Ageing of Motor Neuron

MOTOR NEURON AGEING

HERE WE BREAKDOWN THE SECRETS TO AGEING

The United Nations reported that as of 2020, there are about 727 million people that are 65 years old and above, and by mid-century this number is expected to double.

We often correlate ageing with the onset of many chronic diseases as our organs begin to deteriorate functionally in their respective roles. Indeed, ageing is one of the major contributors to death and reduction of health span.

The lack of understanding in this uncharted field calls for more effort to be put into unveiling the mystery behind ageing and how it will affect the quality of life for us and our future generations.

Through this website, we hope that you will gain a deeper appreciation for your body and recognise how much we truly take our motor neurons for granted.

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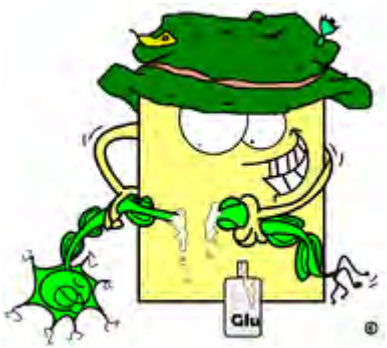
IMAGE SOURCES

MYTHS & MISCONCEPTIONS

Here we breakdown some common misconceptions that one may have heard regarding motor neurons



MYTH 1: NEURONS DO NOT REGENERATE

You've probably heard the saying that adult brains cannot generate any brain cells, and you can only use what you were born with. But is that really true? (Spoiler: we can generate new brain cells! In a process known as neurogenesis)

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MYTH 2: SUPPLEMENTS IMPROVE OUR BRAIN HEALTH

Over 25% of adults over age 50 take a supplement to improve their brain health with the promise of enhanced memory and sharper attention and focus.
Herein lies the problem: there is no solid proof that any of them work.

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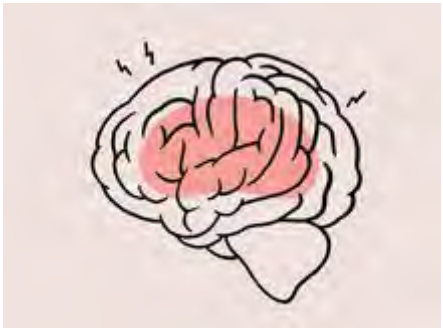

MYTH 3: SIGNIFICANT LOSS OF NEURONS AS WE AGE

Previous findings suggested that we lose about 1% of our brain cells every year throughout our adulthood. This would amount to a shocking 35% to 55% loss of neurons in our brains by the time we are in our 70s and 80s! Is this really true? And does this contribute to our cognitive decline as we age?

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MYTH 4: ONLY OLDER PEOPLE GET ALS

According to the ALS Association, most people who develop ALS are between the ages of 40 and 70 at the time of diagnosis. While it is true that ALS is more common amongst the middle age and elderly population, it is not true that only the older population can get ALS!

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MYTH 5: ALL MOTOR NEURON DISEASES ARE HEREDITARY

Spinal Muscular Atrophy (SMA) which causes progressive muscle degeneration and weakness in children, is one of the rare forms of Motor Neuron Disease (MND) that is inherited. While SMA is always hereditary, it is not true that all other forms of MND are hereditary as well!

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IMAGE SOURCES

+

DO OUR MOTOR NEURONS AGE?

NEUROTRANSMITTERS

Neurotransmitters are chemical messengers of the body that carry messages from neuron to neuron or neuron to muscle. During old age, the terminal endings of our nerves release larger amounts of neurotransmitters when stimulated, causing faster rate of neuromuscular failure.

MITOCHONDRIA DYSFUNCTION

Mitochondria play crucial roles in energy production, metabolism and cell death. As we age, declines in number and function of mitochondria cause reactive oxygen species to accumulate in neurons and cause oxidative stress. This may go on to damage axons, initiating degeneration.

INFLAMMATION

As we age, we experience increased levels of inflammation, marked by a rise in inflammatory markers such as interleukin 6 (IL-6) in our blood and tissues . The senescence of Schwann cells, which is found in our peripheral nervous system, has been associated with increased IL-6.

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MOTOR NEURON DISEASES

ALZHEIMER'S DISEASE

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HUNTINGTON'S DISEASE

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RESEARCH UPDATES

SCIENTIST EXTENDS C.ELEGANS LIFE SPAN

RESEARCH // SEPT 10, 2021

Research carried out in *C. elegans* found that both the loss of SLO-1 and paxilline (pharmacological blockers of SLO-1) resulted in the reduction of motor ageing and extension of life span in young *C.*

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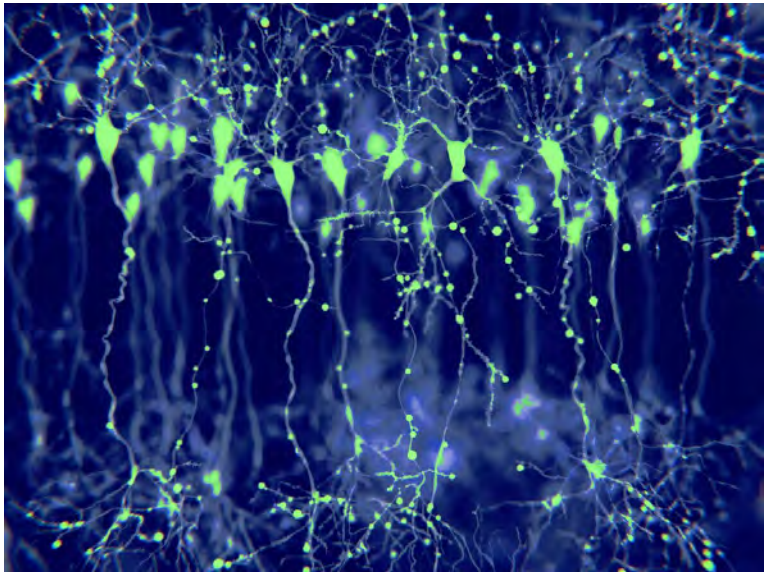

DIRECTLY-REPROGRAMMED NEURONS: A BETTER MODEL FOR DISEASE STUDY

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Scientists have found a more effective method to generate motor neurons that resemble aged neurons. This allows them to better study aging-related neuronal diseases. Learn about their discoveries today!

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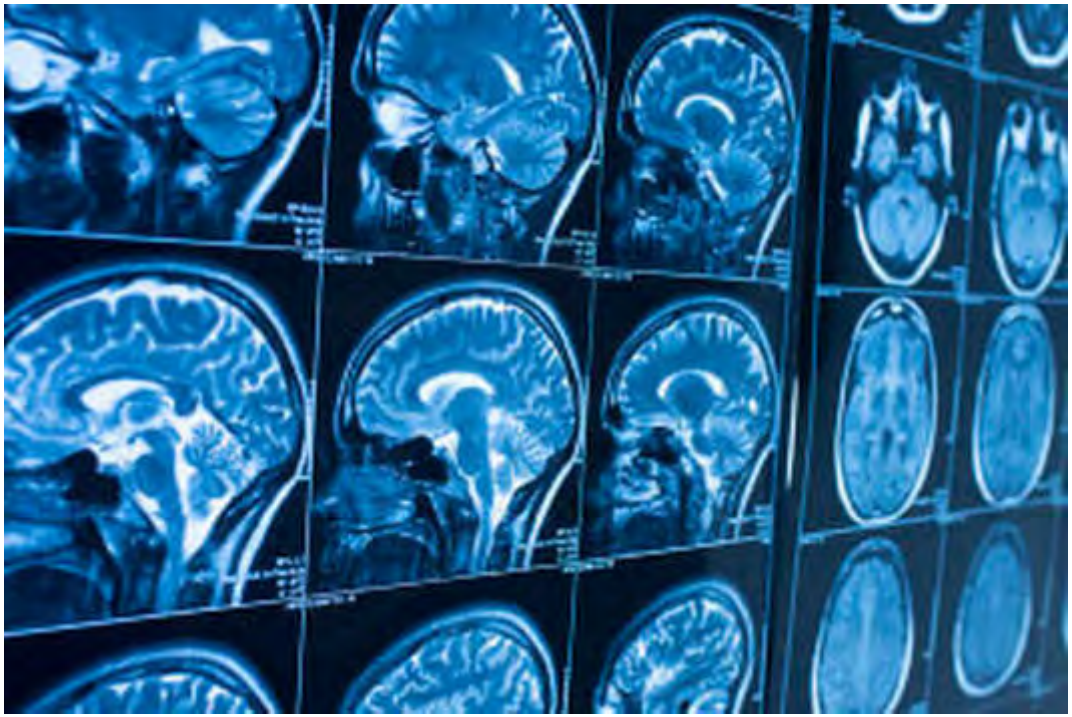

DECODING THE RELATIONSHIP BETWEEN AGEING AND AMYOTROPHIC LATERAL SCLEROSIS: A CELLULAR PERSPECTIVE

STEM CELLS USAGE TO REPAIR DAMAGED NEURON FROM PARKINSON'S DISEASE

RESEARCH // SEPT 22, 2021

Parkinson's Disease is one of the most well know neurodegenerative diseases in the world today. Learn how the top scientists have been trying to tackle the issue, and restore old and sick brains using stem cell transplants!

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RESEARCH // SEPT 20, 2021

With an ageing population comes an inevitable increase in the prevalence of ALS. In this article, we share with you about the overlaps in molecular and cellular changes between age and ALS-associated hallmarks, showing you how cell ageing could potentially be a key contributor to this complex disease.

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TETANUS TOXIN - A POTENTIAL THERAPY FOR MOTOR NEURON AGEING?

RESEARCH // SEPT 16, 2021

As we age, our neurons become a shell of their former selves. In this article, we share with you a potential therapy to restore our neurons back to their former youthful glory!

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Ageing of Motor Neuron

CURIOUS ABOUT AGING OF MOTOR NEURONS?

nctioning in our daily lives. They control our every action, some consciously and others not.

INTRODUCTION TO AGEING

Ageing is a process that affects every single living thing in the world. It is estimated that by 2050, there will be about 1.5 billion people above the age of 65 (World Population Ageing 2020 Highlights, 2020). This may result in an increase in healthcare funding as incidences of age-related diseases arises. With that in mind, it is important to understand what ageing is.

AGEING

"How old are you this year?", is a question most people ask when they first meet. We often correlate age with time but there are instances where the ageing process actually accelerates in young people. Take for example, Progeria or Hutchinson-Gilford Syndrome. Instead of time causing accelerated ageing in Progeria patients, a mutant variant of the Pre-Lamin A protein is unable to be recognised by an enzyme required to cleave it into the intended Lamin A protein (Sinensky et al., 1994). The Lamin A structural protein is normally in charge of maintaining the shape and structure of our nucleus as well as regulate how DNA is condensed in healthy people. This mutation causes the nucleus to become awkwardly shaped as Pre-Lamin A builds up in the nucleus, affecting the cell's ability to divide, and we all know that cell division is an extremely essential process in life. Progeria children look like any other children at birth but rapidly age as they reach preadolescence or adolescence, about ten years within a year (Sinha & Raghunath, 2014). This form of genome instability is similar in the elderly, suggesting that there is much more we can learn about ageing through Progeria and other progeroid patients. This is just a taste of what is to come!

