basic drives, hormone systems, autonomic responses, and instinctive behaviors' (Boehm et al., 2005, p. 690).

Control of behavior in terrestrial mammals

Food odors and pheromones elicit a genetically predisposed hormone response from birth, and this response is linked by GnRH to affects on the behavior of mothers and infants. For example, pheromones associated with lactation and infant nutrition are believed to be responsible for the infant–mother bond (Porter & Winberg, 1999), which makes human pheromones as important to later species-specific social recognition as they are to infant–mother olfactory–visual recognition and bonding in other mammals (Lee, He, & Ma, 2011).

Within minutes of birth, there is also a genetically predisposed, sexually differentiated, GnRH-directed, luteinizing hormone (LH) response in mammalian males, but not in females (Grumbach & Styne, 1992). Activation of the male's LH response involves GnRH (Hoffman, Lee, Attardi, Yann, & Fitzsimmons, 1990), and the GnRH-directed LH response to female pheromones is linked to increased testosterone (T) secretion in the males of many different species (Nyby, 2008).

In mammalian males, the LH response at birth appears to be caused by pheromones associated with food odors emanating from the mother's nipple (Schaal et al., 2009; Schaal, Doucet, Sagot, Hertling, & Soussignan, 2006). Other sensory input and its integration also may be associated with the male's LH and T response throughout life. But the pheromones of a mammalian mother, like those of the honeybee queen, are the only known direct causal link from a sensory stimulus to an immediate hormone response in the brain of male mammals that does not occur with parturition in female mammals.

Sex differences in the effects of pheromones

The GnRH-directed LH and T response in the male is linked to rapid remodeling of the male infant's brain that occurs during the first postnatal 6 months, particularly in areas associated with cognitive tasks, including spatial conceptualization and the emotional processing of visual

[4]Pheromones were first defined as '... substances which are secreted to the outside by an individual and received by a second individual of the same species, in which they release a specific reaction, for example, a definite behaviour, or a developmental process' (Karlson & Luscher, 1959, p. 55). The secretion of these species-specific chemical substances and their transfer between two or more individuals is the basic tenet of pheromonal communication and social selection.

[5]Noradrenergic, dopaminergic, serotoninergic, and opiotergic pathways; inhibitory neurotransmitters (e.g. gamma aminobutyric acid) and excitatory amino acids (e.g. glutamic and aspartic acids); and other brain peptides including pineal secretions (melatonin) and corticotrophin-releasing hormone, and the complex interactions among them are subtle but functional species-specific influences on the electrochemical transmission of neuronal signals that the hypothalamus translates to the chemical signal GnRH.

cues (Sanai et al., 2011). This remodeling of the brain appears to continue throughout life. GnRH and LH cause subsequent changes in levels of other hormones associated with sexual differentiation of the brain and with behavior (see for review, Wizemann & Pardue, 2001). Maternal pheromones that initiate these changes could effectively continue to rewire the developing male brain during the next 6–8 months. This would allow for male and female differences in the developing brain that extend to the next 2–3 years (Sanai et al., 2011).

These effects of pheromones on hormones potentially extend the honeybee model for experiential conditioning of hormone-mediated changes in the honeybee brain to sex differences in the mammalian brain. Affects of pheromones on mammalian behavior incorporate the hypothalamic GnRH pulse generator as the most likely neurophysiological mechanism (Krsmanovic, Hu, Leung, Feng, & Catt, 2009). Positive social interactions associated with pheromones across the organism's lifespan seem to serve as secondary reinforcers that take on the attributes of primary food rewards essential to survival (Jones et al., 2011). Neuroscientifically established reward mechanisms, which have been extensively detailed, link nutrition and social interactions to behavior.

This mammalian model for the development of food preferences and social preferences, which incorporates the effects of nutrition and pheromones on hormones that affect behavior, has clear phylogenetic parsimony. Simply put, throughout the life of individuals, the unique experiences of males and females with food odors and pheromones cause the development of preferences for the physical characteristics of food. These unique experiences also cause preferences for the physical characteristics of potential mates. Females may readily develop the same food preferences as do males, because no evidence suggests that food odors cause changes in the GnRH pulse. But most males and females are genetically predisposed to develop heterosexual preferences for physical characteristics of conspecifics. The difference in the development of sexual preferences in males and females appears to be caused by the sex difference in pheromones and by genetically determined sex differences in the development of the olfactory system (Kang, McCarthy, Cherry, & Baum, 2011), which also appear to be caused by experience-dependent changes in the GnRH pulse.

