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Review

Honey bees as a model for understanding mechanisms of life history transitions

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Abstract

As honey bee workers switch from in-hive tasks to foraging, they undergo transition from constant exposure to the controlled homogenous physical and sensory environment of the hive to prolonged diurnal exposures to a far more heterogeneous environment outside the hive. The switch from hive work to foraging offers an opportunity for the integrative study of the physiological and genetic mechanisms that produce the behavioral plasticity required for major life history transitions. Although such transitions have been studied in a number of animals, currently there is no model system where the evolution, development, physiology, molecular biology, neurobiology and behavior of such a transition can *all* be studied in the same organism *in its natural habitat*. With a large literature covering its evolution, behavior and physiology (plus the recent sequencing of the honey bee genome), the honey bee is uniquely suited to integrative studies of the mechanisms of behavior. In this review we discuss the physiological and genetic mechanisms of this behavioral transition, which include large scale changes in hormonal activity, metabolism, flight ability, circadian rhythms, sensory perception and processing, neural architecture, learning ability, memory and gene expression.
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Keywords: Honey bees; *Apis mellifera*; Behavioral development; Diurnality; Flight metabolism; Thermotolerance; Sensory function

Contents

1. Introduction

Honey bees (*Apis mellifera*) are oviparous, holometabolous insects that live in large colonies usually containing one queen and her progeny, some 20,000–40,000 female workers and 200–300 male drones. Honey bees are

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haplodiploid. Females, queens and workers, arise from fertilized (diploid) eggs laid by the queen. Diploid eggs become queens or workers depending on which cell they are laid in and whether the resulting larvae are fed royal jelly or worker jelly by the bees performing brood care. In contrast, males arise from haploid unfertilized eggs. Male and female larvae undergo a series of larval stages followed by pupation and a full metamorphosis within a cell in the honeycomb. Emerging from the cell as fully formed adult bees, female workers undergo a form of behavioral development termed "temporal polyethism", moving through a series of behaviorally defined life history stages in an age-related fashion (see Fig. 1, adapted from Winston, 1987). Bees perform several different tasks in the hive during the first 2–3 weeks of adult life, including brood care ("nursing") and hive maintenance, and then shift to foraging for nectar and pollen outside the hive for the remainder of their 5- to 7-week life (reviewed in Winston, 1987).

Unlike behavioral development in most animals, movement through these behaviors is exceedingly plastic. In response to the social context and colony needs the individual bees may increase or decrease their rate of development and even return to previous behavioral stages. For example, in colonies deficient in nurses, young bees will continue to tend brood rather than switch to outside tasks (Robinson et al., 1989; Huang and Robinson, 1999). Similarly, in colonies completely lacking young bees, older bees that would normally be foragers often revert to nursing behavior ("reverted nurses"). The effect of colony demography on foraging behavior appears to be due to social inhibition (Huang and Robinson, 1992). Older foraging bees emit ethyl oleate, a component of brood pheromone, which inhibits foraging by younger workers (Leoncini et al., 2004a,b; Pankiw, 2004). In colonies that lack a normal cohort of older foraging bees, younger bees begin to forage precociously—as early as 5 days of age (Huang and Robinson, 1992; Robinson et al., 1989). When normal age foragers are transplanted into a colony containing only young bees, precocious development of foraging does not occur (Huang and Robinson, 1992).

