On the contrary. Wrangham's book comes at a crucial time. Driven by technical accomplishments, the past years have seen huge interest in identifying genes whose adaptive changes underlie human evolution. This enterprise may have, to some extent, shifted the focus away from environmental and in particular cultural drivers of human evolution. Cooking is a key cultural practice of humans and it is Wrangham's merit to identify the clear-cut biological consequences that may have followed in its wake. But, it is important to note that, in his view, clearly the cultural invention came before the biological adaptation. So, it was not a mutation in a gene that primarily conferred a particular advantage, and then was positively selected for, but a learned cultural technique that radically altered our interaction with the environment, in terms of the energy we take in. This changed the selective pressures and of course numerous genetic changes — affecting our jaws, teeth, guts and not least brains — will have ensued.

Moreover, Wrangham's hypothesis points the way to empirical testing of these ideas. So much has been made in recent years of looking for genetic changes underlying increases in brain size or in cognitive capabilities, in particular language. And, while of course the appeal in finding such genes remains and is by no means obliterated by the cooking-human hypothesis, they are inherently difficult to test in a test tube or a mouse model. Wrangham's ideas, by contrast, pave the way for much more straightforward tests. Genes underlying changes in digestive system development and function that have been selected in humans, conceivably could be much more readily tested for physiological effects, simply because metabolism is so much easier to assess than cognitive skill. Despite its seemingly humble status among organ systems, the gut may prove a gold mine for finding some of the key adaptive changes that 'made us human'. Of course, ultimately, what made humans cooks must be due to cognitive capabilities and thus be sought in our brains. It is, after all, this complex interplay between culture and biology that makes studying and thinking about human evolution so uniquely fascinating.

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Quick guide

The mushroom body

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What is a mushroom body? The mushroom body is a prominent and striking structure in the brain of several invertebrates, mainly arthropods. It is found in insects, scorpions, spiders, and even segmented worms. With its long stalk crowned with a cap of cell bodies, a GFP-labeled mushroom body certainly lives up to its name (Figure 1). The mushroom body is composed of small neurons known as Kenyon cells, named after Frederick Kenyon, who first applied the Golgi staining technique to the insect brain. The honey bee brain, for instance, contains roughly 175,000 neurons per mushroom body while the brain of the smaller fruit fly *Drosophila melanogaster* only possesses about 2,500. Kenyon cells thus make up 20% and 2%, respectively, of the total number of neurons in each insect's brain. Kenyon cell bodies sit atop the calyx, a tangled zone of synapses representing the site of sensory input. Projecting away from the calyx is the stalk comprised of Kenyon cell axons carrying information away to the output lobes.

How did mushroom body research start? In 1850, Felix Dujardin showed that the size of the mushroom body was correlated with the complexity of social behavior in different species of bees. Dujardin suggested that mushroom bodies control aspects of insect behavior that are not just simple reflexes and even speculated that they might play a role in 'free will'. Although few researchers have been bold enough to study free will in insects, it is certainly true that arthropods display a wide array of sophisticated behaviors: the bee waggle dance to communicate flower location, learning by observation in *Drosophila*, and elaborate forward-planning and strategy formation by the hunting spider, *Portia*. Modern investigations, begun by Menzel, Erber and Heisenberg, suggest that the mushroom body is an important center for learning and memory. For example, fruit flies learn to associate a specific odor with an electric shock, much like Pavlov's dogs learned that a bell signaled the arrival of dinner. Lesion studies, including a reversible, temporally precise block of mushroom body output using the impressive genetic techniques in *Drosophila,* showed that mushroom bodies are essential for this learning.

What are the inputs and outputs of the mushroom body? In many insects, such as wasps and bees, inputs to the mushroom body come from several different sensory pathways, including smell, taste, vision and hearing. Output regions are less well defined, but one intriguing feature is that the axons of many mushroom body neurons bifurcate, sending one branch towards the midline while the other projects dorsally. Presumably this branching provides identical copies of mushroom body output to different sets of downstream neurons.

How are mushroom bodies made? One of the strangest things about mushroom bodies is their development. They are derived from four neuroblasts that continue to divide throughout much of the lifetime of the animal — in *Drosophila* from the larva until shortly before pupae hatch into adults. In some insect species, mushroom body neurogenesis even continues throughout adult life. During pupation, a fraction of Kenyon cells lose their dendrites and one of their axonal branches. Deprived of inputs, they subsequently re-grow a large dendritic tree, but remain mono-axonal. The reason for this pruning is completely unknown. Remarkably, despite the remodeling of roughly half the larval mushroom body neurons, memories formed in the larval stage can persist into adulthood.