In this section of the blog, we will uncover what motor neurons are and the history of the study of neurons. With that knowledge we will challenge your thinking and bust several common misconceptions regarding our neurons. With clarity and openness, we will then share with you our current understanding of how ageing works! With these foundational concepts, it will be easier for you to navigate through our page on Motor Neuron Diseases and our Blog, which goes in-depth into how we can potentially delay ageing in motor neurons.

Do click on the tabs below!

We hope you enjoy this section and the rest of the website!

WHAT ARE MOTOR NEURONS?

DEBUNKING MYTHS

HISTORY

MECHANISMS OF AGING NEURONS

References

World Population Ageing 2020 Highlights (2020). United Nations Department of Economic and Social Affairs. Retrieved from https://www.un.org/development/desa/pd/sites/www.un.org.development.desa.pd/files/files/documents/2020/Sep/un_pop_2020_pf_ageing_10_key_messages.pdf

Sinensky M., Fantle K., Trujillo M., McLain T., Kupfer A., Dalton M. (1994). *The processing pathway of Prelamin a*. Journal of cell science. Retrieved September 9, 2021, from https://pubmed.ncbi.nlm.nih.gov/8175923/

1. (2014). *Progeria: A rare genetic premature ageing disorder*. The Indian journal of medical research.

Retrieved September 10, 2021, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4140030/%E2%80%8B

Page Authors:

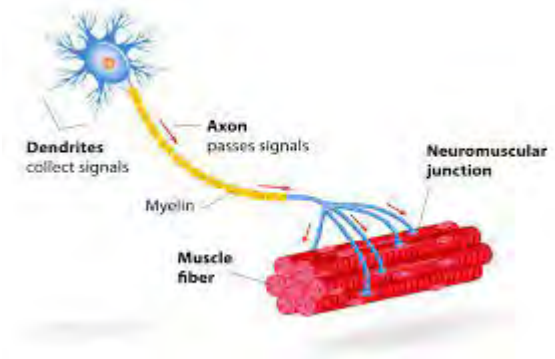
Chua Kevin

Ageing of Motor Neuron

WHAT ARE MOTOR NEURONS?

So what exactly brings the motion to the locomotive known as the human body?

Most of us know that our muscles are what allows us to move, but did you know they would be useless without our motor neurons? Muscle fibers are like obedient well trained soldiers, they generally don't act until they are given a command, at which point they spring into action. That's where motor neurons come in; they are the literal brains of the operation.

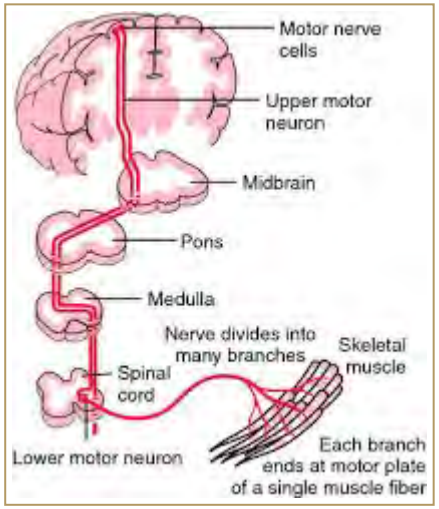


If your muscles were soldiers, the neuron is the commander, giving out specific instructions!

Image source: http://www.mrg-skyline.com/uploads/1/4/6/8/14686040/4.1_notes_-_mr._gs.pdf

Motor neurons are specialized cells that run from our brain all through our spinal cord and are woven within our muscles and organs. They allow us to make voluntary actions like running or jumping, as well as involuntary actions like breathing or swallowing. Without these special cells, there would be no motion to the commotion of our lives!

HOW SCIENTISTS CLASSIFY THEM



The upper motor neuron starts from the brain, while the lower motor neuron begins in the spinal cord

Image source: https://static1.squarespace.com/static/5871553a3e00be90c79a68cd/t/593aa819e3df28fc70a512f2/1497016347702/N14.pdf

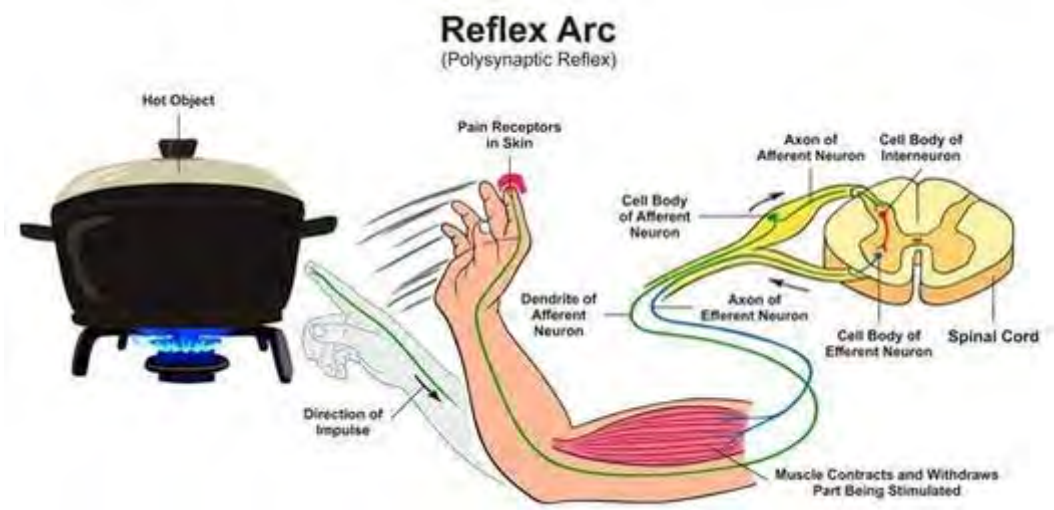
To be a bit more technical, motor neurons are broadly broken down into two groups, *Upper* and *Lower* motor neurons. While they are both referred to as motor neurons, they have vastly different forms and functions. For example, the upper motor neuron uses glutamate to transmit its messages, while the lower motor neuron uses acetylcholine. This is like two computers using different Wi-Fi signals to transmit different messages.

The upper motor neuron also starts right at the top, from the cerebral cortex (the command center for movement in our brain), down through our brain stem and all the way to the bottom of our spine. The lower motor neurons however, start from the spinal cord, where it connects to the upper motor neurons, and innervates throughout our muscles and organs, reaching to the furthest points of our bodies. Together, they form a complete, complex circuit from the top of our heads to the tips of our toes. Almost like our left and right hand, they perform different functions while still meeting in the middle for a handshake.

WHY EVEN BOTHER?

Why even bother classifying them? Well, they do have very different functions. The upper neurons, directly linked to our brain, are required when an action is driven by a thought. They then work together with the lower neurons to bring that "thought" all the way from our brain to the specific effector muscle where that action is carried out.

Our lower neurons however, are capable of reflex actions. Most of us would have had the experience of accidentally grabbing a hot plate. Before we can even *think* of placing the plate down gently using something else to grab it, we've already flicked it away from us, smashing it onto the floor. That sudden "jerk" is thanks to the reflex arc. When our nerves fibers detect a sudden undesired stimulus, they can send a signal along a different pathway, which loops around the spinal cord, ignoring the brain all together, and back into the muscle. Like our earlier soldier analogy, sometimes our muscles need to react quickly to an emergency situation, they have to act before the command center even gets word of what happens. This quick emergency response is referred to as the "Somatic reflex arc", and while it often protects us from danger, it's also the cause of many hot, broken plates!



"Ouch!" You think to yourself, only after you've already dropped the plate!

Image source: https://goprep.co/biology/control-and-coordination

THE MEDICAL SIGNIFICANCE

Now that we're well introduced to our motor neurons, why is this distinction important? This is because the difference in functions means that different clinical symptoms can tell us where exactly the problem lies. For example, a lesion (injury) to our upper motor neuron can cause spasticity or hyperreflexia, resulting in twitching, or stiff muscles, affecting movement and speech. Lesions to the lower motor neurons, however, can cause hyporeflexia or flaccid paralysis, where our muscles can't respond to stimulus, eventually resulting in atrophy. These distinctions are often useful in the characterization of various motor neuronal diseases such as Amyotrophic Lateral Sclerosis (ALS), Multiple Sclerosis (MS) or Spinal muscular atrophy (SMA) like Kennedy disease.

REFERENCES

Motor Neurone. Physiopedia. (2021). Retrieved 28 September 2021, from https://www.physio-pedia.com/Motor_Neurone.

Zayia, L., & Tadi, P. (2021). *Neuroanatomy, Motor Neuron*. Ncbi.nlm.nih.gov. Retrieved 28 September 2021, from https://www.ncbi.nlm.nih.gov/books/NBK554616/.

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Nathaniel Koh Zhi Hao

Ageing of Motor Neuron

HISTORY OF MOTOR NEURON AGEING

Before we dive into learning more about how aging can affect our motor skills or lead to neurodegenerative diseases, let's take some time to appreciate the father of modern neurology, Jean-Martin Charcot.

Jean-Martin Charcot (1825-1893) was a French neurologist and professor of anatomical pathology.

Image Source: https://www.researchgate.net/figure/Professor-Jean-Martin-Charcot-1825-1893_fig1_321639101

Many of you may have heard of Jean-Martin Charcot, back in your biology science class. Charcot was most well known to everyone with his work on hypnosis, hysteria and the discovery of the localizing function in the brain and spinal cord. Nonetheless, he was also the first to describe and diagnose the first known cases of amyotrophic lateral sclerosis (ALS) as a specific neurological disease in the 1960s. That's why ALS is also known as Charot's disease! Other than ALS, his medical work in many other neurological conditions such as multiple sclerosis, Parkinson Disease (PD) and epilepsy had allowed for further research in the neurology field. He was the first to establish a relationship between the clinical features (i.e. resting tremors) of neurological diseases with the pathological changes in post-mortem autopsies (i.e. looking at the brain of the patients who had passed on). His works and medical accomplishments have opened a path to neuroscience, allowing for the development of potential better diagnostics and therapeutic treatments for those affected by neurodegenerative diseases.

FOREFATHERS OF AGING

When we talk about neurodegenerative diseases such as ALS or Parkinson's Disease (PD), we would often associate it with aging as these diseases often surface as one gets older. For example, we tend to see the elderly getting diagnosed with Alzheimer's Disease (AD) or PD, but not so in the young adults. We often hear people talking about the decline or loss of mobility as they age, but have you wondered who was one of the first men to study aging? He was no other than Élie Metchnikoff.

Elie Metchnikoff (1845-1916) was a Russian Imperial zoologist, best known for his pioneering research in immunology.