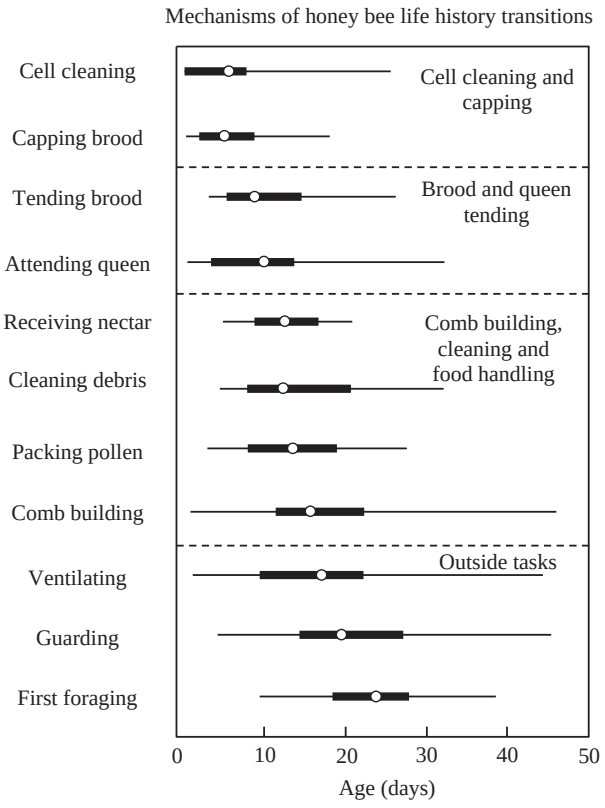

Fig. 1. Age-related task performance (temporal polytheism) by worker honey bees (adapted from Winston, 1987). Workers normally perform tasks inside the colony during early adulthood, and transition to outside tasks as they age. The age at which specific tasks are performed is variable among bees and colonies and subject to genetic background, social interactions, resource availability and other environmental influences (see text).

Juvenile hormone (JH) appears to pace the rate of behavioral development. Although JH treatment can accelerate the hive worker–forager transition, this effect requires several days suggesting JH does not activate the behavior (Elekonich and Robinson, 2000). Furthermore, JH is not required for foraging behavior. Workers lacking JH following removal of the corpora allata (the sole source of JH) on the first day of adult life still become foragers but at older ages and this delay is eliminated with hormone replacement (Sullivan et al., 2000). Adult behavioral development also varies with a colony's genetic background and is sensitive to factors such as weather, season, parasite infestation and colony nutritional status (Kolmes and Winston, 1988; Page et al., 1992; Giray and Robinson, 1994; Huang and Robinson, 1995; Schulz et al., 1998; Giray et al., 1999; Janmaat and Winston, 2000).

As honey bees switch from in-hive tasks to foraging, they undergo transition from constant exposure to the controlled homogenous physical and sensory environment of the hive to prolonged periods in a far more heterogenous environment outside the hive. Within the hive there is little light and the workers actively keep the temperature at 33–35 °C and the humidity near 70% (Winston, 1987). Foraging outside the hive occurs at air temperatures between 10 and 50 °C (Heinrich, 1993) and exposes workers to wind, rain and increased predation. The physiology of honey bees changes as they age and move from non-flying tasks in the hive to foraging, which imparts a suite of different functional demands and energetic requirements. For example, hypopharyngeal glands regress and produce enzymes for processing nectar instead of brood food, body mass decreases, body water content increases and, as we describe in detail below, juvenile hormone levels, metabolic and flight capacity increases (Fluri et al., 1982; Harrison, 1986; Winston, 1987; Huang et al., 1994; Ohashi et al., 1996, 1999; Pontoh and Low, 2002; Robinson and Vargo, 1997). In addition, more complex spatial and sensory information than that encountered in the hive must be integrated to successfully forage (Capaldi et al., 1999, 2000).

2. Honey bees as a model system

The switch from hive work to foraging in honey bee workers offers a valuable opportunity for the integrative study of physiological and genetic mechanisms that produce behavioral shifts and responses to novel ecological challenges. Such an approach is possible only through the study of model systems that simultaneously (a) are the focus of large interactive research communities with basic and applied perspectives, (b) have well-described ecologies, natural behaviors and phylogenies, (c) are well-characterized with respect to natural genetic variation, associated phenotypic variation, and the evolutionary forces maintaining such variation and (d) possess genomes that are sequenced and are (along with their encoded proteins) experimentally tractable (Feder and Mitchell-Olds, 2003). At present, few model organisms satisfy all these demanding criteria because most have yielded genetic and physiological findings without an understanding of their behavior in an ecological-evolutionary context or vice versa. However, the honey bee is among these few exceptions as its evolution, behavior, physiology and genetics are each well represented in an abundant literature (>5000 references) on this species.

