



# HYPOTHALAMIC NEWSLETTER

Welcome to this edition's Hypothalamic Newsletter! We will be discussing the similarities of plant cells and the human brain, the possibility of spinal cord regeneration, nicotine's effect on astrocytes, and more!

## Plant Cells and the Human Brain: They Have More In Common Than You Would Think

Plants and animals are very different species for many obvious reasons, primarily their physiology. But on the cellular level, plants may have common traits with human cells, specifically in axons in the human brain. Axons are cells that are responsible for forming connections that transmit nerve impulses. Axons and plants are similar in regards to their growth, protein content, and the biological roles of the said proteins.

One important similarity is the role of glutamate and glutamate receptors in axons and plants. Glutamate serves as a neurotransmitter in the brain. It has been discovered that glutamate is present in plants as well, and serves as a model of the cell to cell communication, similar to neurological behaviors.

Here, glutamate has the specific role of slowing extension and increasing proliferation (the replication of cells in a single area).

Another interesting similarity is the RHD3 protein. This is a protein found in both plants and axons. In plant cells, it is an important protein for the morphogenesis (shaping) of many organelles as well as cell wall arrangement for proper root growth. However, in humans, this protein is responsible for a hereditary genetic disorder known as Hereditary Spastic Paraplegia (HSP) that causes degeneration of the nervous system, and thus difficulty with motion involving the lower half of the body. This similarity serves as a possible manner of researching HSP for scientists.

So while the human brain and plants are two very different organisms, some of the structures of their cells show some similarities. These similarities teach us more about the physiology and functionality of plant cells and brain cells, and could even give rise to investigations involving neurological disorders that plague humans in the present.

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## The brain can stretch to the size of a pillow

### The Split-brain

In the 1950s and 1960s, Roger Sperry performed a series of experiments to study the functional differences between the left and right hemispheres of the brain. To do so he studied the corpus callosum, which is a large bundle of neurons connecting the two hemispheres of the brain. Sperry severed the corpus callosum in cats and monkeys and found that if the hemispheres were disconnected, they functioned independently of one another, also known as a "split-brain", which enabled animals affected to memorize double the information.

In an attempt to find a treatment for epilepsy, Sperry experimented on the human brain through volunteers who already had a severed corpus callosum. By showing a word to one of the eyes, Sperry found that split-brain people could only show the word shown to the right eye. Next, Sperry showed the participants two different objects, one to their left eye only and one to their right eye only, and then asked them to draw what they saw. All the participants drew what they saw with their left eye but described the object seen with their right eye. As a result, Sperry concluded that the left hemisphere of the brain could recognize speech, while the right hemisphere was unable to. Research by subsequent scientists revealed greater differences in the functions of both hemispheres. For instance, the left hemisphere is generally responsible for analytical tasks, such as calculations and reading

It also serves to understand and learn the language, although the right hemisphere is still involved in language processing to a minor extent. In comparison, the right hemisphere is more efficient at dealing with spatial tasks, such as navigating a maze or reading a map, than the left hemisphere. Nevertheless, it is essential for the two hemispheres to routinely communicate with one another through the corpus callosum. This connection serves as the conduit through which nerve impulses can be transmitted to the contralateral side of the brain and through which the motor control is affected in the reverse direction. The split-brain syndrome is caused primarily via the intentional severing of the corpus callosum through a surgical procedure known as corpus callosotomy. Due to developments of other procedures in the past century that can offset the need for corpus callosotomy, the operation is sometimes done as a last measure for extreme forms of epilepsy in which violent seizures spread from one side of the brain to the other. Preventing the propagation of seizure activity across the hemispheres can significantly improve the patient's quality of life. However, following the operation, patients often develop acute hemispheric disconnection symptoms and chronic symptoms that often are permanent.

### The Possibility of Spinal Cord Regeneration

Due to the non-regenerating nature of the central nervous system in mammals, any injury or damage to the spinal cord leads to the loss of sensory and motor functions within and below the lesion site. As a result, neuronal cell death occurs in the primary motor cortex. Functional recovery after adult mammalian SCI is limited in part by myelin inhibitors of axonal regrowth, in addition to a weak intrinsic neuronal growth response.

