Learning for Life Week 5 Summary 10-24-18

Topic: Brain, Mind and Society

Speakers: Emily Rogalski PhD, Cynthia LaBella MD, Nina Kraus PhD

In this week's session, we learned about *superagers* and how we can use the brain's response to sound in the diagnosis and prognosis of patients with concussion.

There is cognitive decline associated with normal aging, particularly in the realms of attention and memory. Peak memory function occurs around age 30-40 and declines as we age; however, the NU Alzheimers Disease Center has identified nearly 200 adults over the age of 80 whose cognitive function is similar to that of a 50 year old. Emily's work has focused on identifying factors that may be associated with the retention of robust cognitive function in these *superagers.* This work is particularly important as we are living longer, but not necessarily living better. Her study has demonstrated that the brains of the *superagers* when compared with average older adults have a different appearance on imaging studies. Their gray matter (the part of the brain containing the most neurons and involved in the neural functions of sensation, muscle control, emotion and cognition) is thicker, particularly in the area of the anterior cingulate which is the area of the brain responsible for attention. The brains of average older adults shrink over time, yet in *superagers*, this shrinkage is about 2.5 times slower. Microscopic analysis of their brains also demonstrates an increase in the number of Von Economo (VEN) neurons, particularly in the area of the anterior cingulate. While we don't yet understand the implication of this finding, we know that loss of VEN neurons is associated with conditions like Autism, Schizophrenia and Frontotemporal dementia.

Emily's team is also analyzing the psychosocial factors that may contribute to the exceptional cognitive function of the *superagers* and found the following:

They have satisfying, positive relationships with others

They feel that they have a purpose in life

They have a positive attitude towards self and their past

They feel a sense of autonomy, independence and are able to resist social pressures

They have mastery and competence in managing their environment

They are open to new experiences and have a feeling of continued personal growth

So in summary, it seems as if superagers have a combination of **resistance** (the gray matter of their brains is thicker and less subject to atrophy), **luck** (they have more VEN neurons) and **resilience** (they have psychological wellbeing). Emily's team is trying to explain the reasons for these differences.

Cynthia then shifted our focus to the diagnosis and prognosis of concussion. Concussion occurs when the brain oscillates, or moves rapidly within the skull after a blow to the head or body. The connections between nerve cells get stretched during this rapid movement and nerve signaling is disrupted. Until now, the diagnosis of concussion has been clinical. It is based on the patient's history along with signs and symptoms that indicate a concussion has occurred. Ninety percent of the time the physical exam is normal, as is brain imaging. Physicians and athletic directors face the challenge of determining when it is ok for the patient to resume physical and cognitive activity. When has the brain recovered? Visual, cognitive and balance tests are used to indicate recovery; however, these are all effort dependent and somewhat subjective. There may be an incentive for an athlete to return to play prior to full recovery, and a subjective test is susceptible to that interference. What if we had an objective test that could demonstrate the severity of the concussion and the brain's recovery? This is where Nina's work on sound processing in the brain can provide a solution. Nina demonstrated that the brain's cognitive ability influences how we hear sound, and that sound waves and measurable brain waves physically resemble each other. Therefore brain health may be inferred by how well the brain is measuring different features of sound. This tool is much more objective and is being tested as a marker of concussion and recovery. Nina is collaborating with Tory Lindley, Associate Athletic Director at NU, to study this tool in NU athletes. For a detailed look at her work, we encourage you to explore her website:

www.brainvolts.northwestern.edu

Take Home Points:

1. *Superagers* have a combination of resistance (more gray matter in their brain), luck (more VEN neurons) and resilience (better psychological wellbeing)
2. The clinical diagnosis of concussion and particularly recovery from concussion is challenging and subject to bias. Measuring the affected person's brain response to sound may provide a more objective measure of injury and recovery.

really took us into the basics of neuroscience through a glimpse into the labs of two brilliant junior faculty whose work focuses on reward and decision making in the brain.

Genia explained how her lab utilizes genes from the "toolkit of nature" to study how neurons and synapses operate in the brain. Genes from jelly fish allow for fluorescent labeling of neural pathways in the brain and viral genes are used to manipulate neurons. These are just two of the tools used in Genia's lab to understand neural pathways and the interactions between neurons facilitated by neurotransmitters. Without these basic roadmaps of the brain, treatments like deep brain stimulation (which we heard about last week) would not be possible, because physicians would not understand where to place the electrodes to modulate the disease.

The specific work that Genia's lab is focused on is whether or not the neurohormone oxytocin, which is involved in social affect behavior, directly controls the dopaminergic system. The latter is largely responsible for the human reward system. She described a series of experiments that confirm that indeed, oxytocin is significantly involved in stimulating some dopaminergic neurons while inhibiting others. While at this stage, the science is basic, the implications for clinical application in conditions like autism and post-partum depression are significant.

While most of Genia's experiments utilize mouse brains which have a lot of synergy with the human brain, Thorsten's experiments are performed in humans. He employs functional MRI of the brain to visualize the brain's response to olfactory stimuli or smells. Human subjects are exposed to a range of smells which, when used in a variety of experimental designs, allow Thorsten's team to begin to understand how the brain makes choices, and how it learns from experiences to inform future choices. Much of the decision making in our brain occurs in the orbitofrontal cortex (OFC). Thorsten described how an animal who is given cocaine for three weeks is unable to make choices because it behaves as if the orbitofrontal cortex has been damaged. The animal can no longer imagine the outcomes of its behavior. Although this is not yet proven, this research leads to questions and potential implications for patients who have addiction. We believe that the reward and decision making systems are impacted in patients who have addictions. They may not be able to imagine behaviors other than drinking or using drugs that could result in reward, and may not be able to imagine all the consequences of continued addictive behaviors. A new line of research might investigate the outcomes of stimulation of the OFC of patients with addiction. Might that enhance their ability to make different choices?

Take Home Points:

1. We are just beginning to understand the brain's complexity. Research like that of Genia and Thorsten are critical to mapping the neural systems that control complex behavior and emotion like reward and decision making.

2. Once we understand the underlying neural pathways that control behaviors, we can manipulate these pathways chemically or through tools like deep brain stimulation to improve many diseases.