A critical manipulation to discriminate age vs. behavioral effects during honey bee behavioral development is the use of single-cohort colonies (SCCs), which induces precocious foraging (Giray and Robinson, 1994; Huang and Robinson, 1992; Robinson et al., 1989). SCCs made entirely of newly emerged bees use skewed colony age demography to dissociate worker age and behavior. The lack of older workers in the hive causes about 10% of the bees in a single cohort colony to forage precociously-usually at 7–10 days of age (Huang and Robinson, 1992, 1996; Schulz et al., 1998). In a typical colony older bees work outside the hive as foragers while younger bees would work inside the hive, while foragers and hive workers are the same age in a SCC. Critically, SCCs allow the observation and collection of same-aged bees performing different tasks. SCCs initially yield young (precocious) foragers and young (typical age) hive bees, and after a few weeks, old (typical age) foragers and old (over-aged) hive bees (see Fig. 2A). If all of the bees caring for brood in the hive are removed, a percentage of the members of the foraging force will revert to hive tasks

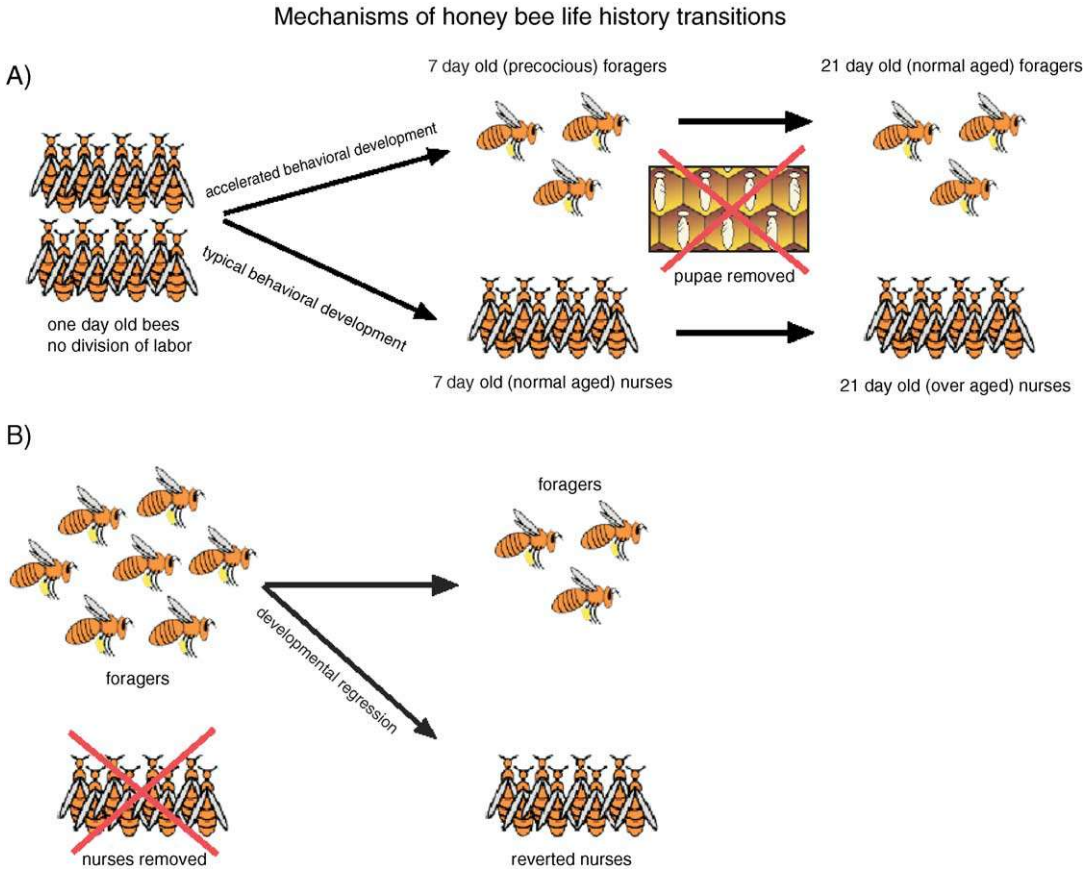

Fig. 2. Behavioral development in a Single Cohort Colony (SCC). (A) In a typical SCC, the colony is established with all newly emerged bees (1 day post-emergence). About 10% undergo accelerated behavioral development thus decoupling the connection between age and behavior. This allows observation of young (normal age) nurses and young (precocious) foragers and later, if no additional cohorts are allowed to emerge, old (over-aged) nurses and old (normal aged) foragers. (B) Reversion SCC, from which the nurses are removed causing some foragers to return to caring for brood. This allows collection of age-matched bees that have foraged but have returned to an earlier stage (nurses) and foragers.