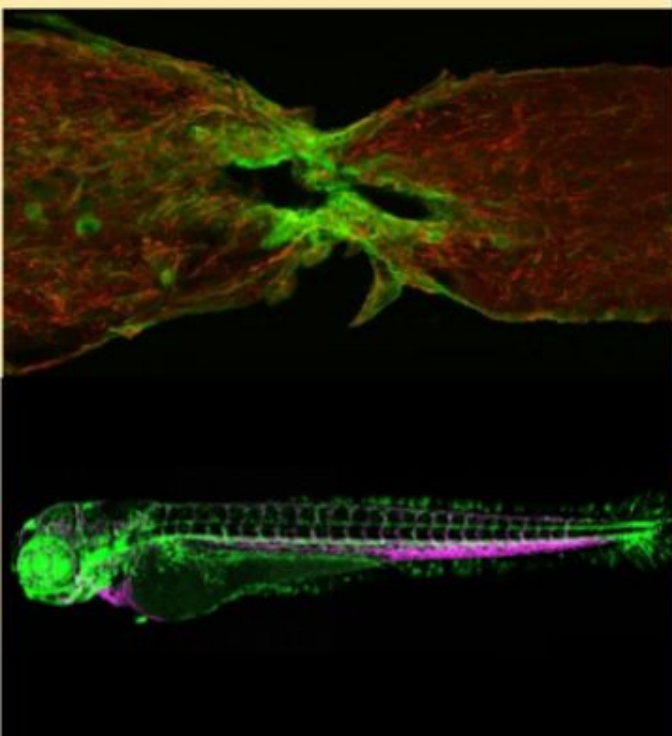
"The amazing thing with zebrafish, and most amphibians and fish, is that if you cut their spinal cord and then leave the animal by itself, within at most a week, the whole spinal cord regenerates itself and the fish will just swim away," says Dr. Tuan Bui, Associate Professor in the Department of Biology at the University of Ottawa. In contrast to mammals, adult zebrafish are capable of neuronal proliferation, regeneration, and functional restoration within 6–8 weeks after complete spinal cord transection via several regenerative processes in addition to surviving upper motor neurons in the brainstem against cell death.

Embryonic neurons of both peripheral and central nervous systems in Zebrafish respond to axonal injury by initiating pro-regenerative transcriptional changes that enable axons to extend and adhere to appropriate targets, to retrieve sensorimotor function

# The Possibility of Spinal Cord Regeneration continued

Adult zebrafish have evolved to develop a paradigmatic vertebrate system to identify novel genes vital for successful regeneration after SCI. Radial glia, such as resident neural progenitors, plays a key role in the remarkable regenerative capacity of the zebrafish spinal cord. According to previous studies, the nuclei of the promote medial longitudinal fascicle (NMLF) and the intermediate reticular formation (IMRF) in the brain stem of zebrafish are the most potent regions for regrowing of descending axons toward the spinal cord.

Since most genes in zebrafish genomes have been highly conserved phylogenetically, the discovery of genes or proteins related to regenerative capacity could address new therapeutic strategies on how to deal with functional recovery after SCI in humans.



# A More Efficient Brain

Sports have various effects on the body and specifically, the brain. Sports by definition is any activity that involves skill and even physician exertion in which an individual/team competes with another individual/team for entertainment purposes. So individuals who play tennis, basketball, hockey, chess, etc, regularly, are more likely to have an efficiently working brain.

Sports promotes more blood flow to the brain, thus enabling your body to build better connections between the nerves within the brain. The effects of better blood flow to the brain include stronger memory, more creative memory, and better developing problem-solving skills. Sports also improve brain function. A study showed that just being a sports fan can have a positive impact on your brain because playing or watching the sport can affect the neural networks supporting our language comprehension.

Various studies show that playing a sport keeps your concentration skills sharp. This is true because sports are very much mind games. Individuals need to plan a strategy in their minds to win or score the goal.

Social interaction comes with a team and a sport for the most part. Talking to people, engaging with individuals is essential for a healthy brain. Sports relax your brain and improve your mood. With more people to interact with, aka teammates, an individual now most likely has fewer problems with social isolation, giving them a better chance to make friends.