Linking pheromone production and distribution to behavior across species

The divergence of invertebrate and vertebrate genomes makes it difficult to compare different forms of the GnRH molecule and its receptor across species. However, the gene, cell, tissue, organ, organ-system pathway that links food odors and pheromones to the brain and to behavior does not change from insects to mammals. As their genetically predisposed, nutrition-dependent, GnRH-directed, hormone-mediated, social potential begins to be realized; mammals mature and produce hormone-dependent, species-specific pheromones just as insects do (Stoddart, 1990; van den Hurk, 2011).

The pheromones of mammals further adult social potential via effects on genes in GnRH-secreting neurons of conspecifics. GnRH secretion influences the secretion of other hormones and affects the mammals' social preferences and their sexual preferences (see for review, Kohl, 2007). As it does in the honeybee model for nutrition-dependent pheromones of the queen, this mammalian model of nutrition-dependent pheromones demonstrates a form of reciprocity. In properly nourished mammals, the pheromones of males and females activate gene expression in neurons of one organism, leading to changes in hormones and in pheromone production that activates gene expression in neurons of another organism, albeit in the absence of a queen, castes, or stereotypical insect behaviors.

Brain development and behavior

In mammals, the more broadly demonstrable and less stereotypical pheromone-driven behaviors are not limited by the tightly controlled social structure of insect colonies. A more developed mammalian brain probably also helps to ensure behavioral diversity. An evolutionary continuum ensures that, in well-nourished mammals that mature sexually, pheromones cause gene expression in hormone-secreting neurons of tissue in the brain. Changes in behavior are required in order for organisms to seek out food odors and pheromones that cause changes in gene expression in hormone-secreting neurons, and those changes in gene expression during an organism's development are required in order for individuals and species to survive.

This reciprocity between brain development and behavior in insects and in mammals better defines the term epigenetic, using all the links in a sequence of events from stimulus to gene activation and expression to neural activity to behavior and back out again (Alaux, Maisonnasse, & Le Conte, 2010; Bell & Robinson, 2011; Grozinger, Sharabash, Whitfield, & Robinson, 2003). The most sought-after sensory stimuli in any species that reproduces sexually are food odors and pheromones. Reciprocity can be represented as a sensory stimuli seeking organ system found in animal species from invertebrates to mammals that seek satiation via hormone-mediated affects on conditioned behaviors. The organ systems of all organisms seek satiation associated with sensory stimuli throughout life.

Reciprocity involving pheromones

In mammals, the neurophysiological and behavioral reciprocity that is required for sexual reproduction is

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perhaps best demonstrated via the link from pheromones to LH. Mammalian pheromones directly alter the secretion of GnRH, which is required for LH secretion (Hoffman et al., 1990). LH secretion indicates that nutritional needs have been met (Caronia et al., 2011). LH is also an important indicator of fertility (Brodin, Bergh, Berglund, Hadziosmanovic, & Holte, 2009) and of steroid hormone-mediated mammalian brain development (Dugger, Morris, Jordan, & Breedlove, 2008). This brain development includes LH-driven changes in ratios of white:gray matter (Peper et al., 2008) as well as pheromone-driven, LH-mediated neurogenesis in the hippocampus (Lau, Yau, & So, 2011; Mak et al., 2007; Peper et al., 2010). All the aforementioned epigenetic links to the social environment and to sexual behavior are reciprocal and are associated with nutrition (Speder, Liu, & Brand, 2011) and with learning and memory via hippocampal neurogenesis.

The LH-mediated development of neuroendocrine and neuroanatomical differences is also consistently linked to differences in social behavior and sexual behavior. Specific genes and their protein products have been linked to GnRH-dependent LH secretion (Wu et al., 2011), to fertility, and to the sense of smell (Mitchell, Dwyer, Pitteloud, & Quinton, 2011; Silveira, Trarbach, & Latronico, 2010). Fertility, reproduction, and a number of other functions in vertebrates are dependent on the pituitary synthesis and secretion of LH (Roch, Busby, & Sherwood, 2011). Decline in olfactory acuity and specificity has been linked to aging and to neurodegenerative diseases such as Alzheimer's (Cheng, Cai, & Belluscio, 2011).