Are mushroom bodies analogous to a particular area of the human brain? At different times

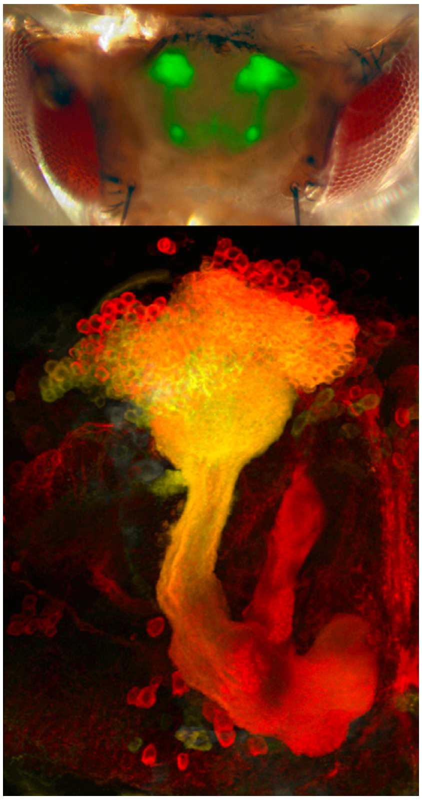

Figure 1. Mushroom bodies of *Drosophila*.

Top panel: anterior view of a fly head dissected to reveal GFP-labeled mushroom bodies. Lower panel: close-up of the mushroom body color-coded for depth. Kenyon cell bodies at the top send out a bulging array of dendrites immediately below, while the axons bundle together to create a stalk before bifurcating to form two output lobes.

by different people, the mushroom body has been considered loosely analogous to three different regions in the mammalian brain: first, the hippocampus, because of its involvement in learning and memory; lesioning the mushroom body in cockroaches impairs their memory for spatial locations, much like hippocampal lesions do in rodents. Second, the cerebellum, again because of its involvement in learning, particularly of precisely timed motor movements; both the mushroom body and the cerebellum are composed of densely packed tracts of axons that make contact with dendrites of large neurons that insert into the tracks like a comb. Third, piriform cortex, because both piriform and mushroom body are only two synapses away from the sensory layer of the olfactory system.

Perhaps a more illuminating way to view the mushroom body is from the perspective of how sensory information is represented there. Although the neurons that provide olfactory input to the mushroom body respond broadly to many odors, mushroom body neurons are very odor-selective and responses appear to be relatively sparse. Sparse representations are a hallmark of learning and memory centers — if neurons respond very selectively to particular stimuli, then memories can also be accurately formed and recalled. From this perspective, the mushroom body is typical of memory centers in the brain in general.

What do mushroom bodies do? Perhaps because it is so prominent and accessible to lesion studies and physiology, sometimes it seems that mushroom bodies are involved in all interesting insect behaviors. One example is olfactory learning and memory: a great deal of work has focused on understanding how sparse representations arise in the mushroom body, and how learning modifies those activity patterns. Surprisingly, these studies revealed a connection between sparseness and oscillatory neuronal activity, such as one sees in the brain waves of human EEGs. The selectivity of Kenyon cell spiking arises from the timing of the inputs. Synaptic excitation and inhibition arrive in rapidly alternating waves. Only during the brief peaks of these oscillations can sensory inputs lead to the generation of action potentials in Kenyon cells. Thus, like the waves on an EEG, insect neural circuits also exhibit oscillatory activity. In this case, the oscillations create highly stimulus-selective neural responses, a role they are also likely to play in the human brain. Imaging experiments that track neuronal calcium levels suggest that learning modifies mushroom body response properties. Specifically, output from a particular region of the mushroom body is augmented after learning. Understanding how these observations of global activity relate to changes of individual mushroom body neurons is the next step in understanding how this circuit creates associative memories.

What else does the mushroom body do? There is a well-established connection between sleep and memory. For example, sleep can prevent a newly established memory from degrading. By the standard definitions — altered brain activity, increased arousal threshold, less movement — insects do sleep. Blocking mushroom body output alters a fly's sleep patterns, affecting the duration of sleep intervals. Perhaps the mushroom body can act as a gate, uncoupling sensory input from behavioral output during sleep. Another role for the mushroom body is during decision-making: like the rest of us, flies confront choices. Normal flies abruptly and consistently switch between two different choices when one is more salient. However, one study indicated that blocking mushroom body output causes this sharp switch to become a smooth transition instead. It is unclear what this means but perhaps it is another instance where the mushroom body acts as a gate or switch, this time enabling the fly to crisply decide which stimulus to follow. All things considered, maybe Dujardin wasn't too far off when he considered that the mushroom body is what elevates insect behavior above the reflexive. Its role in associative learning, sleep and decision-making suggests that it may serve as a gateway, selectively coupling input from different senses to appropriate behavioral output. It certainly seems fair to ask: is the mushroom body where the fly makes up its mind?

Where can I find out more?

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