Image Source: https://en.wikipedia.org/wiki/%C3%89lie_Metchnikoff

Although Mechnikov was more known for his discoveries in innate immunity, he was also involved in the development of one of the earliest concepts of aging. Did you know he drank sour milk everyday because he had a theory that toxic bacteria in our gut caused aging and that lactic acid produced by probiotic bacteria (like those present in our yogurt drinks) could help slow down aging and improve healthspan? Nevertheless, he was the first to come up with the term "gerontology", which refers to the study of aging and longevity and thus he was often referred to as the father of gerontology. Mechnikov proposed that gerontology is a multidisciplinary study as old age cannot simply

that time, human senescence (i.e. biological aging of our cells) was viewed as a slow, chronic process

nikov then postulated that if these aging processes within the body could be controlled, then one could

enjoy a longer and more productive and healthy life until natural death.

Besides Mechnikov, there were a few other forefathers of aging that had contributed greatly to the gerontology field. One of them was Ignatz Leo Nascher, the founder of "geriatrics". Geriatrics aims to prevent and treat diseases and disabilities associated with old age in older adults and thus improving the health of the elderly.

Ignatz Leo Nascher (1863-1944) was an Austrian-American doctor and gerontologist.

Image Source: https://www.geni.com/people/Ignatz-Nascher/6000000017147442394

Like Mechnikov, Nascher also believed that the pathological aging processes could be reversed. He developed a medical model of aging which attributes the process of aging and death to disease pathologies in senescence (i.e. cell ages and stops dividing). Apart from the medical and biological context of aging, Nascher also suggested that exercise and mental stimulation are important in maintaining vigor of mind and body as one ages.

The passion and hard work in the field of gerontology has led many other researchers around the world to study the biology of human our different organs! With the road of gerontology and neuroscience as well as the intermarriage of

these two fields paved by these amazing forefathers , we are able to better understand the aging of our brain, in particular, motor neurons. In this blog, we hope to share with you about the aging of motor neurons, burst some myths and common misconceptions you may have about motor neuron aging and dive deep into some of the exciting recent research breakthroughs in this field!

REFERENCES

Haas L. F. (2001). Jean Martin Charcot (1825-93) and Jean Baptiste Charcot (1867-1936). *Journal of neurology, neurosurgery, and psychiatry*, *71*(4), 524. https://doi.org/10.1136/jnnp.71.4.524

Kumar, D. R., Aslinia, F., Yale, S. H., & Mazza, J. J. (2011). Jean-martin charcot: The father of neurology. *Clinical Medicine & Research*, *9*(1), 46–49. https://doi.org/10.3121/cmr.2009.883

Mackowiak, P. (2013). Recycling metchnikoff: Probiotics, the intestinal microbiome and the quest for long life. *Frontiers in Public Health*, *1*, 52. https://doi.org/10.3389/fpubh.2013.00052

Martin, D. J., & Gillen, L. L. (2014). Revisiting gerontology's scrapbook: From metchnikoff to the spectrum model of aging. *The Gerontologist*, *54*(1), 51–58. https://doi.org/10.1093/geront/gnt073

Tan, S. Y., & Shigaki, D. (2007). Jean-Martin Charcot (1825-1893): Pathologist who shaped modern neurology. *Singapore Medical Journal*, *48*(5), 383–384.

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Yen See Wai, Steffany

Ageing of Motor Neuron

YTH 1: NEURONS DO NOT REGENERATE

Image Source: Weebly

You've probably heard the saying that adult brains cannot generate any brain cells, and you can only use what you were born with. But is that really true? (Spoiler: We can actually generate brain cells! In a process known as neurogenesis)

In this ground-breaking research, researchers autopsied hippocampi from 28 previously healthy individuals aged 14-70 who had died suddenly. The researchers from Columbia University and New York State Psychiatric Institute found that even the oldest brains they studied produced new brain cells. Nevertheless, older individuals form fewer new blood vessels within brain structures and have reduced cell-to-cell connectivity. All of these could have contributed to the reduced cognitive-emotional resilience in old age.

Another Spain study further analysed the brain tissues from 45 patients aged 52 to 97 who had been diagnosed with Alzheimer's before death. Surprisingly, even in these individuals, fresh brain cells were found, including in the oldest 97 year old individual, even though their brains only had between half and three quarters as many fresh neurons as individuals with healthy brains. Perhaps, with this new discovery, if brain scans can one day detect newly-formed brain cells as a marker for early diagnosis of Alzheimer's disease, then there might be potential to prevent or delay the onset of cognitive symptoms of Alzheimer.

Citation:

Cell Press. (2018). Older adults grow just as many new brain cells as young people. www.sciencedaily.com/releases/2018/04/180405223413.htm

Moreno-Jiménez, E. P., Flor-García, M., Terreros-Roncal, J., Rábano, A., Cafini, F., Pallas-Bazarra, N., Ávila, J., & Llorens-Martín, M. (2019). Adult hippocampal neurogenesis is abundant in neurologically healthy subjects and drops sharply in patients with Alzheimer's disease. Nature medicine, 25(4), 554–560. https://doi.org/10.1038/s41591-019-0375-9

MYTH 2: SUPPLEMENTS IMPROVE OUR BRAIN HEALTH

Image Source: https://www.dreamstime.com/healthy-diet-proper-nutrition-supplements-vitamins-cartoon-style-vector-illustration-healthy-diet-proper-nutrition-supplements-image192763739

A recent survey found that about 25% of adults over age 50 take a supplement to improve their brain health with the promise of enhanced memory and sharper attention and focus. Herein lies the problem: there is no solid proof that any of them work.

There's strong evidence that certain diets — like the Mediterranean diet and the DASH diet (rich in vegetables, fruits and whole grains) -

, according to Dr. Gad Marshall, associate medical director at the Center for Alzheimer Research and

Treatment at Harvard-affiliated Brigham and Women's Hospital. "These diets contain foods with large amounts of these vitamins and minerals," he says. "But what is not clear is whether it's the combination of nutrients in these diets that's beneficial, or whether it's specific ones or even certain amounts, or some other factors." Moreover, there has been limited studies and evidence to show that the isolated vitamins or supplements improve brain health.

A familiar instance to us would be the omega-3-fatty acids, otherwise known as fish oil, a staple in many diets and commonly found in fatty fish like salmon and mackerel, as well as in leafy green vegetables, vegetable oils, nuts and seeds. Studies have found an association between higher intake of fish and a lower risk of cognitive decline. However, omega-3 supplements haven't shown the same effect. In fact, any benefit seems to come from a greater intake of fish and not from taking fish oil supplements.

Given the lack of evidence on the benefits of expensive supplements, perhaps the next time you're intending to take a pill of supplement, why don't you consider investing in making lasting lifestyle changes like exercising and following a plant-based diet instead?

Citation:

Gestuvo, M., & Hung, W. (2012). Common dietary supplements for cognitive health. Aging health, 8(1), 89–97. https://doi.org/10.2217/AHE.11.92

Global Council on Brain Health. (2019). "The Real Deal on Brain Health Supplements: GCBH Recommendations on Vitamins, Minerals, and Other Dietary Supplements." http://www.GlobalCouncilOnBrainHealth.org.

Harvard Health Publishing. (2019). Don't buy into brain health supplements. https://www.health.harvard.edu/mind-and-mood/dont-buy-into-brain-health-supplements

MYTH 3: ALL OUR COGNITIVE FUNCTIONS DECLINE AS WE AGE BECAUSE OF SIGNIFICANT LOSS OF NEURONS

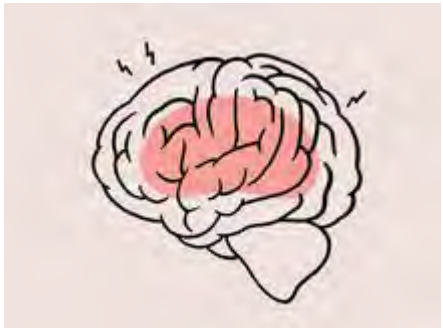

Image Source: https://www.healthline.com/health/depression-physical-effects-on-the-brain#Brain-inflammation

"The older we grow, the wiser we become" – a saying we're all acquainted with, and perhaps, there is some element of truth in it.

Cognition refers to the way we think, and encompasses many different types of thinking skills. For instance, the speed at which we can respond (processing speed), our ability to remember objects (general memory), and our knowledge of words and their meaning (vocabulary knowledge). These cognitive domains show different patterns of change across adulthood.

Findings from 1950s to 1980s regarding loss of neurons in the brain suggested that we lose about 1% of our brain cells every year throughout our adulthood. This would amount to a shocking 35% to 55% loss of neurons in our brains by the time we are in our 70s and 80s! These findings in the earlier days had led to the misconception that the loss of neurons in our brains was part and parcel of human ageing and was the contributing factor to cognitive declines such as processing speed and general memory in our old age.

Thankfully, it is now proven (with more modern techniques) that these early estimates did not take into account age-related brain shrinkage. In fact, we have minimal loss of neurons with ageing, with an estimate of about only 2% to 4% across our lifespans! In actuality,

only when we have neurodegenerative diseases (such as Alzheimer's disease, Parkinson's disease and

others). Hence, if we age without neurodegenerative diseases, we do not lose a significant amount of neurons! This explains why some of our cognitive functions such as vocabulary knowledge does not decline with age. On average, we will reach our peak word knowledge in our 60s, and our performance will not markedly decline after that. Besides conventional wisdom, older people also score higher on tests of social wisdom. For instance, when given a biographical sketch of a stranger, they are better judges of character. Moreover, they are also more tactful at settling a conflict and can better regulate their own emotions and find meaning in their lives. Seems like we truly do become wiser, the older we grow!

So what leads to the prevalent cognitive decline in the aged? It is actually because of changes at the synapses of neurons that are still alive. The good thing is, since neurons are still alive, therapeutically-speaking, we can still aim to intervene in a way that makes these synapses healthy again!

Citation:

Kavé, G., & Yafé, R. (2014). Performance of younger and older adults on tests of word knowledge and word retrieval: independence or interdependence of skills?. American journal of speech-language pathology, 23(1), 36–45. https://doi.org/10.1044/1058-0360(2013/12-0136)

Murman D. L. (2015). The Impact of Age on Cognition. Seminars in hearing, 36(3), 111–121. https://doi.org/10.1055/s-0035-1555115

National Institute of Neurological Disorders and Stroke. (n.d.) https://www.ninds.nih.gov/Disorders/Patient-Caregiver-Education/Life-and-Death-Neuron

Peters R. (2006). Ageing and the brain. Postgraduate medical journal, 82(964), 84–88. https://doi.org/10.1136/pgmj.2005.036665

YTH 4: ONLY OLDER PEOPLE GET ALS

Image Source: https://alsnewstoday.com/social-clips/2017/10/06/explaining-progression-als-2/

According to the ALS Association, most people who develop ALS are between the ages of 40 and 70, with the mean age of 55 at the time of diagnosis. A recent study has also shown that normal aging could be an important contributor to ALS. However, it is likely alongside other influences such as genetic, lifestyle and environmental factors. While it is true that ALS is more common amongst the middle age and elderly population, it is not true that only the older population can get ALS!

