

Synapses—More is Not Always Better

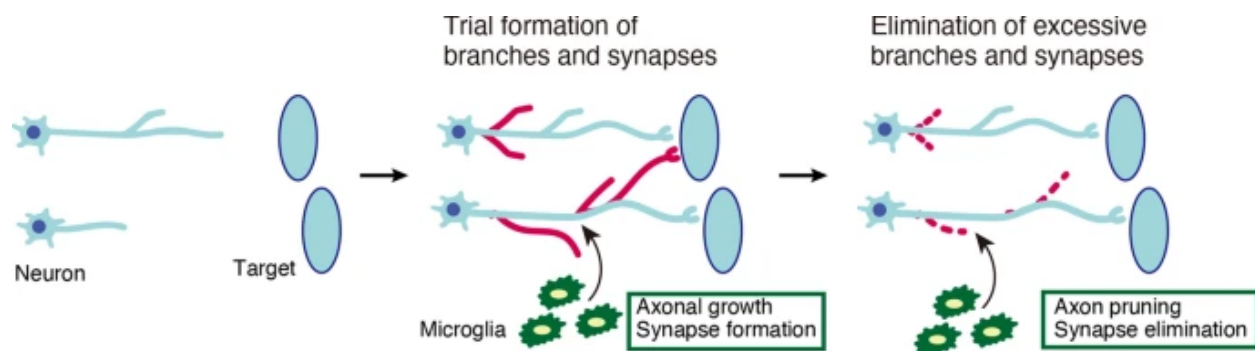
By Victoria Nikityuk

Neurodiversity is a beautiful thing—innovation and creativity rely on people who think differently. In some cases, people who are neurodivergent lead healthy, productive lives. They do not need treatment or cures—what they need is for the world to be more accepting and supportive of neurodivergence. But in some cases, people who are neurodivergent struggle because the differences in their brain prevent them from engaging with the world at all. They might struggle to attend school, hold a job, make friends, and may require life-long medical care. People with severe forms of autism often fall into this category. According to the Centers for Disease Control, one out of 36 children in the US is diagnosed with autism (Maenner, et. al., 2020). There are many forms of autism; some children have difficulty adapting and learning various skills like controlling their emotions, others may have more severe cognitive disabilities and/or the inability to engage in social-emotional interactions with others. The CDC estimates that 25-30 percent of children diagnosed with autism are nonverbal, have severe intellectual disability and engage in self-harm (Center, 2022). Individuals who fall within this severe category spectrum *may* have issues with being overstimulated by their surroundings, making it difficult for them to function in this sensory-simulating world.

Autism has been identified as a disorder of the nervous system, and one aspect of the disorder in some individuals is differences in the pruning of synapses in the brain (Faust, et al, 2021). Synapses connect different brain regions to each other by enabling brain cells (neurons) to send electrical signals. Imagine it as a map application on your phone giving you 100 different routes to get from point A to point B. Similarly, we are born with an abundant number of neuronal networks that have thousands of potential routes for electrical signals! Luckily our map applications show us the best route based on estimated time of arrival by removing the long undesired round about roads. This process of removal of undesired paths also occurs in the brain too. Usually, around the age of 2, we experience our first massive wave of synaptic pruning in the cerebral cortex, and there is a second pruning event in the teenage years (Johnson, 2003). During these pruning events, synapses are pruned (removed) to help refine and sharpen the neuronal networks, to ensure communication between the 86 billion neurons in our brain is as efficient as possible.

Synaptic pruning is not simply cell death of neurons, but the removal of the connections or pathways between specific neurons; it is like removing 95 of the 100 routes from the map app. Looking at the image below, the magenta and light blue colored branches are called axons. The point at which axons contact their target neuron is referred to as a synapse. Synapses are the site at which electrical signals from one neuron in one region of the brain is transmitted to another neuron in another region of the brain. By having that extra magenta colored synapse on the target region as seen in the 2nd section of the image below, that target area will receive more signals than needed. The body will create cells (microglia) to “prune” the branches so that we have a single straight path to our target! If this event doesn’t happen, the excess amount of signal

received or sent can leave the patients with an excessive amount of neurotransmission, which has been linked to autism and epilepsy (Lee et. al., 2015). Although it may seem like more neuronal connections would be better, it turns out that having too many roads is not always the best for us.



