The Death of a Neuron

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I stare up the steep radial glial cells as my friends all disappear, excitedly climbing to teir new destination. It was only a few days ago we were all born from the dividing stem cells in the great proliferation. Our human, Amy, was conceived four weeks ago and has only just begun forming her brain and spinal cord. From the minute I was born, I knew I was destined to be a hippocampal neuron and ever since then, I've been waiting to start my migration with my friends, most of whom will end up in the same location as me.

I start my journey up the radial glial cell. Just as the long climb begins to discourage me, I hear a familiar voice shout, "Ned, we've almost made it!" I look to my right and see my first friend, Nate, shimmying his way up beside me. Seeing his excited self gives me the encouragement I need to keep climbing and reach our destination. Suddenly, we both hear a booming voice call out, "Alright young neurons, it's time to aggregate." Without any thought, our cell bodies begin moving into the formations we've been programmed to create. As more of us hippocampal neurons assemble, our home structure will be formed. Nate and I examine the vast empty space in awe; this will be our home for the rest of our neuronal lives. In the distance, we see the faint lights of previously established neurons coursing with electricity. Over the next few weeks, Nate and I change significantly as we grow, developing axons and dendrites along the way. Our bond grows strong as our growth cones guide us to connect to each other and our friends by synapses. Friendships and connections are critical and a few of the outcast neurons didn't make it over the next few weeks; quite a few lost some synaptic connections. Meanwhile, Nate and I began to grow myelin on our axons and establish ourselves as the official neurons of the hippocampus.

Life for the next few decades in Amy's hippocampus was smooth and easy. Everyday my neighbors and I excitedly transmitted acetylcholine and other neurotransmitters to make new synaptic connections as Amy made memories. Nate and I loved receiving and laughing over chemical gossip from the sensory neurons about the latest cactus our human Amy hurt her hand on because we kept forgetting to create the memory of her pain. Nate had even made a synaptic connection with a lady neuron, while I lost a connection with the annoying neighbor who refused to ever do his job. It seemed as if nothing could go wrong.

One busy morning, after Amy's 66th birthday, while all the neurons were aglow and forming new connections, the happy memories made after yesterday's party, I noticed something peculiar. I moved my dendrite gently to nudge Nate, signaling him to inconspicuously look at the strange shape in the distance. He turned back to whisper, "what is that, Ned?" to which I responded, "I don't know, but it sure doesn't look like any neuron I've ever seen." We decided to ignore the strange mass and brush off this unusual event. We continued about our busy day of transmitting chemical messages. Just as the receptors of my dendrite were about to receive an inflow of GABA from Nate's terminal button, we heard a screech from our neighbor Nelly, "What is happening to my microtubules?" All the neighboring neurons turned to look as Nelly, normally a very excited neuron, began to shrivel and darken. "My tau, I think it's tangling!" We all helplessly looked as her dendrites disconnected from her neighbors and she shriveled into herself and died. Nate and I looked at each other instantly, sensing a problem: something was happening in our hippocampal home.

"What's all the commotion," bellowed the voice of the eldest neuron, grandfather Neil. He was quickly answered with nervous voices explaining the death of Nelly. Concern clouded his soma as he somberly said, "This isn't the first occurrence. These deaths have been happening all over the hippocampus. I've received messages that it's taking a toll on Amy's memory." Without hesitation, Nate yelled out, "Sir, have you seen the large masses as well?" I gave him a look, but he didn't notice. "Yes, those have just started appearing. I'm afraid I know what this means." He paused, "The end is approaching my friends" he said ominously. Gasps echoed throughout the hippocampus, and neurons shuddered in fear. I signaled to Nate and asked what Grandfather Neil meant. He replied, "only the worst thing that could possibly happen to a neuron in the hippocampus." Still confused, I questioned him again. "Alzheimer's, Ned. Remember decades ago when Amy learned about it in school? It means this is the end for us, we're all going to end up like Nelly." In shock, I replied, "What? No, there must be some way to-" just as I was finishing my thought, Grandfather Neil called out again: "Hold on, I've just received word from the frontal lobe neurons that Amy has decided to see a neurologist about treatments. There is still hope." Neurons began to glow with excitement as exciting messages of hope were transmitted throughout the hippocampus. I, on the other hand, had just noticed another mass, this one much closer. I asked Grandfather Neil to explain to me exactly what it was. "That, son, is an amyloid plaque, formed when the wrong cut is made by beta and gamma-secretase enzymes on the amyloid precursor protein, causing small fragments of beta-amyloid to form and creating toxic plaques that interfere with our functions as neurons", he explained. I finally understood. However, the looming plaque looked even more threatening than before.

Over the next few weeks, I noticed it became harder and harder to produce and transmit acetylcholine. We got messages that Amy had begun taking Razadyne, supposedly to help prevent the breakdown of acetylcholine, but we weren't seeing the effects. Over the next few months, more and more neurons died and the plaques kept appearing. Nate and I tried to stay positive and keep our connection strong but one day, the inevitable happened. Amy had been losing memories for over a year, and today something felt off. I was talking with Nate when, all of a sudden, one of my microtubules collapsed. He instantly sensed my panic and tried to send glutamate, anything to electrify me again, but our connection had already broken. I could feel the tangles beginning to form and everything became difficult as I struggled to stay alive. I could sense Nate calling out to me, but the last thing I saw was a looming amyloid plaque, and then everything went dark.

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