A bottom-up/top-down reward mechanism

Further evidence for consideration of the gene, cell, tissue, organ, organ-system pathway that links odors directly to hormones and behavior comes from studies of affective neuroscience. An accumulation of evidence now indicates that genetically predisposed, instinctual, unconditioned, emotional behaviors and feelings emanate from homologous brain functions in all mammals (Panksepp, 2011). This evidence emphasizes the need to demonstrate the reciprocity of the gene, cell, tissue, organ, organ-system pathway in models of human behavior.

The homologous brain functions involved in human behavior appear to be regulated by higher brain regions, but the molecular basis of their neurophysiological interactions can be readily compared to insects like the honeybee. For example, as mentioned above, food choice in foraging honeybees is mediated by hormones (Wright et al., 2010). These hormones, serotonin and dopamine, function as neurotransmitters in mammals, and they have been linked to the control of hunger, depression, anxiety, obsessions, physical activity, reward mechanisms, and eating disorders such as anorexia and bulimia in women (Bailer et al., 2011, 2012). Serotonin and dopamine are known to be involved in the interactions among hormones and neurotransmitters that cause changes in the secretion of GnRH in mammals (Grumbach & Styne, 1992; Wada et al., 2006).

It is becoming clearer that the primary emotional functions of affective processing associated with the gene, cell, tissue, organ, organ-system pathway and with food acquisition are the foundation for secondary-process learning and memory mechanisms, which interface with tertiary-process cognitive-thoughtful functions and behavior (Panksepp, 2011). This is demonstrable in the following bottom-up sequence: (1) food odors and pheromones; (2) GnRH; (3) LH; (4) steroidogenesis and feedback; (5) white matter/gray matter development; (6) hippocampal neurogenesis; (7) learning and memory; and (8) behavior.

Behaviors associated with the neurophysiological rewards of food acquisition and reproduction typically reactivate the sequence that conditions the hormonal responses and behavioral affects that are associated with food odors and pheromones. This relatively simplistic representation of an 8-stage sequence incorporates the gene, cell, tissue, organ, organ-system pathway that links sensory input to behavior. It also allows for consideration of how higher and lower levels of control participate in the regulation of the organism via its affective experiences, which may not involve any cognitive-thoughtful functions (Kohl, Atzmueller, Fink, & Grammer, 2001).

Affective disorders might best be approached using the same pathway. As is the case with honeybees and in other animal models, cognition is not required to decode the neurophysiological activity of primal affective experiences. Instead, these primal affective experiences are directly associated with reciprocal relationships involving food odors and pheromones in all animal species. They are only indirectly, if ever, associated with human cognition. Typically, humans are among the animals that do not consciously process the effect of food odors on hormones and their behavior, and it is even rarer for people to think about the effect of pheromones on hormones and their affect on behavior. But it seems that even without thought, food odors and pheromones are primarily responsible for hormone-driven, unconscious affects on the behavior of other animals and on human behavior.

'Neural networks' in beehives and mammalian brains: looking both ways (back or forward)

Conditioned hormonal and behavioral responses to odors associated with food selection and conspecifics in mammals require something like the collective 'neural networks' of beehives. Philosophically and metaphorically, these neural networks extend to mammalian brains.

The concept that is extended is the epigenetic tweaking of immense gene networks in 'superorganisms' (Lockett, Kucharski, & Maleszka, 2012) that 'solve problems through the exchange and the selective cancellation and modification of signals (Bear, 2004, p. 330)'. It is now clearer how an environmental drive probably evolved from that of food ingestion in unicellular organisms to that of socialization in insects. It is also clear that, in mammals, food odors and pheromones cause changes in hormones such as LH, which has developmental affects on sexual behavior in nutrient-dependent, reproductively fit individuals across species of vertebrates.