Ultimately, sports provide stress relief. Sports burn off more of the stress hormone, adrenaline too, which can promote relaxation. This is why many doctors recommend girls be active during their period to reduce cramps because exercising and playing a sport releases endorphins and adrenaline. Endorphins are hormones that block pain receptors in your brain, thus helping to stop pain signals from your period cramps. So overall, take up a sport to play because it does much more benefit than harm.



## Nicotine's effect on astrocytes

In the United States, as of 2017, over 500,000 people die per year due to smoking cigarettes and its associated cardiovascular, cancer, and respiratory diseases. Despite knowing the health risks associated with nicotine exposure, almost 35 million Americans continue to smoke cigarettes as of 2017. Its addictive effects can be explained by looking at the effect nicotine can have on the central nervous system, specifically in glial cells, including astrocytes. These astrocytes support communication between neurons by regulating and controlling synaptic activity.

Previous studies have suggested that in various regions of the brain, microglia and astrocytes have nicotinic acetylcholine receptors.

Cell proliferation is when there is an increase in cell quantity due to the growth and division of a cell. In a recent study, Aryal and colleagues found that when astrocytes were exposed to 0.1 and 1  $\mu\text{M}$  of nicotine when observed 24 hours later, there was an increase in cell proliferation. Specifically, at 0.1  $\mu\text{M}$  of nicotine, Aryal and colleagues saw a 5% increase in cell proliferation, and at 1  $\mu\text{M}$  of nicotine, an 8% increase in cell proliferation was observed. Additionally, they also observed an increase in calcium activity in the cell soma and processes, compared to astrocytes not exposed to nicotine.

Additionally, Aryal and colleagues found that blocking these nicotinic acetylcholine receptors using antagonists, called mecamylamine, and in turn blocking the ability for binding to these receptors, inhibited astrocyte remodeling and reversed the increase in calcium release and activity previously observed following nicotine exposure.

This suggested that nicotinic acetylcholine receptors on astrocytes may be a critical target in understanding the addictive potential of nicotine. Overall, the novel study by Aryal and colleagues suggested that the role of nicotinic acetylcholine receptors include modulating the increased astrocyte processing and calcium signaling caused by exposure to nicotine.



## Cotard's Syndrome

Unfortunately, most of us have been made grimly aware of the fragility of life, and the ever-present, cruel randomness of the prospect of death. What we perhaps are not as familiar with, however, is the irrational, perpetual belief that we are deceased. Those that suffer from Cotard's syndrome experience exactly this; delusions in which the patient believes that they or their body parts are dead, already deceased, or simply do not exist. Often accompanied by severe depression and other mental illnesses, Cotard's syndrome involves nihilistic delusion and is often referred to as 'walking corpse syndrome. Nihilism, the belief that nothing has any value or meaning, is the primary symptom associated with the disorder, inciting patients to believe themselves to be 'rotting away' or to never have existed in the first place.

## Cotard's Syndrome Continued

While anxiety, hallucinations, hypochondria, guilt, and a preoccupation with death are common identifiers, a 2011 study found that 89% of cases are closely linked to depression, with persons under the age of 25 developing specifically bipolar depression, despite the average age for developing the disease being approximately 50. Women have also been reported as more likely to develop the disorder. Beyond mental illness, Cotard's syndrome can be an indicator of brain infections, brain tumors, dementia, epilepsy, migraines, multiple sclerosis, Parkinson's disease, and stroke.

As far as treatment options extend, the most popularized is that of electroconvulsion therapy, or ECT, also a common treatment for severe depression which involves passing small electric currents through the brain with the intent of creating small seizures while the patient is under anesthesia. Despite its popularity, it also conveys significant risks, such as memory loss, confusion, nausea, and muscle aches. The preferred method of treatment is usually less drastic, and doctors may refer patients to antidepressants, antipsychotics, mood stabilizers, and psych and behavioral therapy. However, in the treatment of severe cases of Cotard's syndrome, such as reviewed by the NCBI, ECT was looked on most favorably as being the most effective treatment.

