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Food for thought: an interview with Ana Domingos

Ana Domigos holding 'diet' and 'regular' soft drink cans.
Image credit: Roberto Keller

Ana Domingos of the Gulbenkian Science Institute in Portugal has forged a career learning why we like certain types of food. By looking at the reward system of the mouse brain, she has revealed pathways that explain why animals prefer sugar, and perhaps why it may factor so strongly in the Western diet.

Domingos' work is often described as the neurobiology of calorie addiction, but she believes that may be a bit misleading. "I would be careful with the word addiction," she told eLife. "Addiction to a substance requires that in the absence of consumption of that substance, there are withdrawal syndromes, which can come in the form of pain or anxiety. Withdrawal from sugar, to my knowledge, does not create any of this." Unlike other types of addiction, there does not appear to be a tolerance effect with sugar, where animals require increasing amounts to achieve the same rewarding effect.

Rather than addiction, Domingos describes our preference for sugar in terms of how the pleasure sensors of the brain (and the associated dopamine release) guide our actions. "Neuroeconomics is an area of neuroscience that tries to understand how people and animals make choices, and how the brain encodes those choices," Domingos said. Traditionally, however, most people studying this area only use electrophysiology and fMRI, which correlate behaviors to gross neuronal activity or blood flow in the brain, respectively. "My approach was [to use] molecular genetics to find specific neurons that are responsible for certain behaviors."

"During my Ph.D. I got training in molecular genetics and making transgenic animals (those with intentionally altered genes) so that we can control neuronal activity," she said. At that time, optogenetics — a way of manipulating certain genes in neurons so that the cells can be activated by flashes of light — didn't exist. So Domingos, who was working with Leslie Vosshall at The Rockefeller University, used a different trick to achieve the same goal. "[I took] advantage of a gene (OR83B) that Drosophila melanogaster expresses in olfactory neurons. By manipulating the presence of this gene I could activate certain combinations of neurons, and then compare the difference between Combination A, Combination B or Combination C." Using such transgenic tools, she was able to map neural circuits to behaviors.

Sugar cubes in a bowl
Image credit: Kurtis Garbutt

According to sales data in journals such as Beverage Digest, which is an important publication for scientists in the food industry, there is on average a three-fold difference in the sales of regular soft drinks compared to Diet alternatives using artificial sweeteners. This big difference in sales has been consistent since 1947, when sweeteners were first introduced onto the market. "If there is a historical trend in market behavior," Domingos said, "that tells me that there may be a biological explanation."

While Domingos was a postdoc, optogenetics hit its stride. Working with Jeffrey Friedman at Rockefeller she used a sensor to detect when mice drank from the water bottles in their cages. By coupling this with a transgenic mouse that had light-sensitive dopamine neurons, she was able to optically stimulate the pleasure centers of the brain when the animal drank certain fluids. Though the mice had a natural preference for sugar water (sucrose), she was able to trick the animal into liking water flavored with an artificial sweetener (sucralose) by stimulating dopamine release with a light pulse whenever the mouse licked the water bottle.

In her recent study, Domingos used optogenetics to find that the pathway from taste receptors to reward was more complex than initially thought. She discovered that if a laser activated a certain non-dopamine releasing population of brain cells called melanin concentrating hormone (MCH) neurons, the animal would once again be drawn to artificial sweetener. Moreover, without these neurons, mice did not prefer sugar to artificial sweeteners. She concluded that there is a linked activation of dopamine neurons through the MCH brain cell pathway.

By teasing apart the effects of different nutrients on the brain, Domingos is on a mission to educate people about what our bodies require to stay healthy. "Trying to find out what nutrients satisfy the needs of a person makes much more sense in biological terms than trying to find the calorie content that a person needs to eat."

Domingos wants to create similar maps from receptors to the pleasure centers of the brain for other types of nutrients. One area she is particularly interested in investigating is how signals from fatty foods, which are sensed in the intestine, reach the brain.

By Brian Mossop - Freelance science and technology writer

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