The original environmental drive of food odors and their effect on LH shares remarkable homology with the function of a sex pheromone in yeast that links pheromones to LH and to reproductive fitness via nutrition in mammals (Maeda et al., 2010). The fact that the sex pheromone of a yeast species elicits an LH response from the cultured pituitary cells of a mammal (Loumaye, Thorner, & Catt, 1982) exemplifies an evolutionary continuum across species. The effect of sex pheromones on GnRH in mammals links them to LH and to sexual selection for other sensory signals of reproductive fitness. This homology from yeasts to mammals also differentiates the similar effects of food odors on hormones across *some* species from the species-specific behavioral affects of sex differences in pheromones in all species that sexually reproduce (Kohl, 2007).

Physiopathology or genetically predisposed variability in the effects of food odors and pheromones on hormones and behavior?

The same pathway that links food odors and pheromones to hormones and behavior is well known to be involved in the physiopathology of systemic diseases. In mammals, this pathway to behavior is epigenetically linked to genetic predispositions for proper nutrition and to shaping of different adult phenotypes. Fowden et al. (2006) provide examples of what can go wrong with nutritional influences at each step: gene, cell, tissue, and organ. They list errors directly associated with intrauterine and postnatal nutrition that can result in the systemic physiopathology of diabetes and hypertension in rats and indicate that results of these epigenetic effects extend to people.

The FDA Critical Path Initiative

Given the importance of understanding how food odors and nutrition epigenetically influence individual survival in other mammals, it is not surprising that a reiteration of the 'FDA Critical Path Initiative' (Marts & Resnick, 2007) stresses the need to approach the development of human sexual behavior, which is required for our species survival and beneficial to human well-being, by using the same pathway that links food odors and pheromones to the behavior of honeybees and humans.

Including the interactions among the gene, cell, tissue, organ, organ-system pathway (Wizemann & Pardue, 2001) allows sexual differentiation of the brain and behavior to be detailed in the manner that was suggested by Diamond, Binstock, and Kohl (1996) and more recently by McCarthy and Arnold (2011). These details are in obvious accord with what has been neuroscientifically known for several decades about organization and activation of the brain and behavior (Naftolin, 1981). Neuroscientists can now incorporate the role of epigenetic influences of food odors and pheromones, as well as *in utero* effects of endocrine disruptors on GnRH (Wolstenholme, Rissman, & Connelly, 2011) and on mate choice (Jasarevic et al., 2011). For example, endocrine disruptors and pheromones may act on species-specific and sex-specific GnRH feedback pathways to alter the estrous cycle and alter pubertal onset via changes in gene expression that result in significant physiological and behavioral changes throughout life (Cao, Mickens, McCaffrey, Leyrer, & Patisaul, 2011).

Theory revisited

Indeed, researchers can speculate that dietary differences in primate species alter the production of dehydroepiandrosterone sulfate (DHEAS) in a manner similar to what we think occurs with endocrine disruptors (Harris & Waring, 2008). This could have a significant impact on the metabolism of DHEAS, which appears to be the precursor to primate-specific ratios of specific metabolites of steroid hormones such as androsterone (A) and etiocholanolone (E). The A/E ratio is a measure of individual physical fitness in men (Aguilera et al., 2009) and has been linked to sexual preferences (Margolese & Janiger, 1973). Less speculation is required with regard to the effects of endocrine disruptors on GnRH, the effects of plant odors on the hormone estradiol in women (Fukui, Toyoshima, & Komaki, 2011), and the effect of pheromones on hormones associated with mate choice. Collectively, effects on hormones help to extend animal models of food selection and social selection to sexual selection because they involve the same pathway. In theory, this GnRH-directed neurophysiological pathway may be the FDA's 'Critical Path', which is recommended for crucial consideration in the development of new therapeutic drugs. In fact, it incorporates the hypothalamic GnRH pulse as the epigenetically effected neurophysiological mechanism that links the effects of food odors and pheromones to the secretion of other hormones and to the affects of many different hormones on behavior.

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Integration of olfactory/pheromonal conditioning into clinical psychology: The American Society of Addiction Medicine (ASAM) policy statement

The Public Policy Statement: Definition of Addiction (ASAM, 2011) represents a paradigm shift that may move the current practice of clinical psychology forward. It dictates the adoption and integration of neuroscientific principles that are required in order to understand differences between genetically predisposed brain disease, naturally occurring variations of behavioral development, and choice. These neuroscientific principles include focus on how sensory input influences behavior. The statement specifically mentions food and sex along with drugs and alcohol; each seems to chemically condition changes in hormones and in behavioral responses. Although no link between cause and effect is mentioned by ASAM, these principles could incorporate the GnRH neurophysiological mechanism and levels of LH, which link food odors and pheromones to chemically conditioned behaviors.