including brood care (now a "reversion colony"). These individuals have been foragers and are the same age as the colony's foragers but now are behaviorally and physiologically at an earlier developmental stage (see Fig. 2B).

In addition to SCCs, honey bee researchers have developed a number of other manipulations which increase the usefulness of the honey bee as a model system sensu Feder and Mitchell-Olds (2003). The best known of these is the training of bees to specific feeding stations, individual markings and observation hives as used by von Frisch (1964) and his students in his Nobel Prize winning work on the honey bee dance language. Using cohorts of known age bees, as for a SCC described above, researchers can set up colonies with specific multiple-aged cohorts (reviewed in Huang and Robinson, 1999) to look at the role of age in socially mediated effects on behavior and physiology. As is the case for many other animals, honey bees can be cross-fostered (e.g. Pankiw et al., 2002) to separate the role of genotype from that of developmental environment. Colonies containing adult workers of mixed genotypes can also be made to investigate the genotypic influences on any number of individual and colony traits (e.g. Page et al., 1992, 2000). Physical characters of bee colonies can be manipulated in many ways to facilitate data collection such as adding modified entrances to remove pollen (e.g. Todd and Bishop, 1940), collect dead bees (e.g. Gary and Lorenzen, 1984), manipulate flight distance, or mark and/or capture bees individuals as they leave or return (e.g. Capaldi et al., 2000). Colonies with an entrance modification which allows regular workers but not larger "big-backed" workers with attached raised tags that increase their size to pass can keep some members of a group from flying to test the role of flight activity in physiology, neurobiology or subsequent behavior (e.g. Withers et al., 1995). The role of the queen and her pheromone secretions have been investigated using colonies where the queen's geneotype differs from that of the workers or where the queen is removed and her presence simulated with pheromone (e.g. Slessor et al., 1988). Additionally, bee behavior and physiology has been manipulated with numerous pharmacological treatments (eg. Ben-Shahar et al., 2003), pheromones (e.g. Grozinger et al., 2003, also see below) and other odors (e.g. Wright and Smith, 2004).

3. Diurnality

The onset of foraging also marks a transition from relatively constant arrhythmic activity to diurnal activity patterns. At night, foragers enter a sleep-like state in the hive (Kaiser and Steiner-Kaiser, 1983; Sauer et al., 2003) and in a sense make the transition between a homogenous and heterogenous environment each day. As worker bees age, they develop a circadian rhythm (Stussi and Harmelin, 1966; Toma et al., 2000) but their behavioral rhythms are task-dependent. Workers who are caring for brood work around-the-clock while workers who forage only work during the day (Moore et al., 1998). These behavioral rhythms are socially mediated-reverted nurses loose their behavioral rhythmicity (Bloch and Robinson, 2001). Honey bee circadian rhythms are entrained by cycles of both light and temperature and act to coordinate foraging behavior with appropriate flight temperatures, sun compass navigation and the timing of visits to specific floral sources with nectar availability (reviewed in Moore, 2001). Foraging age bees are positively phototactic. Phototaxis is modulated by the honey bee *foraging* gene (*Amfor*) which encodes a cGMP dependent protein kinase (PKG). Increases in PKG activity cause precocious foraging and are correlated with increases in positive phototactic behavior (Ben-Shahar et al., 2003). Like other animals, honey bee circadian rhythms are influenced by *Period* gene expression in the brain (Toma et al., 2000; Bloch et al., 2003). However, the mechanism underlying the plasticity in behavioral rhythms and its relationship to the circadian rhythm is unknown (Bloch and Robinson, 2001).