In fact, symptoms can strike at any age. Even those in their young 20s and 30s can get ALS as well! One such person is the famous physicist Stephen Hawking who had a rare early-onset of ALS. He was diagnosed at the age of 21 and lived with the disease for over 50 years! We still do not know why ALS strikes some individuals and not others. In other words, the causes of ALS are still in the debates, but evidence from researches are pointing towards both genetics and environment!

Citation:

ALS Association (n.d.). Who gets ALS? https://www.als.org/understanding-als/who-gets-als

National Institute of Neurological Disorders and Stroke. (2013). Amyotrophic Lateral Sclerosis (ALS) Fact Sheet | National Institute of Neurological Disorders and Stroke. Nih.gov. https://www.ninds.nih.gov/Disorders/Patient-Caregiver-Education/Fact-Sheets/Amyotrophic-Lateral-Sclerosis-ALS-Fact-Sheet

Pandya, V. A., Patani, R. (2019). Decoding the relationship between ageing and amyotrophic lateral sclerosis: a cellular perspective. Brain, 143(4), 1057–1072. https://doi.org/10.1093/brain/awz360

MYTH 5: ALL MOTOR NEURON DISEASES ARE HEREDITARY

Image Source: https://www.istockphoto.com/es/vector/hombre-en-silla-de-ruedas-gm1310222238-399697651

Unbeknownst to all, most people who develop Motor Neuron Disease (MND) have no family history of MND. Spinal Muscular Atrophy (SMA) which causes progressive muscle degeneration and weakness in children, is one of the rare forms of MND that is inherited. While SMA is always hereditary, it is not true that all other forms of MND are hereditary as well.

Interestingly, only about 10% of all MND cases are actually hereditary, with the other 90% happening sporadically. There are no actual defining causes of MND identified just yet! However, instead of just a single cause, it is believed that many different factors are actually at play when it comes to the development of sporadic MND.

Some possible factors suggested thus far are exposure to chemicals and toxins, engaging in strenuous physical activities, recurrent head trauma and smoking.

t regular strenuous exercise increase the risk of developing ALS in people who are genetically

predisposed to them. (Before this discovery, exercise as a risk factor for ALS has been considered controversial). This has led to the next steps of developing tests to identify people most at risk and also to further discover environmental risk factors which also predisposes one to MND.

Finding out the causes of motor neuron deaths in sporadic MND is paramount in bringing us tremendously closer to developing more effective, and hopefully even curative, treatments or to come up with preventive measures!

Citation:

Better Health. (n.d.) Motor Neuron Disease (MND). https://www.betterhealth.vic.gov.au/health/conditionsandtreatments/motor-neurone-disease#causes-of-mnd

Julian T.H., Glascow N., Barry A.D.F., Moll T., Harvey C., Klimentidis Y.C., Newell M., Zhang S., Snyder M.P., Cooper-Knock J., Shaw P.J. (2021). Physical exercise is a risk factor for amyotrophic lateral sclerosis: Convergent evidence from Mendelian randomisation, transcriptomics and risk genotypes. https://doi.org/10.1016/j.ebiom.2021.103397

Kolb, S. J., & Kissel, J. T. (2015). Spinal Muscular Atrophy. Neurologic clinics, 33(4), 831–846. https://doi.org/10.1016/j.ncl.2015.07.004

McDermott, C. J., & Shaw, P. J. (2008). Diagnosis and management of motor neurone disease. BMJ (Clinical research ed.), 336(7645), 658–662. https://doi.org/10.1136/bmj.39493.511759.BE

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Loh Jia Hui & Ho Hui Tong

MECHANISMS THAT CAUSE THE AGEING OF MOTOR NEURON

and health complications such as diabetes, cataracts and strained mobility (WHO *Ageing and Health*,

n.d.), the decrease in the capacity of the motor neuron is just one of the many. In this case, we define ageing as the breakdown in communication between the brain which acts as the transmitter of the motor neurons, the peripheral nervous system and finally the skeletal muscles which are the final receiver of the motor neurons. This relationship between the motor neurons and its respective transmitters and receivers mirrors that of a wifi router and its connecting devices. Just like the wifi router that sends a signal to its respective devices for them to receive, the brain and peripheral nervous system also delivers a similar signal via a motor neuron to allow for the muscles to receive and respond accordingly. The presence of poor wifi reception due to the presence of multiple competing devices or random networks nearby is likewise similar to the failure of communication between motor neurons and its receptors due to possibly an increase in neural noise and random background activities (Hong & Rebec, 2012).

In both cases these irregular background noises create erratic signals to the receiving ends, resulting in the failure to deliver the desired signals. The direct effect of ageing on neural noise has yet to be determined, however studies have shown direct relations between factors of ageing and increase in neural noise. One such example would be the increase in glutamate upon ageing and the eventual accumulation of it around the neurons, resulting in the failure of signal transmission (Farrand et al., 2015).

Image source: http://www.clker.com/clipart-146809.html

Neurotransmitters and aging

Neurotransmitters are chemical messengers of the body that carry messages from neuron to neuron or neuron to muscle. During old age, the terminal endings of our nerves release larger amounts of neurotransmitters when stimulated. Although this seems like an effective way to improve message transmission at our neuromuscular junctions, it has actually been observed to cause a faster rate of neuromuscular failure.

Excitatory receptors receive chemical signals to bring about movement, while inhibitory receptors receive signals to stop movement. As we age, adenosine receptors in our neurons become modified such that the number of excitatory adenosine receptors increases while inhibitory adenosine receptors decrease. These receptors are crucial in controlling responses to stimulation. Changes in their ratios cause our neuromuscular junctions to preferentially select to activate inhibitory receptors instead of excitatory receptors as we age (Manini et al., 2013). This decreases excitatory neural function and decreases the ability to produce muscle force.

Mitochondria dysfunction, oxidative stress and aging

Mitochondria play crucial roles in energy production, metabolism and cell death. They also buffer calcium ion loads in the cell responsible for excitation-contraction signalling in neurons.

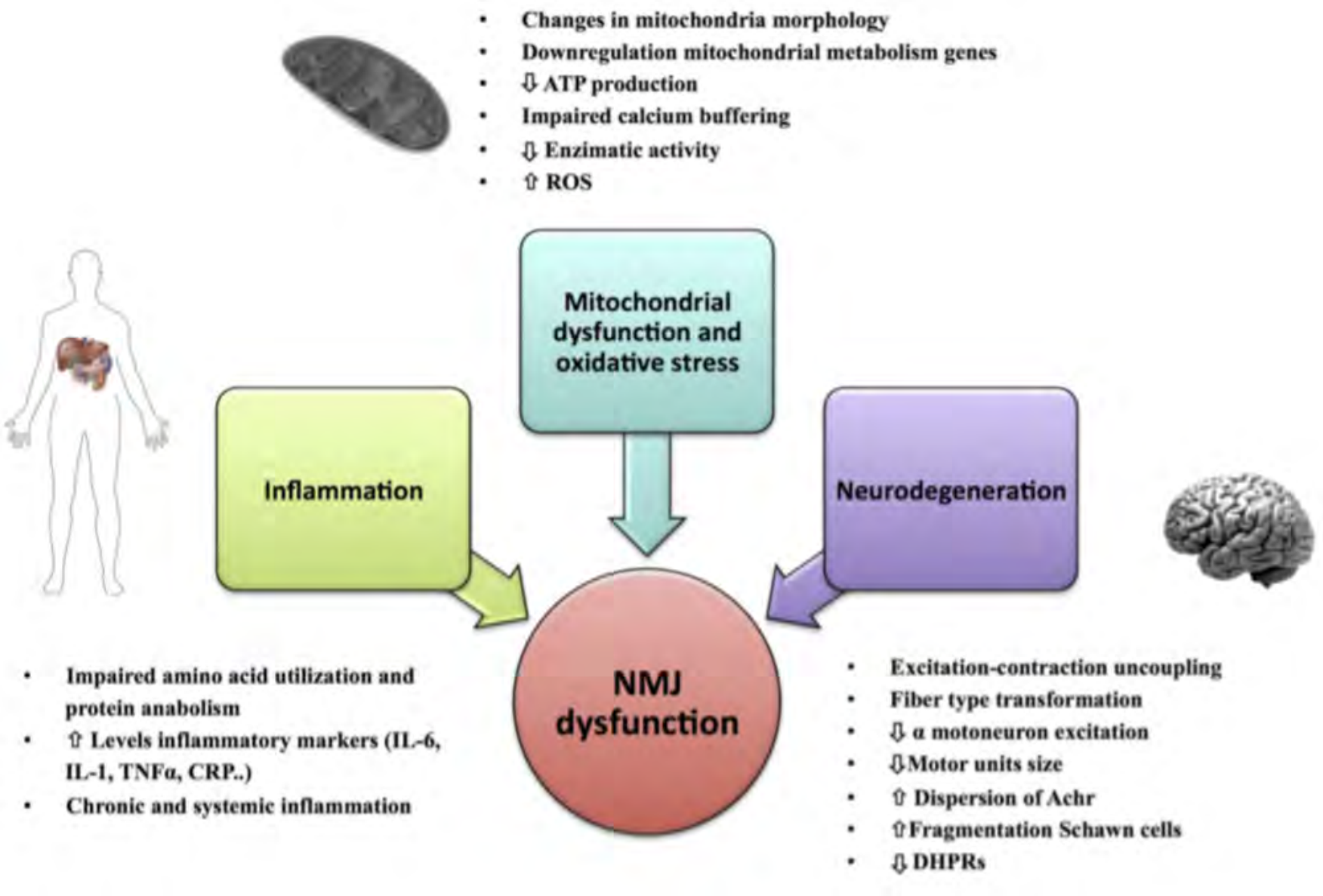
As we age, declines in number and function of mitochondria cause increased levels of oxidation. Mitochondrial nitric oxide and hydrogen peroxide accumulate in the mitochondria, and these reactive oxygen species cause oxidative stress. This may go on to damage axons, initiating degeneration. Schwann cells, which are key players in our peripheral nervous system, are rich in fatty acids, causing them to be major substrates for reactive oxygen species and thus vulnerable to accumulation of oxidative damage (Manini et al., 2013).

Myelinated peripheral nerves were also found to be oxidatively damaged during aging. This causes inflammation, and increases accumulation of aggregated proteins (misfolded protein clusters), lipofuscin (found in lysosome) adducts (Jang & Van Remmen, 2011). As such, high oxidative stress affects neuromuscular maintenance.

Inflammation and ageing

ased levels of inflammation, which is measured by increased levels of inflammatory “markers” in the

blood and tissues, such as interleukin 6 (IL-6), interleukin 1 (IL-1), tumor necrosis factor alpha (TNF-alpha), and C-reactive protein. Schwann cell senescence has been associated with increased IL-6, suggesting roles of inflammation in age-related changes in axon regeneration (Gonzalez-Freire et al., 2014).



