Developmental nutritional environment reduces honey bee resilience to virus infection

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Early-life nutrition can have long lasting or permanent effects on the phenotype. Because of the sensitivity of juvenile development to environmental input, the nutrition an individual receives in early stages of life can lead to morphological, physiological, neural, and epigenomic changes that permanently alter their adult phenotype (Gilbert 2017). In turn, these alterations can have important consequences for the behavior, health, and reproductive success of the individual. For example, when zebra finches experienced low food conditions as chicks, their spatial associative learning as adults was impaired, however their spatial associated learning was enhanced (Kriengwatana et al. 2015). In humans and non-human mammals, mounting evidence shows that early-life nutritional deprivation leads to decreased adult survival and reproductive output (rev. in Lummaa and Clutton-Brock 2002); effects which can span generations as even the offspring of these individuals may be underweight and underdeveloped (Albon et al. 1987; Meikle and Westberg 2001; Burton and Metcalfe 2014). Similar effects of early-life nutrition occur in insects. For example, when nutritionally deprived as juveniles, adult female cockroaches had reduced reproductive lifespan; an effect that could not be reversed with enriched diet as adults (Barrett et al. 2009). Although animals may be able to buffer some of the effects of early-life nutritional stress by reallocating resources to critical functions during development (Birkhead et al. 1999), or by adopting alternative life history strategies as adults (Emlen 1997; Wang et al. 2006), these compensatory mechanisms can be costly (Birkhead et al. 1999). The effects of early-life nutrition are long-reaching, with the potential to shape all aspects of the adult phenotype.

The honey bee *Apis mellifera* has served as a workhorse for understanding how nutrition shapes development. Honey bees are social insects that live in colonies comprised of sterile workers, male drones, and a single reproductive queen. Whether a developing larva will become a worker or queen is driven by the diet she receives. Female larvae are fed a high quality diet for 3 days post-hatching, at which point the nurse bees that provisioning the larvae may switch to feeding them a lower quality diet, assuring that they will develop into workers. However, if a larva remains on the high quality diet, it will develop into a queen (Winston, 1987). The nature and timing of this developmental switch has been thoroughly studied, and a clear picture is emerging of how nutrition mediates critical gene expression cascades and hormonal modulation to determine caste fate (Kucharski et al. 2008; Kamakura 2011; Mutti et al. 2011; Roth et al. 2019). Despite the vast work on honey bee queen/worker development as a model for disentangling environmental and genetic determinants of phenotype, we know very little about the effects of developmental nutrition on adult phenotype within the worker caste. However, we know that a worker’s developmental environment can have important lifelong effects, including their ability to forage and recruit foragers (Scofield and Mattila 2015), their aggressiveness (Rittschof et al. 2015), and their cooperativeness (Walton et al. 2018) as adults.

For honey bee workers, adult nutrition is important for pathogen resilience. The health of managed honey bees is in constant jeopardy due to the multitudinous pathogens and pests that infect and infest colonies. An improved diet can mitigate these effects by maintaining immunocompetence (Alaux et al. 2010). Namely, the detrimental effects of infection by the microsporidian *Nosema ceranae* can be offset by pollen, quantity (Jack et al. 2016), quality, and diversity (Di Pasquale et al. 2013). Honey bee colonies also face infection by many viral pathogens, transmitted largely by the mite *Varroa destructor*. Israeli acute paralysis virus (IAPV), which has been associated with large-scale colony loss (Cox-Foster et al. 2007), produces distinct pathological phenotypes including shivering, paralysis, and death in a relatively short and repeatable window (Maori et al. 2009). As such, IAPV provides a valuable system to use an economically relevant honey bee virus to investigate whether different types of nutritional stimuli can affect the resilience of bees to disease. Emerging research has highlighted the importance of adult nutritional environment in mitigating the effects of IAPV (Dolezal et al. 2019; Rutter et al. 2019). However, the long-lasting effects of larval diet on viral resistance is not well understood.

In this study we combine two different experimental nutritional manipulations to investigate how developmental nutrition affects bees’ resilience to virus infection and then seek to understand the underpinnings of these differences. We find that both of these nutritional treatments cause observable reductions in resilience to infection, providing evidence for the importance of developmental nutrition in producing worker bees that are patent against infection as adults. These results have important ramifications in our understanding of the interplay within the network of environmental stresses faced by pollinators. It also shows how honey bees can provide a valuable model for studying how developmental nutrition canalizes adult phenotype, even focusing just within the worker caste. Because honey bees experience complex social interactions in addition to simple differences in nutritional stimuli, this system has ripe potential for parsing apart nutritional from other social stimuli in honey bees.

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