Circadian rhythms may also be important for the physiological support of foraging behavior. JH titers in foraging bees are consistently higher than those of bees working in the hive, even on their first foraging flight (Jassim et al., 2000; Elekonich et al., 2001). Increased JH titer causes degeneration of the hypopharyngeal glands and a shift from producing brood food to production of alpha-glucosidase, amylase and glucose oxidase, the enzymes needed to process nectar into honey (Winston, 1987; Kubo et al., 1996; Ohashi et al., 1999). High JH titers also promote degradation of the fat body and consequent decreases in hemolymph vitellogenin, the most common storage protein in the hemolymph (Fluri et al., 1982). As brood food is highly proteinaceous, decreases in fat body and vitellogenin levels further mark the switch from a bee well suited to caring for young to a bee well suited for flying, carrying heavy loads (in relation to body size), and processing nectar. In addition, there is a diurnal rhythm in JH titer in foragers that is not present in pre-adult bees (Elekonich et al., 2001; Elekonich and Robinson, unpublished data). Interestingly, the timing of the diurnal peaks in JH titer match the timing of the peaks in *period* mRNA expression with the highest titers during the mid-subjective night (Toma et al., 2000; Elekonich et al., 2001). However, it appears that JH titer does not influence diurnal locomotor activity as allactectomy has no effect on circadian locomotor rhythm, nor does treatment of young bees with methoprene, a JH analog, accelerate the onset of circadian behavior (Bloch et al., 2002).

It may be that the high titers and diurnal rhythms of JH support foraging physiology directly. In other insects, JH affects muscle properties directly influencing muscle maturation (Rose et al., 2001) and initiating muscle degeneration and ovarian development in post-dispersing insects in preparation for reproduction (reviewed in Dingle and Winchell, 1997). For example, *Gyrllus firmus* females from

the flight-capable morph (which possess fully developed flight muscles) show a large-amplitude daily cycle in JH, while females from the flightless morphs (which possess underdeveloped flight muscles) have a much smaller amplitude JH cycle (Zhao and Zera, 2004). In addition, JH treatment of flight-capable females induces ovarian growth and muscle histolysis (Zera and Cisper, 2001). JH also effects both cellular and whole animal metabolism. JH treatment increases cytochrome oxidase activity and mitochondrial protein synthesis in a cell line derived from *Drosophila* (Stepien et al., 1988). Allatectomized honey bee foragers have lower metabolic rates and are flight deficient compared to controls. However, this difference is abolished with methoprene treatment (Sullivan et al., 2003).

4. Metabolism and flight capacity

Adult honey bees go from being unable to fly during the first day following eclosion to generating spectacular rates of metabolism and aerodynamic power (up to 0.8 W g^{-1} and 0.2 W g^{-1}, respectively; Roberts and Harrison, 1999) that enable later work outside the hive, traveling up to 8 km from the hive and carrying loads nearly equivalent to their body mass during foraging and undertaking (removal of dead individuals from the hive). The development of flight ability generally occurs in two distinct periods, the first being the 3–4 days following eclosion and the second typically at 14–21 days post-eclosion during the transition from hive work to foraging. Day-old bees that are physically agitated (a manipulation generally assumed to induce maximal metabolic capacity) can generate metabolic rates of only 0.1 W g^{-1} and are isothermic with the surrounding air. Hovering 2-day-old bees have metabolic rates approaching 0.3 W g^{-1} and have an increased ability to raise their muscle temperatures above that of the surrounding environment; coincident with the increase in metabolic capacity of young bees are dramatic increases in thoracic pyruvate kinase and citrate synthase activities as well as thoracic glycogen levels (Neukirch, 1982; Harrison, 1986; Moritz, 1988; Fewell and Harrison, 2001; Harrison and Fewell, 2002). Flight metabolic rates, thoracic enzyme levels and thoracic glycogen levels remain relatively constant over the 1–3 week period when the bees work within the hive. Then, at the onset of foraging, there is an approximate 15% increase in agitated flight metabolic rate, coincident with an approximate doubling of thoracic glycogen levels (Harrison, 1986; Fewell and Harrison, 2001). Cytochrome concentrations of honey bee flight muscle also increase by an order of magnitude from 1 to 20 days after eclosion (Herold and Borei, 1963).

