Diseases 2

[00:00:00.61] Now we're going to cover some degenerative and developmental disorders that may be solvable by neural engineering solutions. Now, this is going to be far from a comprehensive list and there are many other conditions that neural engineering treatments would be appropriate for. But I just can't cover them all here. So I'm going to cover some of the most common ones that are seen.

[00:00:24.25] Among the most common is Parkinson's disease, which is caused by the death of neurons in the substantia nigra. The substantia nigra is part of the basal ganglia, which is a group of regions that contribute to movement. And we're going to go into more detail on that when we do the motor unit of the course later.

[00:00:41.98] At the bottom of this slide, you can see a diagram that shows a healthy brain, which has the substantia nigra clearly visible. "Substantia nigra" is Latin for "black stuff" and that name is very appropriate. On the right is a person's brain who has Parkinson's disease. And the substantia nigra neurons are gone. They've died.

[00:01:02.59] The symptoms of Parkinson's disease don't typically appear until about 90% of the neurons are already dead. And these symptoms include the classic tremor as well as slow movement, difficulty starting movements, rigidity and poor balance. Cell death is caused by clumps of alpha-synuclein protein, which are called Lewy bodies. This also contributes to Lewy body dementia, which is a separate disorder from Parkinson's, but has very similar cellular pathology.

[00:01:35.20] It's increasingly believed that the Lewy bodies appear across the brain and they just hit the substantia nigra especially hard. The death of the substantia nigra unbalances the circuitry of the basal ganglia, which normally has an elaborate system of increases and decreases in activity depending on stimulation or inhibition passing through the sequence of regions. And the loss of the substantia nigra seriously inhibits that function.

[00:02:04.15] The primary first-line treatment is L-DOPA, which is a dopamine precursor molecule. So the brain can turn L-DOPA into dopamine. And it's an oral medication that the person just takes everyday. And only about 4% of the L-DOPA actually travels to the brain and gets turned into dopamine. In all people who take L-DOPA, the medication eventually will stop working because it augments the missing dopamine that the substantia nigra neurons normally are producing, but ultimately, it's not enough anymore.

[00:02:39.82] So the next treatment is deep brain stimulation, which we're going to return to in more detail in the next lecture when we cover common neural engineering devices that are already on the market. It's one of the most common neural engineering devices that's currently available. And it involves stimulating remaining portions of the basal ganglia in order to restore some normal function.

[00:03:10.24] Huntington's is another degenerative disease which causes movement abnormalities. In the case of Huntington's, it causes unintentional or incomplete movements,

abnormal eye movements, a characteristic writhing movement, and poor coordination. It's caused by a genetic mutation in the Huntington protein gene, which is shown on the right side of this slide. It's usually inherited. In about 90% of patients, at least one of their parents had Huntington's.

[00:03:38.89] This mutated protein causes cell death, but the mechanism of how exactly the mutated Huntington's disease causes cell death isn't known. And it primarily affects the chordate and the putamen, which is collectively called the striatum. And then the symptoms eventually spread to other parts of the basal ganglia and then to the cortex.

[00:03:58.93] The mean survival rate after diagnosis with Huntington's disease is 20 years. But because the symptoms are severe and there is no cure, the suicide rates are unfortunately very high. A medication called tetrabenazine can help alleviate the symptoms, but it can't prevent the progression and it can't cure the disease. And unfortunately, Huntington's disease most commonly onsets between the ages of 30 and 50 and 8% of cases onset before the age of 20.

[00:04:34.36] Amyotrophic Lateral Sclerosis, ALS, also known as motor neuron disease or Lou Gehrig's disease, is caused by the degeneration of motor neurons in the motor cortex and in the body. There's no cure for ALS and there's no treatment that can help slow progression. In most individuals, they see a gradual weakening and loss of control over their muscles. And in up to half of patients, they also see some cognitive dysfunction, which is dementia-like, in about 15% of patients. So they lose memory as well as cognitive function.

[00:05:10.16] It usually onsets between the ages of 55 and 75. And about 10% of cases are inherited. And half of those patients die within 30 months of their diagnosis, mostly from respiratory failure. But 10% survive 10 years or more, including the most famous case of ALS, which is Stephen Hawking, who has survived for over 50 years since his diagnosis.

[00:05:37.41] Multiple sclerosis is thought to be an autoimmune and genetic disorder. The nervous system is thought to recognize myelin as a threat and attack the myelin and the glia that are providing it. Regardless of its cause, it results in the focal loss of myelin throughout the central nervous system and in the peripheral nervous system. And it specifically is caused by the loss of oligodendrocytes, which are a type of glia that produce the myelin, and the neurons themselves are not harmed. The principal symptoms include double vision or blindness, muscle weakness, poor sensation, lack of coordination, and sometimes cognitive symptoms, especially risky decision making.

[00:06:24.21] It comes in multiple types, most commonly, the relapsing-remitting type, which comes and goes. And the symptoms will come. They will persist for months to years. And then they will remit; they will go away for a while.

[00:06:39.75] But some cases are progressive. And it's highly sensitive to stress. A person who has relapsing-remitting multiple sclerosis can also switch to having the progressive type and this is especially triggered by stressors.

[00:06:56.25] A new study suggests that a combination of chemotherapy and a transplant of the patient's own treated bone marrow may help reset the immune system and stop it from recognizing myelin as a threat. But this treatment is very risky and it hasn't been proven in large trials to work. The trial that demonstrated this only had about 25 people in it. Other than that, the primary treatments are mobility aids.