The Neuromuscular Junction: Aging at the Crossroad between Nerves and Muscle

Image source: https://pubmed.ncbi.nlm.nih.gov/25157231/

References

Ageing and health. (n.d.). Retrieved 5 October 2021, from https://www.who.int/news-room/fact-sheets/detail/ageing-and-health

Farrand, A. Q., Gregory, R. A., Scofield, M. D., Helke, K. L., & Boger, H. A. (2015). Effects of aging on glutamate neurotransmission in the substantia nigra of Gdnf heterozygous mice. *Neurobiology of Aging*, *36*(3), 1569–1576. https://doi.org/10.1016/j.neurobiolaging.2014.11.017

Hong, S. L., & Rebec, G. V. (2012). A new perspective on behavioral inconsistency and neural noise in aging: Compensatory speeding of neural communication. *Frontiers in Aging Neuroscience*, *4*. https://doi.org/10.3389/fnagi.2012.00027

Gonzalez-Freire, M., de Cabo, R., Studenski, S. A., & Ferrucci, L. (2014). The Neuromuscular Junction: Aging at the crossroad between nerves and muscle. *Frontiers in Aging Neuroscience*, *6*. https://doi.org/10.3389/fnagi.2014.00208

Manini, T. M., Hong, S. L., & Clark, B. C. (2013). Aging and muscle. *Current Opinion in Clinical Nutrition and Metabolic Care*, *16*(1), 21–26. https://doi.org/10.1097/mco.0b013e32835b5880

Jang, Y. C., & Van Remmen, H. (2011). Age-associated alterations of the neuromuscular junction. *Experimental Gerontology*, *46*(2-3), 193–198. https://doi.org/10.1016/j.exger.2010.08.029

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Ageing of Motor Neuron

MOTOR NEURON DISEASES

JRON DISEASE AND WHY DOES IT MATTER TO ME?

Motor Neuron Diseases (MNDs) is a rare disease that affects the nervous system, especially the brain. MNDs causes weakness and even paralysis over time resulting in difficulty in daily activities. Although some people are able to survive for years with MND, they would eventually succumb to its debilitation and pass away (NHS, n.d.). There are currently no known cures for MNDs but several treatments exist to help curb the symptoms posed to help reduce the burden it has on a person's daily life - we tackle these progress in research on the Blog page, so do take a look after going through the following subpages below.

Although Motor Neuron Diseases (MNDs) are rare, they are still detrimental to the people who suffer from them. Conditions like Amyotrophic Lateral Sclerosis saw the rise of using internet culture to bring awareness to the debilitating disease with the ice bucket challenge. The challenge had people pour a bucket of ice water on themselves and nominate friends to do the challenge as well as donate to ALS research. Before the challenge, there was little publicity about the disease apart from notable figures like Lou Gehrig, Stephen Hawkings and Mao Zedong.

In this section, we aim to share with you several facts about notable MNDs as well as their symptoms.
We have a long way to go in MND research, so we hope to inspire you to pursue research in these diseases as well!

ALZHEIMER'S DISEASE

PARKINSON DISEASE

HUNTINGTON'S DISEASE

AMYOTROPHIC LATERAL SCLEROSIS

PRIMARY LATERAL SCLEROSIS

References

NHS. (n.d.). *Motor Neurone Disease*. NHS choices. Retrieved September 19, 2021, from https://www.nhs.uk/conditions/motor-neurone-disease/.

Header image reference: https://cpb-ap-se2.wpmucdn.com/blogs.auckland.ac.nz/dist/2/96/files/2021/05/robina-weermeijer-IHfOpAzzjHM-unsplash-1080x675.jpg

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Ageing of Motor Neuron

ALZHEIMER'S DISEASE

r's Disease?

Alzheimer disease (AD) is a progressive neurodegenerative disease and is the cause of the majority of dementia cases.

Patients with AD experience the loss of memory, speech problems, poor judgements, and other symptoms. Even though AD itself is not fatal, the complications that arise due to the lack of ability to take care of oneself can be fatal.

Hence this resulted in AD being ranked as the top 7 cause of death in the world.

Image Source: https://www.associazionepropsy.org/lalzheimer-aspetti-psicologici/

Most of the people diagnosed are 65 years old and above.

WHAT ARE THE SYMPTOMS OF ALZHEIMER'S DISEASE

1. Memory Loss

An early sign of Alzheimer's disease is forgetting information that were learned shortly. Others include the need to repeat the same questions multiple times or forgetting important dates.

2. Difficulties in managing familiar tasks

Alzheimer's patient usually have difficulty completing daily tasks such as remembering the controls for the TV or even the usage of a microwave.

3. Problems with speech

Patients usually have trouble participating in conversations. They may have difficulty recalling certain words that are normally used.

4. Misinterpretation of time and places

For some people, they might lose track of the current season, date and time. Occasionally, they may also forget how they end up at their current location.

5. Frequent mood swings

People with Alzheimer's tend to experience sudden mood swings and personality changes. Extreme emotions such as depression, confusion or anxiousness might also be experienced.

6. Poor judgement

A person living with Alzheimer's may have trouble in judgement or decision making. They might not be able to judge distance or provide less care for their personal grooming.

IMAGE REFERENCES

WHAT CAUSES ALZHEIMER'S DISEASE?

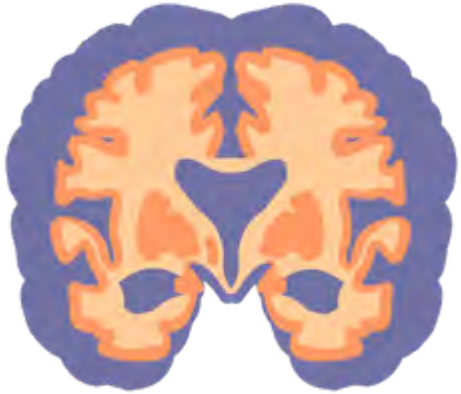

Image Source: https://favpng.com/png_view/symmetry-orange-cartoon-brain-png/C28cTMP8

AD is caused by the abnormal accumulation of the protein fragments in the brain. One of the proteins is known as beta-amyloid plaques which build up outside the neurons.

Another protein is known as protein tau which builds up and tangles inside the neurons.

The beta-amyloid plaques and tau result in the death of the neurons by preventing neuron to neuron communication and preventing transport of essential nutrients to neurons respectively.

How can Alzheimer's be treated?

AD cannot be definitively diagnosed until after death.

series of tests to

make a diagnosis. These tests include problem-solving tests, memory tests, blood tests and brain imaging. Inputs from family members on patients' behaviour and family medical history can also be useful. Even though there is no cure for AD, there are medications to manage the symptoms.

With 99% clinical trials of AD drug development ending up in failure, aducanumab is the only approved medication used to treat AD. However, as aducanumab has been approved under the accelerated approval pathway, the true effectiveness of this treatment has yet to be unveiled.

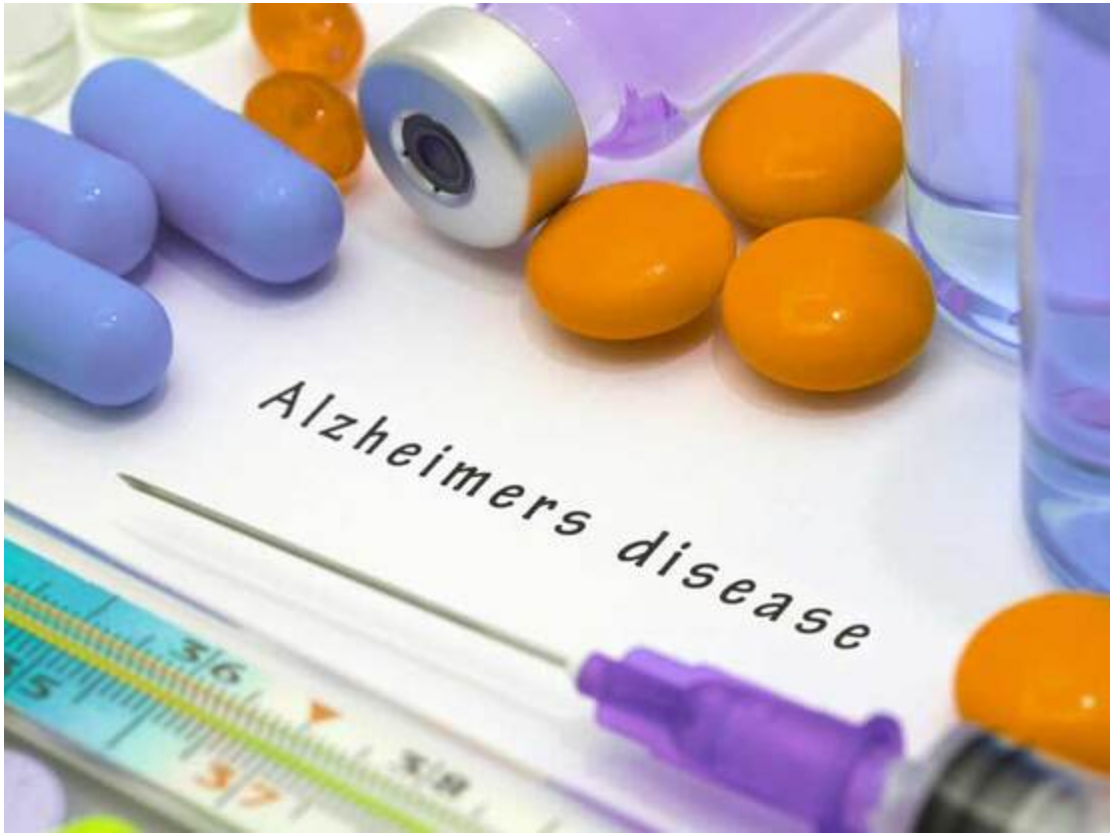

Image Source: https://mangyte.vn/news-khong-tu-y-mua-thuoc-dieu-tri-alzheimer-613900.html

SEVERITY OF ALZHEIMER'S DISEASE

Image Source: https://www.hide-fujino.com/blog/2006/04/11/53431/

Severe dementia due to AD resulting in the lack of self-care can cause complications such as malnutrition and prolonged confinement to bed. Such complications drastically increase the risk of acute conditions that can result in death. One such example is pneumonia, the most common cause of death among patients with AD.

In 2019, the World Health Organisation reported that AD together with other types of dementia is ranked as the 7th leading cause of death. However, this may be underestimated. AD patients that passed on due to pneumonia may have their primary cause of death listed as pneumonia rather than AD even though AD have in fact caused the acute condition.

REFERENCES

Alzheimer’s Association (2021). 2021 Alzheimer's disease facts and figures. *Alzheimer's & Dementia*, *17*(3), 327–406. https://doi.org/10.1002/alz.12328

Cummings, J. L., Morstorf, T., & Zhong, K. (2014). Alzheimer’s disease drug-development pipeline: few candidates, frequent failures. *Alzheimer's research & therapy*, *6*(4), 1-7.