Structural and regulatory proteins of the flight muscle may also be changing as honey bees age and transition to flight-dependent behaviors. For example, honey bees express different troponin-T (TnT) isoforms in their thoraces at 1-day vs. 5-day post-eclosion (Domingo et al., 1998), suggesting that calcium-dependent regulation of muscle contraction is altered in an age-specific manner consistent with the acquisition of functional flight capability. Likewise, the mixture of TnT isoforms also changes during maturation of the flight muscles of the dragonfly *Libellula pulchella*, with correlated changes in calcium sensitivity of muscle activation, twitch contraction kinetics and other indices of aerodynamic power output during free flight (Fitzhugh and Marden, 1997; Marden et al., 1999, 2001).

The development of flight and metabolic capacity in honey bees is also influenced by circulating juvenile hormone (JH) levels, which rise before the onset of foraging (Jassim et al., 2000; Elekonich et al., 2001) and typically are much higher in foragers compared with nurses (reviewed by Bloch et al., 2002). Allatectomized honey bees still become foragers, but at an older age than intact bees. Treatment with the JH analog methoprene after allatectomy eliminates this delay (Sullivan et al., 2000). Hence, JH does not activate foraging, but rather influences the pace at which honey bees develop into foragers. Mortality during the first orientation flight of foragers is higher in allatectomized honey bees than in sham and untreated honey bees (Sullivan et al., 2000, 2003). Furthermore, allatectomized honey bees have significantly reduced groundspeeds during orientation flights, decreased flight ability and lower flight metabolic rates relative to sham and untreated honey bees (Sullivan et al., 2003).

5. Thermotolerance

Honey bees foragers regularly experience air temperatures above and below those maintained in the hive, and utilize several physiological mechanisms that allow them to regulate their flight muscle temperatures between 36 and 46 °C, the range permitting maximal flight muscle force production (Coelho, 1991). For example, honey bees elevate metabolic heat production during flight in cold air temperatures by increasing their wingbeat frequency (Harrison et al., 1996; Roberts and Harrison, 1999) and dissipate excess heat during flight in hot temperatures by evaporation (Heinrich, 1980; Roberts and Harrison, 1999). When foragers are outside of the hive but not flying, they maintain flight muscle temperatures by regulating shivering thermogenesis, a tetanic contraction of the flight muscles against a skeletal stop (Esch et al., 1991; Goller and Esch, 1991).

At the cellular level, muscle proteins and resultant function are protected from heat-damage in part by the expression of the heat shock proteins (Hsps) which are highly-conserved molecular chaperones that participate in the maturation, maintenance, and degradation of diverse proteins in both unstressed and stressed cells (Parsell and Lindquist, 1993; Feder and Hofmann, 1999; Gething, 1997; Morimoto et al., 1994). Like almost all organisms, honey bees increase Hsp expression in response to high temperatures, but have a higher Hsp induction temperature than

isothermic insects such as *Drosophila* (Severson et al., 1990; Elekonich and Robinson, unpublished). The normal hive temperatures of 33–35 °C do not cause elevated levels of *hsp70* mRNA in honey bees, but does induce Hsp expression and cause high mortality in *Drosophila* (Krebs and Feder, 1997a). Honey bees held at 43 °C for 4 h exhibit highly elevated levels of *hsp70* mRNA in their brains and experience no mortality (Elekonich and Robinson, unpublished). Similar and potentially higher expression may be expected in the flight muscles, which can reach 49 °C during foraging at very high air temperatures (Cooper et al., 1985; Coelho, 1991; Roberts and Harrison, 1999; Stabentheiner et al., 2002).

