Did you know that our motivation to learn decreases with age? A recent study by the Graybiel Lab from the Massachusetts Institute of Technology (MIT) identified a key neural circuit underpinning motivational learning that is compromised with age.

This circuit lies in the part of our brain known as the basal ganglia, a collection of structures involved in movement, habit formation, and emotion. Specifically, the Graybiel lab studies specialized clusters of cells called striosomes found in the striatum—one of the functional units of the basal ganglia. These cells have been implicated in cost-benefit decision making that enables organisms to weigh the pros and cons of a particular decision and act according to their analysis.
As ocean temperatures continue to rise due to climate change, widespread algae blooms proliferate, releasing domoic acid, a toxin that has given rise to a plague of epilepsy in communities of ocean mammals. One such animal, a 7-year-old sea lion named Cronut, recently underwent groundbreaking neurosurgery with the aim of reversing his sudden-onset epilepsy.

Seizures and sea lions

by Elizabeth Burnette

Although striosomes were known to be involved in this type of decision making, the mechanism by which they mediated cost-benefit analysis remained unknown. This led the Graybiel lab to ask: what happens to striosomes as mice learn to make these kinds of decisions?

Conditioning experiments conducted by the researchers showed increased activity in mice striosomes during value-based associative learning. The researchers determined that striosomes act as an integrating center and filter for sensory and emotional information used to make value-based decisions. Next, the MIT scientists looked at how striosome activity changed with age. Using the same conditioning experiments with older mice, they observed less activity in the striosomes while learning cost-benefit behaviors, which leads to a prolonged learning phase signaling a decreased efficiency and motivation to learn. Upon artificially activating the striosomes during learning of tasks, the old mice showed increased engagement and restored efficacy levels of learning. Screening of drugs targeted at increasing striosome activity is already underway. This study might hold the key to teaching old dogs new tricks and increasing mental engagement to maintain healthy minds into old age.
Domoic acid poisoning in marine mammals causes damage to the hippocampus, almost identical to the Temporal Lobe Epilepsy most commonly seen in humans. Damage to inhibitory interneurons in the hippocampus essentially “removes the brakes” on electrical currents in the region, causing seizures which in turn can further damage this circuitry. In this way, epilepsy can often worsen over time.

By transplanting new MGE cells, researchers are able to restore the damaged inhibitory neuron population in the hippocampus. These inhibitory cells then clamp down on the electrical activity that causes seizures, rescuing healthy brain activity. This technique has shown great success in mice, with an 84-88% reduction in seizure activity and behavioral deficits - more than 6 months after the treatment. However, Cronutt is the first higher-order mammal to receive this surgery and we cannot expect this surgery to be conducted in humans anytime soon. However, hopefully, this novel treatment may benefit many more sea lions, otters, and other marine animals in the years to come.

More on the authors..

**Arielle Hogan** Arielle received a B.S. in Biology and a B.A. in French from the University of Virginia in 2019. She is now currently pursuing a Ph.D. in Neuroscience in the NSIDP program at UCLA. Her research primarily focuses on bioinformatics approaches to studying CNS injury and neural repair.

**Elizabeth Burnette** Elizabeth is pursuing a PhD in Neuroscience at UCLA, in the lab of Dr. Lara Ray. Her research uses neuroimaging and psychoneuroimmunology methods to study the neurobiology of addiction in clinical populations. Her dissertation project explores the role of neuroinflammation in alcohol use disorder.