As was referred to in many case studies, patients presenting with Cotard's are at greater risk of suicide attempts, malnutrition and starvation as a result of a refusal to eat and drink, and detachment from society and reality, as they are unable to believe in their

existence. This complicates the maintenance of healthy social interaction and the upkeep of hygiene, which often results in skin and teeth deterioration.

Our knowledge of this perplexing disorder is far from extensive, and research continues to be conducted into its causes and biological consequences. Cotard's syndrome is one of the many examples of the complex and fascinating nature of our brains, demonstrating how disorders that only seem plausible in fantasy novels or on our favorite television shows can exist all around us. The magic of medicine, therefore, is far from fictional, and with each of its peculiar nuances is an opportunity for scientific discovery and revolutionary breakthroughs.



## Brain Development in Early Childhood

Toddlers – running, laughing, crying, naughty little beings free from the clamor and chaos of everyday activity. But there's more to these children than what we see on the outside. Their bodies – brains, more specifically, undergo critical processes necessary for developmental and cognitive growth. In fact, in its entire lifetime, the human brain changes and develops the most from the time of birth to five years of age. Therefore, everything a toddler interacts with and experiences – people, places, scents, objects – directly influences the developmental growth of their brains.

The brain is a complex organ filled with neuron cells. Neurons are units of the nervous system responsible for receiving signals from the outside world and accordingly relaying signals across the body. Most importantly, the connections made between neural cells are what allow our brains to function the way they do. There are more neural connections made in early childhood years than any other time in life, making this stage of life very critical. As connections intertwine and develop between different areas of the brain, the human can perform more complex tasks. Positive experiences and everyday interaction with the outside world foster neural connection growth.

## Brain Development in Early Childhood

The heavy influence of outside stimuli on a child's brain development is the reason why there is a significant amount of emphasis placed on loving relationships, safety, exposure, and interaction in early childhood years. Positive stimulation provides the foundational connections needed for higher-level thought, emotion, and coordination required later on in life. This is why reading, playing, and talking with young children is critical for brain development. On the other hand, a lack of quality and care during early childhood years can prevent critical neural connections from forming. As a result, vital brain functions such as cognitive thinking abilities, problem-solving, communication, regulation, etc. are negatively affected – in some cases, not even formed. Exposure to impoverishment, stress, abuse, violence, drugs, etc. early on in life are examples of experiences that prevent ideal brain stimulation and have long-term consequences on the human. Nihilism, the belief that nothing has any value or meaning, is the primary symptom associated with the disorder, inciting patients to believe themselves to be 'rotting away' or to never have existed in the first place. It is important to realize that every child's growth curve is different, and developmental stages are not reached at the same time. A developmental "milestone", for example, a first step, a first word, a first wave, can be studied to gauge when other changes in a growing child may start to appear. While the rate at which a child's brain develops is influenced by a variety of factors, exposure to more stimuli and an environment that enables neural connections influences this process. So, the next time you see a young child

playing with wooden building blocks, running and squealing in the sand, laughing loudly, or obsessing over an object that may seem insignificant to you, take a few moments to appreciate the stimuli and its beneficial influence on the child's brain and development.

## Memory Making Involves Extensive DNA Breaking

It's been known for a long time that brain cells snap DNA in places to express genes for learning and memory. However, a new study suggests that Brain cells snap DNA in more places and in more cell types than previously realized to express genes for learning and memory.

Study senior author Li-Huei Tsai, Picower Professor of Neuroscience at MIT and director of The Picower Institute for Learning and Memory, says that "We wanted to understand exactly how widespread and extensive this natural activity is in the brain upon memory formation because that can give us insight into how genomic instability could undermine brain health down the road,". They were testing to see how widespread the process is, and what would happen over time. The brain heals all these breaks, but it gets harder and harder as you get older. This can be the cause of neurodegeneration. It was also found that scarier memories cause a lot more breaks in DNA. Fear learning techniques were used on mice for another study, and it shows that the secreting hormones were caused by stress. Stimulating these hormones in mice given the same results. "More research will have to be done to prove that the DSBs required for forming and storing fear memories are a threat to later brain health, but the new study only adds to evidence that it may be the case, the authors said." This is all further evidence to lead to the bigger point, that this leads to threats to brain health later on.