Hsp70 protein levels vary with tissue type in heat-stressed *Drosophila* (Krebs and Feder, 1997b; Michaud et al., 1997). Likewise, honey bee foragers returning from a trip express greater amounts of Hsps in their thoraces relative to nurse bees, yet there is no significant difference in head Hsp70 expression between the two groups (Roberts and Elekonich, in press). One explanation for this result is that foragers have hotter thoraces, but not heads, than hive bees. While this is true in some circumstances (Stabentheiner, 2001; Stabentheiner et al., 2003), another possible explanation for elevated levels of expression in forager thoraces is that elevated Hsp70 expression is necessary to assist protein degradation, repair, maturation and replacement needed by the heavily taxed forager flight muscles (conservatively estimated to contract over 4 million times per day based on 5 h of flight per day and 240 wingbeats per second; Winston, 1987; Harrison et al., 1996). Over-expression of Hsp70 in mouse skeletal muscle similarly protects against muscle damage (McArdle et al., 2004). We are currently investigating the effects of age, behavior, time-of-day, season and tissue-type on muscle protein damage and Hsp expression.

Expression of Hsp70 family proteins increases with age in worker bees (Severson et al., 1990). However, constitutive expression of *hsp70* mRNA in the brain measured with quantitative real time-polymerase chain reaction is significantly higher in foragers than in age-matched hive bees (Elekonich and Robinson, unpublished) suggesting that *hsp70* transcription may reflect task rather than age. Since bees typically progress through tasks as they age, the earlier protein data may reflect the fact that older bees are also foraging bees. These differences in brain mRNA are not entirely surprising because the expression of a number of genes in the brain including other Hsps are correlated with behavioral task (foraging vs. hive-work; Whitfield et al., 2003).

6. Neural and sensory function

Changes in the neuropil volume, dendritic arborization, and levels of neurochemicals in both the mushroom bodies and antennal lobes of the honey bee brain occur in concert with behavioral development and its subsequent changes in physiology. In addition to the changes in brain gene expression described earlier, these experience-dependent changes in neural architecture and function may reflect changes in information processing and sensory thresholds in response to the greater complexity of foraging tasks relative to hive work. Honey bee foragers make use of visual, auditory, and olfactory information while locating flowers, assessing the sugar content of the nectar, communicating the quality and location of the food to other foragers and repeatedly navigating between the hive and food sources (Winston, 1987). To support this complex task, changes in sensory system sensitivity and learning occur as bees change tasks (Capaldi et al., 1999).

Arguably the most studied areas of the insect brain, the mushroom bodies receive olfactory, visual and mechano-sensory inputs and are involved in both spatial and olfactory learning and memory (Roman and Davis, 2001; Menzel, 2001). Mushroom body neuropil increases in size in adult bees concurrent with increases in JH. However, changes in neuropil volume do not depend on JH, as such changes happen even in allotectomized bees where JH titers are negligible (reviewed in Fahrbach et al., 2003). Dendritic length and branching increase with increasing foraging experience (Farris et al., 2001) and individuals with the greatest foraging experience at a given age have the largest mushroom body neuropil volume (reviewed in Fahrbach et al., 2003).

It is likely that the transition from hive work to foraging requires increased visual and olfactory abilities on the part of foraging bees. There are few studies of the developmental regulation of the visual system in insects. Recently, Sasagawa et al. (2003) found in honey bees that levels of mRNA coding for the photopigments arrestin and green-sensitive opsin vary diurnally and are affected by light. However, arrestin mRNA levels increase as bees age while opsin levels appear to reflect task, being higher in foragers than in hive bees. In contrast, the development of the olfactory system is better described. The antennal lobes of the honey bee brain comprise the primary olfactory neuropil and are connected to pre-motor areas in the protocerebrum and to the mushroom bodies (Heisenberg and Gerber, 2002). Olfactory sensory neurons from the antennae converge in the antennal lobes onto spheres of neuropil called glomeruli, which can be readily identified in different individuals. Two specific glomeruli change increase in volume with the shift from in-hive tasks to foraging. Furthermore, antennal lobe morphology differs between bees collecting nectar and those collecting pollen (Winnington et al., 1996; Sigg et al., 1997).