Different types of pruning occur at each of the two major synaptic pruning events. During the first pruning event, at the age of 2, signals are fine tuned; we will still see the magenta branches, just not as many as before (Johnson, 2003; Faust et. al., 2021). During the second major pruning event in the teenage years, the remaining magenta branches interfering with efficient neuronal transmission will be pruned (Johnson, 2003; Faust et. al., 2021).

Scientists are working to identify both genetic and environmental factors that confer risk of autism. The data clearly shows that autism is a highly heritable disorder; genomic studies have revealed 102 genes strongly associated with autism. But it is also clear that environmental factors, like industrial chemicals, drugs, maternal autoantibodies, and pesticides also play a role. For example, different components found in plastics have been shown to increase risk of autism (Zaheer, et. al., 2022). From the bottles that we drink to the plastic storage containers we use every day, we are exposing ourselves to harmful material which could negatively impact not only our health, but the health of future generations. Who would have thought that plastic compounds could interfere with signaling pathways in the brain?

As of now, there are no treatments for people with severe autism, but the disorder is a growing concern due to its increasing prevalence. In the US alone the prevalence of autism has increased over 300% over the past two decades. This fast-rising increase aligns with environmental factors being a major driving force, a notion that has been supported by epidemiological studies. Many in the public focus on vaccines as a potential risk factor, when this is the one environmental factor that has been exhaustively excluded as an autism risk factor. Instead, we should be boycotting plastics and organophosphate pesticides—both of which can dangerously impair brain development. Hopefully, scientists will continue to reveal the environmental factors that pose risk of severe autism. It is important for us to keep in mind that to protect the synapses of future generations, we should first protect our environment by reducing the prevalence of known risk factors.

References:

- Chaste, P., & Leboyer, M. (2012). Autism risk factors: genes, environment, and gene-environment interactions. *Dialogues in clinical neuroscience*, 14(3), 281–292. <https://doi.org/10.31887/DCNS.2012.14.3/pchaste>
- Centers for Disease Control and Prevention. (2022, March 28). *Signs and symptoms of autism spectrum disorders*. Centers for Disease Control and Prevention. Retrieved April 26, 2023, from <https://www.cdc.gov/ncbddd/autism/signs.html>
- Faust, T. E., Gunner, G., & Schafer, D. P. (2021). Mechanisms governing activity-dependent synaptic pruning in the developing mammalian CNS. *Nature reviews. Neuroscience*, 22(11), 657–673. <https://doi.org/10.1038/s41583-021-00507-y>
- Fujita, & Yamashita, T. (2021). Mechanisms and significance of microglia–axon interactions in physiological and pathophysiological conditions. *Cellular and Molecular Life Sciences : CMLS*, 78(8), 3907–3919. <https://doi.org/10.1007/s00018-021-03758-1>
- Johnson. (2003). Development of human brain functions. *Biological Psychiatry (1969)*, 54(12), 1312–1316. [https://doi.org/10.1016/S0006-3223\(03\)00426-8](https://doi.org/10.1016/S0006-3223(03)00426-8)
- Lee, B. H., Smith, T., & Paciorkowski, A. R. (2015). Autism spectrum disorder and epilepsy: Disorders with a shared biology. *Epilepsy & behavior : E&B*, 47, 191–201. <https://doi.org/10.1016/j.yebeh.2015.03.017>
- Maenner MJ, Warren Z, Williams AR, et al. Prevalence and Characteristics of Autism Spectrum Disorder Among Children Aged 8 Years — Autism and Developmental Disabilities Monitoring Network, 11 Sites, United States, 2020. *MMWR Surveill Summ* 2023;72(No. SS-2):1–14. DOI: <http://dx.doi.org/10.15585/mmwr.ss7202a1>
- Zaheer J, Kim H, Ko IO, Jo EK, Choi EJ, Lee HJ, Shim I, Woo HJ, Choi J, Kim GH, Kim JS. Pre/post-natal exposure to microplastic as a potential risk factor for autism spectrum disorder. *Environ Int*. 2022 Mar;161:107121. doi: 10.1016/j.envint.2022.107121. Epub 2022 Feb 3. PMID: 35134716.
- Zeidan J, Fombonne E, Scora J, Ibrahim A, Durkin MS, Saxena S, Yusuf A, Shih A, Elsabbagh M. Global prevalence of autism: A systematic review update. *Autism Res*. 2022 May;15(5):778-790. doi: 10.1002/aur.2696. Epub 2022 Mar 3. PMID: 35238171; PMCID: PMC9310578.