Header Image Source: https://theuncoverreality.in/2021/07/22/evidence-of-sustained-benefits-of-pimavanserin-for-dementia-related-psychosis-medicine/

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Ageing of Motor Neuron

PARKINSON'S DISEASE

n's Disease?

Parkinson disease (PD) is a progressive neurodegenerative disease that affects movements. Patients with PD experience tremors, muscle stiffness, problems in balancing and other symptoms.

Even though the disease itself is not fatal, complications due to the higher risks of falls can be fatal. Being the fastest growing neurological disorder, PD raises a concern as experts predict the number of people with PD to reach 12 million by 2040.

Image Source: https://photostockeditor.com/clip-art-vector/download/995735910

People that are diagnosed with PD are usually people of age 60 and older.

Males are also more likely to have PD as compared to females.

WHAT ARE THE SYMPTOMS OF PARKINSON'S DISEASE

1. Tremors

An early sign of Parkinson's disease is having tremors on the hand at rest. However, shaking can also be normal after vigorous exercise, high level of stress, or after an injury.

2. Slowed movements

Parkinson's patient experience a slow down in motor movement, Bradykinesia. Motor coordination such as buttoning a shirt or slow handwriting are signs of bradykinesia.

3. Loss of smell

Patients usually have trouble picking up certain scents. Patients can no longer recognise everyday food through the use of smell.

4. Dizziness

For some people, they might experience frequent dizziness and a loss of balance when they stand up after sitting for a period of time. This indicates a low blood pressure which is connected to Parkinson's disease.

5. Masked face

People with Parkinson's disease have a serious, depressed or angry look to their face when they are at rest. This occurs even if one is not in a bad mood.

6. Sleep problems

A person living with Alzheimer's may have trouble falling asleep, experiencing insomnia. Some on the other hand might have intense dreams.

IMAGE REFERENCES

WHAT CAUSES PARKINSON'S DISEASE?

Image Source: https://www.differencebetween.com/difference-between-parkinsons-and-myasthenia-gravis/

PD is caused by the damage of nerve cells responsible for producing dopamine. However, the reason for the destruction of nerve cells is unknown. Ongoing research is still being done to understand the cause.

How can Parkinson's be treated?

Similar to AD, there is no definitive test to diagnose PD. Specialists would have to diagnose based on medical histories, symptoms and doing physical and

There is however, no cure for PD.

Often, medications such as these can be taken to reduce your symptoms. One common and effective medication taken is Carbidopa-levodopa. Levodopa is a chemical that can be converted to dopamine whereas Carbidopa can prevent levodopa from converting outside the brain. With increased levels of dopamine, the symptoms will be greatly reduced.

Image Source: http://indoamericanhospital.in/blog/best-spine-hospitals-kerala/

SEVERITY OF PARKINSON'S DISEASE

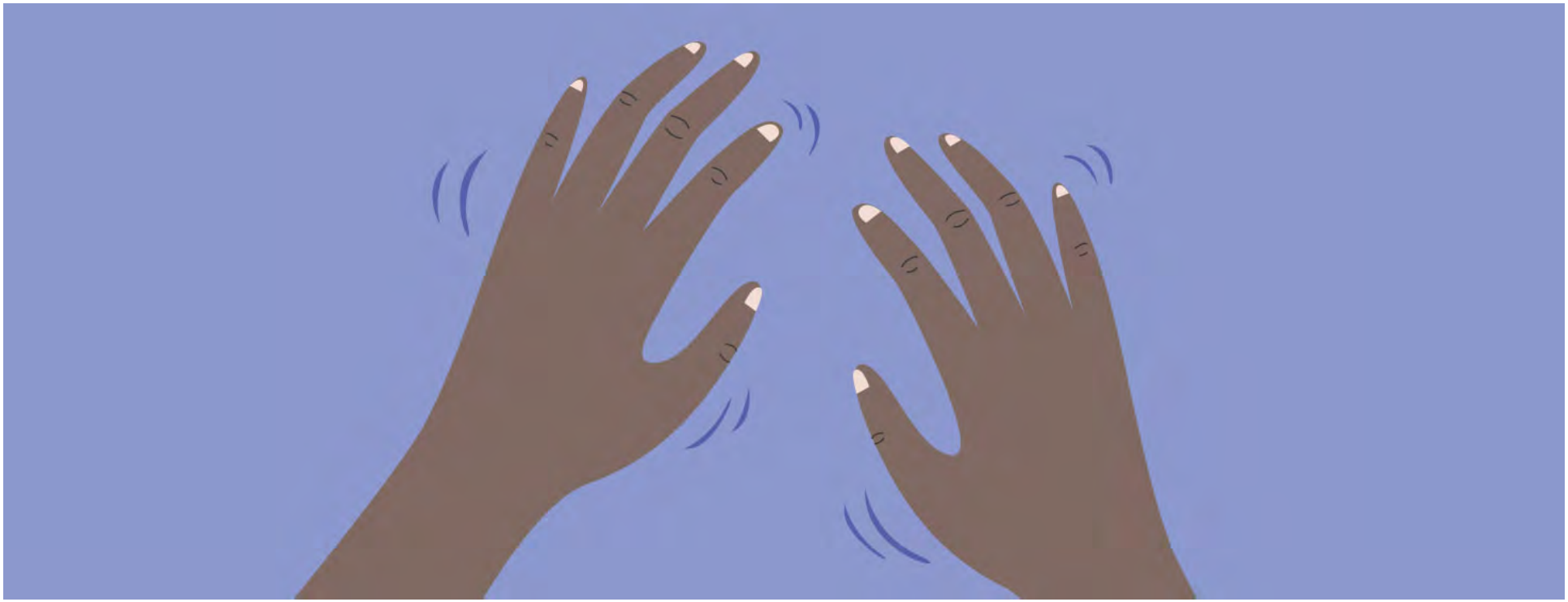

Image Sources: https://parkinsonsdisease.net/answers/differences-essential-tremor

Even though PD itself is not fatal, complications resulting from PD can be fatal. Due to the impaired movement, falls is one of the most common cause of death among PD patients. Fatality can happen due to serious falls or during surgery to treat the injuries.

PD is known to be the fastest growing neurological disorder in the world. The number of people with PD doubled to over 6 million from 1990 to 2015. It is estimated that this number will continue to increase due to ageing of the baby boomer generation. The number is estimated to double again to over 12 million by 2040.

REFERENCES

Dorsey, E. R., Sherer, T., Okun, M. S., & Bloem, B. R. (2018). The emerging evidence of the parkinson pandemic. Journal of Parkinson's Disease, 8(s1). https://doi.org/10.3233/jpd-181474

Mayo Foundation for Medical Education and Research. (2020, December 8). Parkinson's disease. Mayo Clinic. Retrieved September 29, 2021, from https://www.mayoclinic.org/diseases-conditions/parkinsons-disease/symptoms-causes/syc-20376055.

Header Image Source: https://eliteayurveda.com/blog/causes-and-risk-factors-that-influence-parkinsons-disease/

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Ageing of Motor Neuron

HUNTINGTON'S DISEASE

ɔn's disease?

Huntington's disease is an inherited disease that results in the degeneration of nerve cells in the brain.

This disease usually appears in people who are in their thirties or forties. Huntington's disease usually diminishes a person's ability to perform normal daily activities such as thinking and moving.

Image source: https://post.medicalnewstoday.com/wp-content/uploads/sites/3/2020/05/GettyImages-1188431917_thumb-732x549.jpg

Individuals with a parent having Huntington's disease are at a high risk of inheriting it. Although the disease usually appears in the thirties or forties, there are instances where the disease begins in childhood.

WHAT ARE THE SYMPTOMS OF HUNTINGTON'S DISEASE

1. Difficulty in moving

Some individuals might not experience uncontrolled movement but develop difficulty in muscle movement instead. This rigidity in muscles increases the chance of falling which might result in severe injuries to individuals.

2. Uncontrolled movement in muscles

People with Huntington's disease would experience involuntary and unpredictable muscle movements. This usually occurs when individuals are feeling anxious or distracted.

3. Slurred speech

Neuromuscular disorders usually result in the slurring of speech. Individuals often find it difficult to pronounce certain words or mumble in the middle of conversations.

4. Lethargic in daily activities

Individuals with Huntington's disease are usually lethargic. The lack of energy is potentially due to the lack of sleep which arises from insomnia.

5. Cognitive & Judgement changes

As the disease progresses, individuals often have difficulties with their judgement or decision making. This might be reflected in the difficulty in driving, prioritising unimportant task or even the inability to learn new things.

6. Cognitive & Behavioural changes

A change in behaviour is usually noticed as an early sign of Huntington's disease. Individuals commonly experience mood swings and depression that may cause sudden hostile outburst or even suicidal thoughts.

IMAGE REFERENCES

WHAT CAUSES HUNTINGTON'S DISEASE?

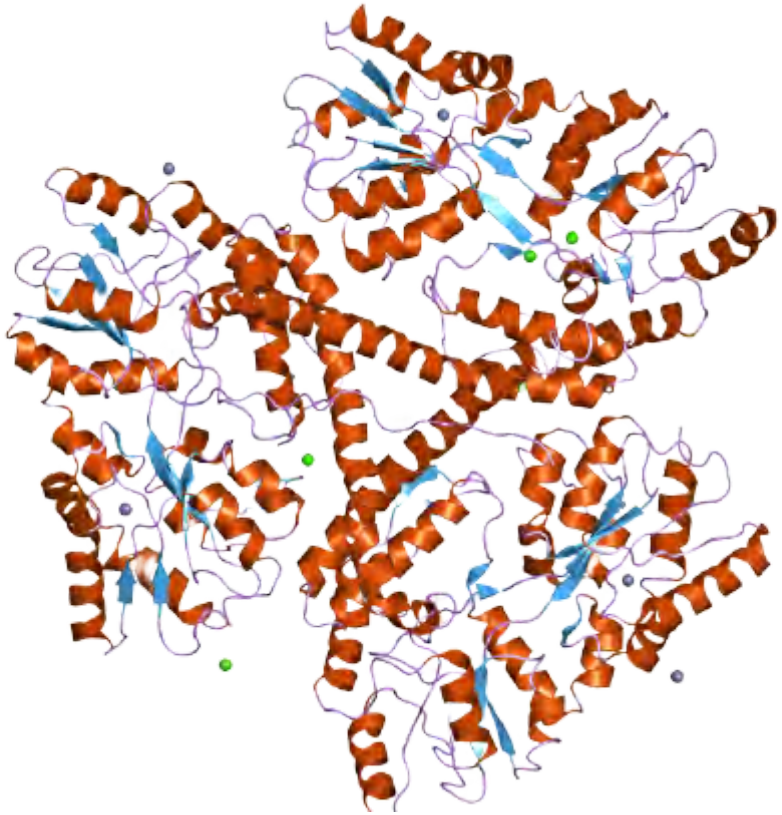

Image source: https://banner2.cleanpng.com/20180418/jrw/kisspng-huntingtin-huntington-s-disease-mutation-antisense-dendrite-5ad808dbc1d012.8140358115241074837939.jpg

HD is an inherited genetic disease that is passed down from parent to child.

