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Aging: A Young Mind in Old Bees

A new surprising study suggests that various cognitive abilities and motosensory functions remain perfectly intact as honeybee workers age. How do these findings fit in with a buzzing life?

Stephanie Jemielity and Laurent Keller

You can't reach old age by another man's road. These are Mark Twain's words on the observation that each person is affected by a slightly different palette of ailments when getting older. From the speed of our heart beat to cognitive abilities and locomotor functions, there is a general decline in performance with age in humans. This phenomenon, often referred to as functional senescence, has also been documented in many other species. Although the speed and onset of decline may vary with genetic and environmental factors, functional senescence is thought to be the prime culprit for the widely observed environment-independent increase in mortality rate with age — demographic aging — as well as the limited lifespan of organisms [1]. In a new study reported in this issue of *Current Biology*, Rueppell and colleagues [2] challenge this view with evidence that several behavioral and motosensory functions are not subject to an age-related drop in performance in honeybee workers.

To determine the association between functional senescence and demographic aging, Rueppell *et al.* [2] subjected 26- to 52-day-old worker bees that had started foraging to a series of well-established behavioral tests. They found no negative association between the age of foragers and their ability to respond to light, their responsiveness to sucrose, their ease at associative olfactory learning or the speed at which they exit the hive upon external perturbation. At the demographic level, however, signs of aging were clear: the mortality of foraging workers increased significantly with age during the behavioral experiments, and residual lifespan decreased significantly with age across forager cohorts transferred to undisturbed laboratory cages.

The apparent decoupling of demographic and specific physiological aging patterns in the honey bee workers are in sharp contrast with findings in *Drosophila*, where similar behavioral tests revealed a clear decrease in performance with age (reviewed in [3]). Rueppell *et al.* [2] suggest that this discrepancy might stem from the particular social life characteristic of the honey bee and other social insects. Indeed, the evolution of social life in bees, ants, wasps and termites has been accompanied by an almost 100-fold increase in average lifespan compared to their solitary ancestors [4]. In our view, however, there is currently no theoretical reason to expect that functional senescence should be entirely absent from social insect workers. Rueppell *et al.*'s [2] reasoning is based on a review by Amdam and Page [5], which provides an interesting explanation for why the lifespan and aging rate of honey bee workers is so extraordinarily plastic compared to other organisms. But there is no reason to expect, nor do Amdam and Page [5] attempt to conclude, that plasticity in aging rate should lead to a complete lack of functional senescence.

That some physiological traits in honey bee workers do show a decline in performance with age is supported by a recent study [6] which measured the age-specific resistance of workers to three different physiological stressors. The results showed that resistance to oxidative stress, starvation and heat stress was significantly better in 10-day old nurse bees than in 50-day-old 'overage nurse bees' (worker bees that had been experimentally forced to continue nursing activity). This finding cannot be due to differences in activity between young and old workers, because both groups performed similar tasks. Furthermore, the result is unlikely to be caused by higher nutritional reserves in younger bees, since lipid stores in young and overage nurse bees were comparable.

There are several possible explanations for the seemingly contradicting findings of the two

honey bee studies. The behavioral tests performed by Rueppell *et al.* [2] might simply be less 'energetically demanding' than the stress resistance tests performed by Remolina *et al.* [6]. But this would not account for functional senescence exhibited by *Drosophila* in similar behavioral tests [3]. Alternatively, it might be that some behavioral and physiological traits decline more slowly than others because they have different effects on fitness in different age classes. The four behaviors investigated by Rueppell *et al.* [2] are central to efficient foraging: these traits may be specifically selected to remain functional in older worker bees, which are much more likely to forage than younger bees. More generally, traits that have greater effects on fitness in older ages might possibly decline more slowly than traits having lower effects. If this prediction holds, it is conceivable that different species exhibit different patterns of functional senescence. For instance, while individuals from one species might be more prone to cognitive decline, individuals from other species might be more sensitive to physiological ageing or lowered immune defense. In other words, the road to old age might not only take different turns for each individual, but also for each species.

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Human Evolution: Thrifty Genes and the Dairy Queen

Two new studies of genes that have experienced positive selection since the origin of pastoral agriculture help explain the incidence of lactose tolerance and diabetes, but cast considerable doubt on the popular thrifty genes hypothesis.

Greg Gibson

Lactose intolerance means different things to different people. To a modern American it might mean an unwanted rest stop a short while after a visit to the Dairy Queen; to an early pastoralist it might have meant the difference between life and death. Milk is both a source of nutrients and of water in arid climates, but it can also be the cause of diarrhea and dehydration. The ability to digest the lactose in milk has thus been estimated to confer a fitness advantage as high as 5 to 10 percent, one of the strongest known selection differentials in human adaptation [1].

Much of the ability to digest dairy products rests with persistence into adults of expression of the *LCT* gene, which encodes lactase-phlorizin hydrolase [1]. In a remarkable new study, Sarah Tishkoff and colleagues [2] show that at least two independent regulatory mutations affecting *LCT* expression confer lactase persistence in northern Europe and east Africa. The two polymorphisms are 100 base pairs apart in the thirteenth intron of the *MCM6* gene, which lies 14 kilobases upstream of *LCT*. They both drive elevated expression of a reporter gene in intestinal cell lines, and both explain a sizeable portion of lactose tolerance in their respective populations.

It is possible to estimate whether there has been positive selection on alleles using a method called extended haplotype homozygosity analysis (EHH; Figure 1) [3]. The idea is to ask how much of the chromosome surrounding the selected site has been swept along with it during its increase in frequency. The northern European allele appears to be a little older, but it is striking that in both cases the persistence haplotypes are typically homozygous for well over a megabase, whereas the ancestral haplotypes associated with lactose intolerance are often only a few kilobases long. Further analysis allows dating of the selective sweeps [4], admittedly with very wide confidence intervals, to 5,000–10,000 years ago, and this puts both events coincident with the domestication of cattle. It is hard to refute that this is a lovely example of the coevolution of genes and culture [2].

Such signatures of selection are precisely what would be predicted of so-called thrifty genes. Jim Neel [5] proposed 45 years ago that the high incidence of diabetes in modern humans is a result of positive selection for alleles that confer the ability to rapidly sequester rare caches of carbohydrates as fat that would tide us over during famine. This thriftiness has supposedly become harmful in modern times as the rapid storage of an endless supply of energy-dense foods leads to obesity and eventually the emergence of insulin resistance.

There is certainly variation for weight gain and diabetes susceptibility in humans; these two traits are heritable and genetically correlated, and it seems plausible that fat reserves might help out during times of food shortage. Unfortunately, these three preconditions for natural selection