[00:07:25.30] Epilepsy is defined as the condition of having two or more seizures. So having one seizure, you had a seizure. Having two seizures, you now have epilepsy. Epilepsy can come from focal seizures, which come from a specific location in the brain every single time, or generalized seizures, which can come from anywhere in the brain and there isn't a specific location that is causing the seizures every single time.

[00:07:52.78] Focal epilepsy generally causes specific symptoms, often twitching or uncontrollable laughter or babbling or other specific focal symptoms that are very specific. But generalized epilepsy causes either grand mal seizures, which are the classic flopping on the floor and writhing that everybody recognizes from TV, or an absence seizure where the person just goes blank and is completely unresponsive. Epilepsy is caused by the hyper-excitability of neurons either within a specific area in focal epilepsy or just across the brain in generalized epilepsy.

[00:08:36.46] And this hyper-excitability-- so the neurons are more likely to fire than they should be-- can cause the neurons to synchronize so they're firing in waves. And they shouldn't be firing in waves. And this causes electrical activity to spread in ripples across the cortex.

[00:08:54.76] Most people who have epilepsy can be controlled perfectly well by medications that help reduce the excitability of neurons. So they just take a pill or a couple of pills a day and it prevents the spread of seizures. But in some people, the medications don't work or they don't work well enough and in those individuals, we can do surgery to remove the specific part of the brain that is causing the seizures. And this is obviously only an option for focal epilepsy, not generalized epilepsy. But if you remove the tissue that's causing the seizures, then you don't have seizures anymore.

[00:09:32.20] I also wanted to briefly mentioned Alzheimer's disease, which is not currently a target of neural engineering, but it is something that frequently comes up in questions about neural engineering. Unfortunately, the damage due to Alzheimer's disease is too diffuse and the system-level consequences to the cortex and other parts of the brain are not well enough understood that we would require a significant amount of cellular-level neural engineering in order to address it. What happens is that you get tangles of this tau protein that I mentioned when we talked about CTE that destroy cellular structure and intracellular transport.

[00:10:12.77] And that's picture A on the left here. You've got these tangles of tau protein aggregating inside of the cells. Alzheimer's is also characterized by these plaques, like plaques on your teeth, of amyloid beta protein, which builds up on the outside of the cells. And it prevents molecules from flowing in and out as freely.

[00:10:38.68] And it causes cell death broadly across the brain, primarily starting in the temporal lobe and then spreading throughout the rest of the cortex in most types of Alzheimer's, and cognitive degeneration. And one of the primary theories of why people with Alzheimer's have good days and bad days is that one of the first things that Alzheimer's affects is the ability not to store memories, but to retrieve memories. So it's harder for the brain to locate the memories and bring them up into the active state, but they're still there, at least to begin with.

[00:11:19.18] Finally, I want to review a couple other conditions that don't neatly fit into either of those categories but are still major targets for neural engineering. First, amputations and congenital missing limbs. These are not precisely a nervous system problem. It's not caused by damage or degeneration of the nervous system specifically. But it is one of the most important targets for engineering research today.

[00:11:45.31] And the goal of neural engineering research with regard to prosthetics is to develop a design that can read a motor signal from the nervous system, peripheral or central nervous system, translate that into a command to the device, sense from the environment, sense touch or proprioception information, deliver that sensation to the nervous system, and to move dexterously, which requires a high quality, jointed prosthetic and a power source. All of these same design principles for designing a prosthetic to replace a missing limb would also apply to various forms of paralysis except that the intent in that case would be to either control an external device such as a wheelchair or robotic arm, an orthotic, which-- in contrast to a prosthetic, which replaces a missing limb-- an orthotic encases an existing limb and helps provide strength or stability-- or to control the person's own body by bypassing the spinal cord injury and stimulating and reading from the person's own body directly.

[00:13:01.34] Muscular dystrophy and related muscular disorders are also a major target of neural engineering. So there's many different types of muscular dystrophy. They all cause progressive weakness and muscle deterioration.

[00:13:15.20] It's not a nervous system disorder, but it can be potentially helped by neural engineering because it would amplify the nervous system signal. The most common type of muscular dystrophy or Duchenne muscular dystrophy is caused by a faulty muscle protein called dystrophin, which makes the muscles very weak and underdeveloped. It can also cause some significant respiratory issues.

[00:13:40.94] But the motor signals are intact and they reach the muscles accurately. So it could be potentially treated by a neural engineering device that reads from the peripheral nervous system what the person is trying to do and then could control an orthotic that encases the person's limbs and provides strength that they lack. Any treatment for muscular dystrophy would also have to account for the respiratory symptoms of the disease, as well.

[00:14:13.20] So in conclusion, neural engineering-- why does it matter? Engineering can contribute solutions to various diseases, disorders, and injuries that are distinct from other areas of study such as pharmacology or surgery and where other solutions are not available.

[00:14:30.50] So we've spent a lot of time in this course so far reviewing neuroscience and neuroanatomy, which we need to consider whenever we're discussing injury treatments. We can't just discuss the engineering components. We also have to discuss the biological interfaces. And the nervous system presents unique challenges to both medical treatments and specifically, technology-based treatments. Over the course of the next few lectures, we're going to review what we can do right now in neural engineering and what we wish we could do and targets for further research.