A mutation in chromosome 4 is responsible for Huntington's disease. If a HD parent decides to have a child, there is a 50% chance that the child inherits this chromosome 4 carrying the mutation resulting in a child with HD. However, if the child does not have HD, the child will

not develop the disease or pass it to the next generation.

How can Huntington's disease be treated?

Although there is no direct treatment for HD, there are medications to help curb the symptoms.

Such treatment usually involves modulating the neurotransmitter which can help control both emotional and movement difficulties.

Antipsychotic drugs such as risperidone/olanzapine or haloperidol are used to mitigate uncontrolled movement as well as emotional outburst.

However, these drugs would worsen the condition of patients with difficulty in muscle contractions. Drugs used are susceptible to side effects that causes further fatigue. Hence, these medications are only to be taken during a symptom outburst.

Image source: https://www.pharmalive.com/wp-content/uploads/2020/08/uniQure-Begins-First-in-Human-Gene-Therapy-Trials-for-Huntington%E2%80%99s-Disease-BioSpace-8-4-20.jpeg

SEVERITY OF HUNTINGTON'S DISEASE

Image source: https://c.neh.tw/thumb/f/720/comhiclipartixagi.jpg

Individuals with adult-onset Huntington's disease usually have a live about 10 to 30 years left after signs and symptoms start to arise. This could be further escalated if the individuals sustain heavy injuries from falling or gets an infection.

[illegible] more progressive as compared to adult-onset counterpart. Hence, adolescent who shows sign of

Huntington’s disease usually only able to live for another 10 to 15 years.

References:

National Institute of Neurological Disorders and Stroke (2020), Huntington's Disease: Hope Through Research. National institute of health (20-NS-19). https://www.ninds.nih.gov/Disorders/Patient-Caregiver-Education/Hope-Through-Research/Huntingtons-Disease-Hope-Through

Header image source: https://d3b6u46udi9ohd.cloudfront.net/wp-content/uploads/2019/11/01061906/living-iwth-huntingtons.png

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Ageing of Motor Neuron

AMYOTROPHIC LATERAL SCLEROSIS

lateral sclerosis?

Amyotrophic lateral sclerosis (ALS) is a progressive nervous system disease that is caused by damage to both the upper motor neuron and the lower motor neuron.

ALS is also often termed as the Lou Gehrig's disease named after a baseball player who was diagnosed with it.

This progressive disease begins with muscle twitching and usually progresses up to the inability to eat, breathe, talk and move, ultimately leading to fatality.

image source:

https://upload.wikimedia.org/wikipedia/commons/thumb/3/36/Using_a_head_mounted_laser_to_point_to_a_communication_board.jpg/290px-Using_a_head_mounted_laser_to_point_to_a_communication_board.jpg

The average age of diagnosis is around 55 with ages ranging from 40 to 75.

WHAT ARE THE SYMPTOMS OF AMYOTROPHIC LATERAL SCLEROSIS

1. Difficulty in walking

The first signs of ALS usually appears on your lower limb starting with one leg. Walking tend to feel awkward which might result in falling down.

2. Clumsiness in hand movement

ALS patients might also experience early signs beginning with their arms. Grip strength becomes inconsistent and patients might drop items uncontrollably.

3. Slurred speech

Patients usually have trouble participating in conversation. They may have difficulty pronunciating certain words that are normally used.

4. Swallowing difficulties

Difficulty in swallowing arises in later stages of the disease, also known as dysphagia.

5. Abnormal twitching

Patients with ALS might experience sudden abrupt twitching in muscles such as the arms, shoulders or tongue.

6. Cognitive & Behavioural changes

A person living with ALS tend to go through various changes in emotions despite a lack of stimulus.

IMAGE REFERENCES

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WHAT CAUSES AMYOTROPHIC LATERAL SCLEROSIS?

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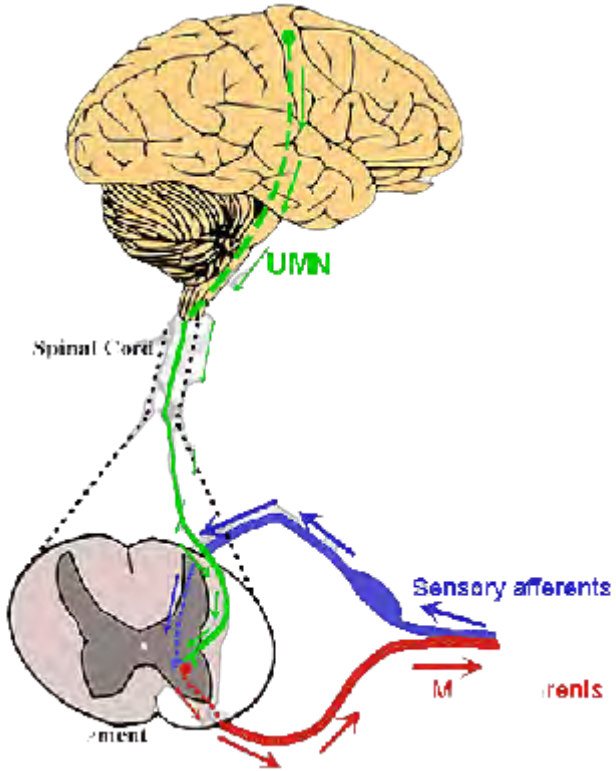

Image sources: https://e7.pngegg.com/pngimages/38/691/png-clipart-brain-amyotrophic-lateral-sclerosis-upper-motor-neuron-lower-motor-neuron-brain-brain-amyotrophic-lateral-sclerosis.png

5~10% of ALS is believed to be inherited leaving the remaining cases to be unknown as of today. However, researchers believe that it could possibly be due to complicated interactions between genetic and environmental factors.

Such environmental factors usually involve the exposure to harmful chemical substances to the body such as nicotine from smoking or other forms of toxin in the environment.

How can ALS be treated?

As of today, there is no cure for lateral sclerosis.

However, progress has been made to curb the symptoms of the illness. A recent finding in early 2021 discovered a drug, AMX0035, that could potentially help extend patients' life expectancy to up to five years. However, the drug is currently still undergoing a phase 3 trial due to the strict policy laid down by the Food and Drug administration.

22 drugs were reported to perform vastly differently in phase 3 to phase 2 in a 2017 FDA report thus solidifying their stand.

Hence, clinical usage for AMX0035 is still far off from practical especially with the long duration required to gather data from the patients.

Image source: https://www.israel21c.org/wp-content/uploads/2017/05/shutterstock_als-768x432.jpg

SEVERITY OF AMYOTROPHIC LATERAL SCLEROSIS DISEASE

Image source: https://w7.pngwing.com/pngs/834/148/png-transparent-hemiplegia-paralysis-cerebrovascular-disease-cerebral-infarction-mahi-mahi-child-toddler-boy.png

There are currently no possible cure for ALS but only treatments towards the general symptoms.

ALS progression is categorised into three stages: early, middle and late. Early symptoms mainly include weakness in muscles in the outer limbs such as hands or legs. Middle symptoms are accompanied with loss of muscle function, usually experiencing muscle paralysis. During

late stages, individuals are mostly paralysed including crucial muscles in the mouth, throat and those involve in breathing. Individuals usually only have 3-5 years remaining once late symptoms starts arising.

References:

National Institute of Neurological Disorders and Stroke (2021). Amyotrophic Lateral Sclerosis (ALS) Fact Sheet. (16-916) https://www.ninds.nih.gov/Disorders/Patient-Caregiver-Education/Fact-Sheets/Amyotrophic-Lateral-Sclerosis-ALS-Fact-Sheet

Sabrina Paganoni MD et al (2021). AMX0035 in Patients With Amyotrophic Lateral Sclerosis, from https://clinicaltrials.gov/ct2/show/NCT03127514.

Header image reference: https://s.abcnews.com/images/Sports/lou-gehrig-file-gty-jef-210601_1622583041719_hpMain_16x9_992.jpg

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Ageing of Motor Neuron

PRIMARY LATERAL SCLEROSIS

eral sclerosis?

Primary lateral sclerosis (PLS) is another progressive nervous system disease that is caused by damage to the upper motor neurons resulting in weakness in muscles as well as stiffness.

PLS usually begins with the legs and spreads through the body over time. PLS cases are divided into two sections, Juvenile primary lateral sclerosis and Adult primary lateral sclerosis.

Image source: https://stemcelltreatmentnow.com/wp-content/uploads/2019/01/Sylvie-Denis-OT.jpg

The most recorded cases of PLS are often of people between ages 40 and 60.

WHAT ARE THE SYMPTOMS OF PRIMARY LATERAL SCLEROSIS

1. Difficulty in moving

The first signs of PLS usually appears on your lower limb starting with the legs, eventually progressing to the upper body parts such as the arms and facial muscles.

2. Clumsiness in hand movement

PLS patients might also experience early signs beginning with their arms. Grip strength becomes inconsistent and patients might drop items uncontrollably.

3. Slurred speech

Patients usually have trouble participating in conversation. They may have difficulty pronunciating certain words that are normally used.

4. Swallowing difficulties

Difficulty in swallowing arises in later stages of the disease, also known as dysphagia.

5. Breathing difficulties

Patients with PLS might experience sudden abrupt twitching in muscles such as the arms, shoulders or tongue.

6. Cognitive & Behavioural changes

A person living with PLS tend to go through various changes in emotions despite a lack of stimulus.

IMAGE REFERENCES

WHAT CAUSES PRIMARY LATERAL SCLEROSIS?

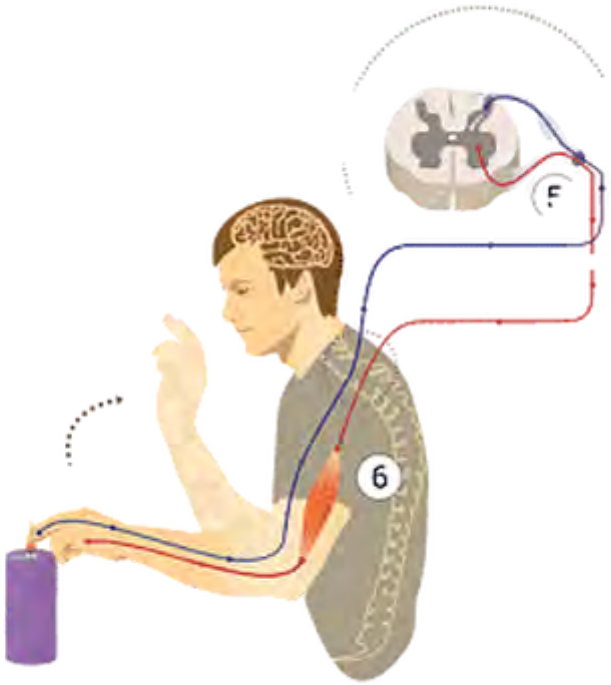

Image source: https://e7.pngegg.com/pngimages/885/404/png-clipart-reflex-arc-amyotrophic-lateral-sclerosis-nervous-system-spinal-cord-muscular-system-angle-hand-thumbnail.png

The underlying cause of adult primary lateral sclerosis is yet to be discovered and it is known that it is not an inherited disease.