The propensity to primarily collect pollen or to primarily collect nectar as a forager is partly determined by genotype. Working with lines of bees selected for pollen or nectar foraging, Pankiw et al. (2001, 2002) have shown that bees from pollen foraging lines are more

responsive to lower amounts of sucrose but that sucrose response thresholds are also influenced by recent foraging experiences. Sucrose response thresholds also decrease as bees age, when octopamine levels increase and JH titers increase (all typical of foragers; Maleszka and Halliwell, 2001; Pankiw and Page, 2003). Increased responsiveness to sucrose is at least in part mediated by manganese levels in the brain. Levels of RNA encoding the manganese transporter *malvolio* in worker honey bee brains reflect manganese levels and increased levels of manganese are associated with increased sucrose responsiveness and precocious foraging (Ben-Shahar et al., 2004). Honey bee foragers and bees working at brood care in the hive learn equally well in associative learning tests but foragers have a longer memory for the learned odor (Ben-Shahar et al., 2000), perhaps reflecting a modification in pre-existing neural pathways with the transition to foraging.

Although JH appears to control the rate of behavioral development and affects flight capacity and metabolism (see above), levels of the biogenic amine octopamine in the brain appear to be the immediate activator of foraging. Using the SCC manipulation described earlier, Schulz and Robinson (1999) showed that levels of octopamine in the antennal lobes are higher in foraging bees than in bees tending brood in the hive regardless of age, while levels of octopamine in the nearby mushroom bodies are higher in older bees regardless of the task they were performing. These differences exist even on the bee's first foraging flight. Oral treatment of entire colonies of bees with octopamine dissolved in sugar syrup increased the number of precocious foragers in a dose-dependent manner—with foraging beginning soon after treatment and stopping as treatment ended. In addition, JH treatment produces bees with forager-like levels of octopamine in their antennal lobes (reviewed in Schulz et al., 2002). Octopamine appears to act by directly affecting perception of task-related stimuli at the level of the antennal lobes. Colonies treated with octopamine show a larger increase in foraging activity upon subsequent exposure to brood pheromone, a volatile chemical secreted from the cuticle of the larvae (Le Conte et al., 1990), than do untreated control colonies (reviewed in Schulz et al., 2002), suggesting that octopamine treatment increases forager perception of the brood pheromone and lowers the response threshold for foraging performance rather than simply increasing foragers overall activity levels.

Pheromone exposure may directly act on foraging behavior and perception of foraging related stimuli. Brood pheromone, is known to increase pollen foraging by stimulating foraging by bees already in the foraging force and recruiting younger bees to the foraging force (Pankiw et al., 1998, 2004). Exposure to queen mandibular pheromone, a substance secreted from the queen mandibular glands (Naumann et al., 1991; Slessor et al., 1988) can decrease JH titers and cause workers to forage at a later age (Robinson et al., 1998). In addition, queen mandibular pheromone increases expression of genes typically higher in nurses and decrease expression of genes typically higher in foragers (Grozinger et al., 2003). Similarly to the interaction between brood pheromone and octopamine, gene regulation in response to queen mandibular pheromone may affect individual workers responses to other environmental cues. However, this remains to be tested.

7. Conclusions

Although honey bees are depicted in Spanish cave paintings dated from 6000BC and the first recorded observations of bee behavior were made by Aristotle, the honey bee model system is just beginning to reach its' full potential. Future research has the potential to fully integrate genetic and physiological approaches to understand honey bee ecology and life-history transitions. Behavioral shifts such as that from hive-work to foraging require the integration of new environmental information with changes in physiology, peripheral receptors, and neural response thresholds and the production of subsequent behavior. Honey bee genomic analysis including recently developed RNAi based techniques (Amdam et al., 2003; Beye et al., 2002; Farooqui et al., 2004; Gatehouse et al., 2004) will allow investigators to identify up-regulation of receptors, enzymes and other functional components that coordinate CNS-based changes in thresholds for relevant stimuli (as suggested for octopamine by Schulz et al., 2002). In addition it will identify changes in the ability of sensory receptors to selectively perceive relevant changes in the environment as the individual bee prepares for and undergoes the transition from hive worker to forager. By measuring gene expression, endocrine, metabolic and neural physiology and behavior in groups of bees, future studies will be able to gain a detailed picture of how the distributed network of changes is integrated at the colony level. With a combination of a sequenced genome, well described natural history including ecology, behavior and development as well as a large, interactive community of researchers with a variety of tools to manipulate all aspects of honey bee biology, the honey bee as a model system will doubtless continue to deserve its description by von Frisch (1964) as an unending "magic well" for the next hundred years.

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