Medical practitioners from ASAM and neuroscientists are more likely than psychologists to be aware that effective FDA-approved therapeutic intervention frequently involves pharmaceuticals that alter feedback on the GnRH neuronal system (Grumbach & Styne, 1992), which is the central neuronal system that is essential to species survival in all vertebrates (Kotitschke, Sadie-Van Gijsen, Avenant, Fernandes, & Hapgood, 2009) *via* its integral involvement in the acquisition of food and in sexual reproduction. ASAM seems to think that clinical psychologists should become more aware of currently accepted neuroscientific facts, which may be important to their understanding of eating disorders and of human sexuality among other things that are not currently understood about the development of behavior.

For example, a prominent sensory psychologist recently made the surprising claim in his book that mammalian pheromones do not exist (Doty, 2010). In contrast, another recent book reviews the latest information on pheromones across species including mammals (van den Hurk, 2011). Clearly, as ASAM indicates, there may even be sensory psychologists who specialize in olfaction, but who are unfamiliar with the neuroscientific facts about food odors and pheromones. Dr. Richard L. Doty, for example, claims that mammals are not like insects when it comes to their response to pheromones, but he ignores the obvious similarities in molecular biology across species. In contrast, Lockett et al. (2012) address the likelihood '... that honey bee colonies accumulate specific DNA methylation patterns with time, in much the same way as do human individuals ...', and their data '... support the honey bee superorganism metaphor extending to the molecular level ...'. Understanding the molecular biology of behavior across species seems to be essential to progress in socioaffective neuroscience.

Socioaffective neuroscience: extending an insect model to humans

The honeybee already serves as a model organism for studying human immunity, disease resistance, allergic reaction, circadian rhythms, antibiotic resistance, the development of the brain and behavior, mental health, longevity, and diseases of the X chromosome (Honeybee Genome Sequencing Consortium, 2006). Included among these different aspects of eusocial species survival are learning and memory, as well as conditioned responses to sensory stimuli (Maleszka, 2008; Menzel, 1983).

In the absence of misleading terms and semantic arguments about what pheromones are (Wysocki & Preti, 2004), food odors and pheromones are simply the chemical signals that epigenetically influence genetically predisposed behavior by influencing hormones. Without their hormonal effects on neural networks of brain circuitry, no species of insect or mammal could survive.

Just as the influence of diet and pheromones can be in the larval stages or in other developmental stages of insects, it can also be in the pre- and postconception stages of mammals, including humans (Fowden et al., 2006; Mennella, Jagnow, & Beauchamp, 2001). For example, pheromones and nutrition could alter levels of maternal hormones, gestational events, and postnatal outcomes *via* their direct effect on maternal GnRH and the placenta. The outcomes might not always be positive, which means the possible effects should not be ignored. That would be like ignoring the likely effects of docosahexaenoic acid in the maternal and postnatal diet on LH and on neuronal development in the mammalian brain (Lassek & Gaulin, 2011).

Conclusion

New data on how genetic predispositions are epigenetically linked to phenotypically distinct neuroanatomy and behaviors is provided in the honeybee model. Across-species comparisons from insects to vertebrates clearly show that the epigenetic influence of food odors and pheromones continues throughout the life of organisms that collectively survive whereas individuals do not. These comparisons also attest to the relative salience of sensory input from the rearing environment. For example, when viewed from the consistency of animal models and conditioned behaviors, food odors are obviously more important to food selection than is our visual perception of food. Animal models affirm that food odor makes food either appealing or unappealing. Animal models reaffirm that it is the pheromones of other animals that makes them either appealing or unappealing.

Socioaffective neuroscience and psychology may progress more quickly by keeping these apparent facts in mind: Olfaction and odor receptors provide a clear evolutionary trail that can be followed from unicellular

organisms to insects to humans (Keller et al., 2007; Kohl, 2007; Villarreal, 2009; Vosshall, Wong, & Axel, 2000).

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