Juvenile primary lateral sclerosis is caused by inheritance of a mutation in a gene called ALS2. ALS2 is responsible for creating a protein called alsin which is essential in normal muscle function. As ALS2 gene is mutated, the protein alsin becomes unstable and thus impairing muscle function.

How can PLS be treated?

There is currently no cure for primary lateral sclerosis.

However, there still exist treatments that are targeted at managing the symptoms.

Such treatments involve medications that help lower the rate of muscle stiffness or physical therapy that improves muscle flexibility.

Motor devices are also used to assist with movement such as a wheelchair, walker or even devices that assist with speech.

Image source: https://spotmeee.com/wp-content/uploads/2020/01/4.jpg

SEVERITY OF PRIMARY LATERAL SCLEROSIS DISEASE

Image source: https://www.cleanpng.com/png-wheelchair-dog-clip-art-wheelchair-rim-cliparts-3748117/

Primary lateral sclerosis could take as long as 20 years for progression to reach its final stages. Even then it varies highly from person to person. There are cases where some lose their entire ability to walk whereas some are able to walk fine with minimal assistance
Although PLS does not shorten life expectancy like ALS, quality of life deteriorates through the weakening of muscles. This creates a higher chance to falls that might lead to heavy injuries.
Hence, people diagnosed with PLS should seek external help to enable them to conduct daily tasks with minimal risk of injuries.

References:

Carmel Armon, Francisco Talavera, Nicholas Lorenzo (2019). Primary Lateral Sclerosis. https://emedicine.medscape.com/article/1171782-overview

Header image reference: https://ak.picdn.net/shutterstock/videos/11312420/thumb/1.jpg

Page Authors:

Soh Qi Hui & Khoo Zhao Chen

Ageing of Motor Neuron

DIRECTLY-REPROGRAMMED MOTOR NEURONS: A BETTER MODEL FOR DISEASE STUDY

9/29/2021 0 Comments

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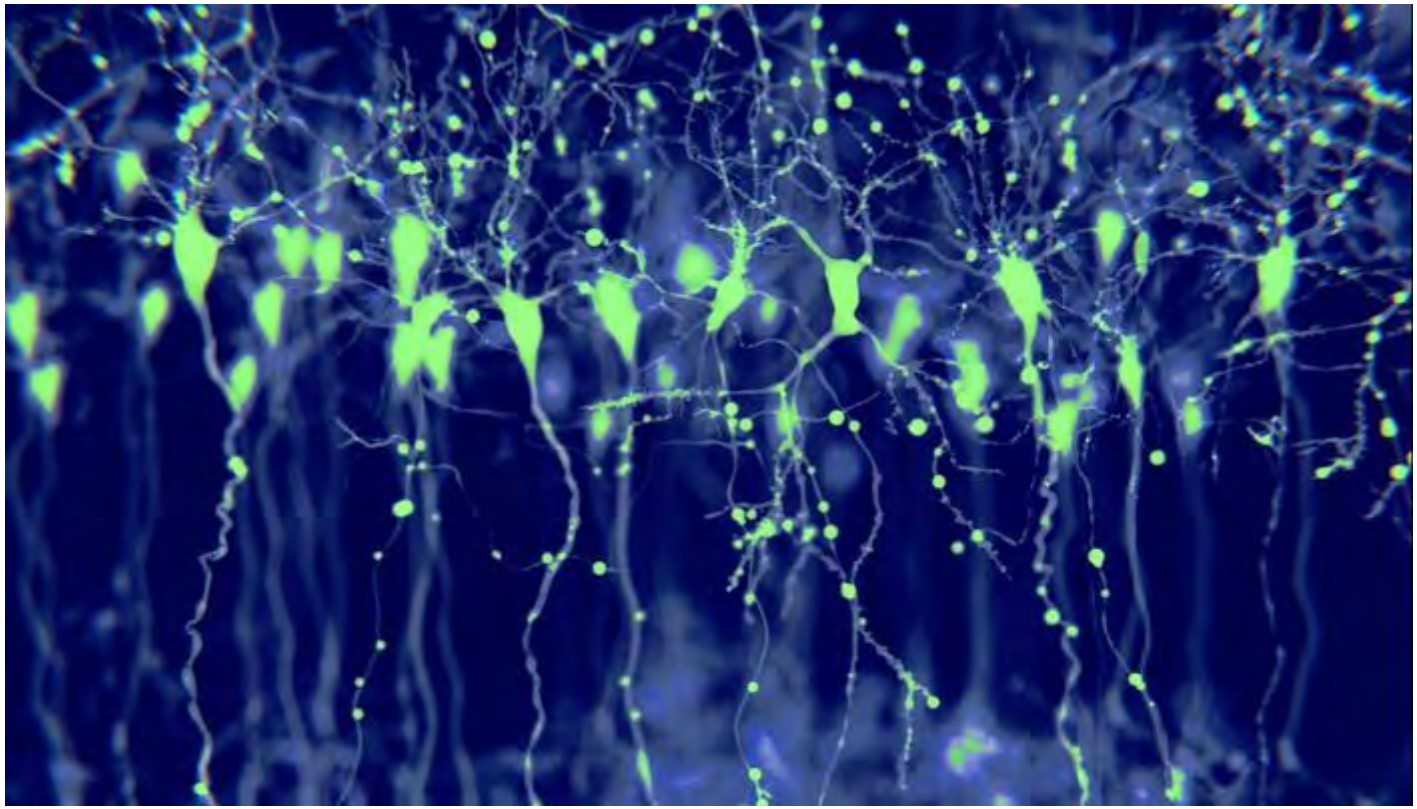

Image Source: https://scitechdaily.com/fluorescent-brain-probe-visualizes-groups-of-neurons-as-they-compute/

What led to the study?

Ageing-related motor neuron diseases can be modelled by generating motor neurons for experimental testing. Current methods to do so are limited in their ability to mimic aged motor neurons, making them less suitable testing models. As such, scientists have been looking for more effective methods to generate motor neurons that retain similarities to aged motor neurons to be used for testing. This would allow more accurate studies to be conducted on age-related motor neuron diseases.

What were the main goals?

The main goals of this study were to:

1. Confirm that the existing method of creating motor neurons from stem cells caused them to be rejuvenated, making them less similar to aged motor cells (and less suitable for testing).
2. Confirm if motor neurons directly converted from normal cells were more similar to aged motor neurons, allowing them to be used for studying late-onset motor neuron diseases better.

How did the researchers do it?

In the laboratory, researchers first converted both young and old fibroblasts (normal connective tissue cells) into stem cells, before finally converting them into motor neurons. They analysed the structures of these motor neurons generated from the stem cells, and compared differences between ones with young and old cell sources. Comparisons were also made with aged motor neurons.

Researchers also converted fibroblasts directly into motor neurons, without turning them into stem cells. They analysed the structures and differences between these directly-converted motor neurons, and motor neurons converted from stem cells. Lastly, they compared differences between both types of neurons and aged motor neurons.

What was discovered?

Motor neurons generated from stem cells were indeed rejuvenated regardless of whether they were originally from young or old fibroblasts. In both cases, the neurons all lost similarities to aged motor neurons. On the other hand, the researchers' new method of generating motor neurons directly from fibroblasts donated from aged and diseased patients were able to maintain similarities to aged motor neurons. This would make this new method more suitable for generating motor neurons used in

Potential novel treatment?

The new method of generating motor neurons in this paper offers a brand new cell model that maintains similarities to aged motor neurons, which scientists need in order to carry out more accurate testing. This makes the new motor neurons more suitable for use in experiments. When more precise cell models are available to be tested on, scientists will be able to study the development of motor neuron diseases with more understanding, allowing them to develop future cures for these diseases.

Reference

Tang, Y., Liu, M., Zang, T., & Zhang, C. (2017). Direct reprogramming rather than IPSC-based reprogramming maintains aging hallmarks in human motor neurons. Frontiers in Molecular Neuroscience, 10. doi:10.3389/fnmol.2017.00359

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For the more scientific-minded individuals, feel free to click on read more to learn more about what the researchers found in-depth!

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USING STEM CELLS TO TREAT PARKINSON'S DISEASE IN MONKEY MODELS

9/22/2021 0 Comments

Image Source: https://www.healthline.com/health-news/what-would-happen-if-monkeys-werent-used-in-research

What led to the study?

Parkinson's Disease is the second most common progressive neurodegenerative disorder and is mainly due to the death of neurons in certain regions of the brain. Current treatments for Parkinson Disease include the use of drug L-DOPA, which only treats the symptoms of the disease, but not its [illegible] With increasing research in deriving neurons from human stem cells, the field has widened [illegible] degenerative diseases through neuronal cell replacement and

transplantation in hope to reverse the pathological progression of such diseases.

What are the main goals?

The main goals of this study was:

1. Demonstrate that clinical-grade stem cells can serve as a reliable source of neurons
2. Demonstrate that the transplantation of these neurons can aid in the recovery of Parkinson Disease
3. Assess any potential side effects that the neuron transplant might have (e.g. cancer, inflammation)

How did researchers do it?

In the laboratory, the researchers produced neuron cells from stem cells through a process known as neuronal differentiation. These neurons were then transplanted into the brains of the monkeys with Parkinson Disease. After transplantation, the monkeys were left to rest before observations of their movement behaviors (i.e. locomotive behaviors) were recorded and tests were done on them to check for signs of cancer or inflammation. Throughout the whole study, the monkeys welfare were well taken care of and ethics approval was obtained before the start of the study.

What was discovered?

Clinical-grade stem cells were able to differentiate into neurons using good manufacturing practices. Subsequent transplantation of these neurons into Parkinson's Disease monkeys were shown to improve their locomotive behaviors (i.e. they had better control over their movements). Safety concerns were addressed and there were no signs of tumor formation or inflammation response in the monkeys that received the neuron transplants.

Precise transplantation of stem cell derived neurons into the brain is a potential promising treatment for Parkinson's Disease patients in hopes to improve their movement.

Reference

Wang, Y.-K., Zhu, W.-W., Wu, M.-H., Wu, Y.-H., Liu, Z.-X., Liang, L.-M., Sheng, C., Hao, J., Wang, L., Li, W., Zhou, Q., & Hu, B.-Y. (2018). Human clinical-grade parthenogenetic esc-derived dopaminergic neurons recover locomotive defects of nonhuman primate models of parkinson's disease. *Stem Cell Reports*, *11*(1), 171–182. https://doi.org/10.1016/j.stemcr.2018.05.010

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DECODING THE RELATIONSHIP BETWEEN AGEING AND AMYOTROPHIC LATERAL SCLEROSIS: A CELLULAR PERSPECTIVE

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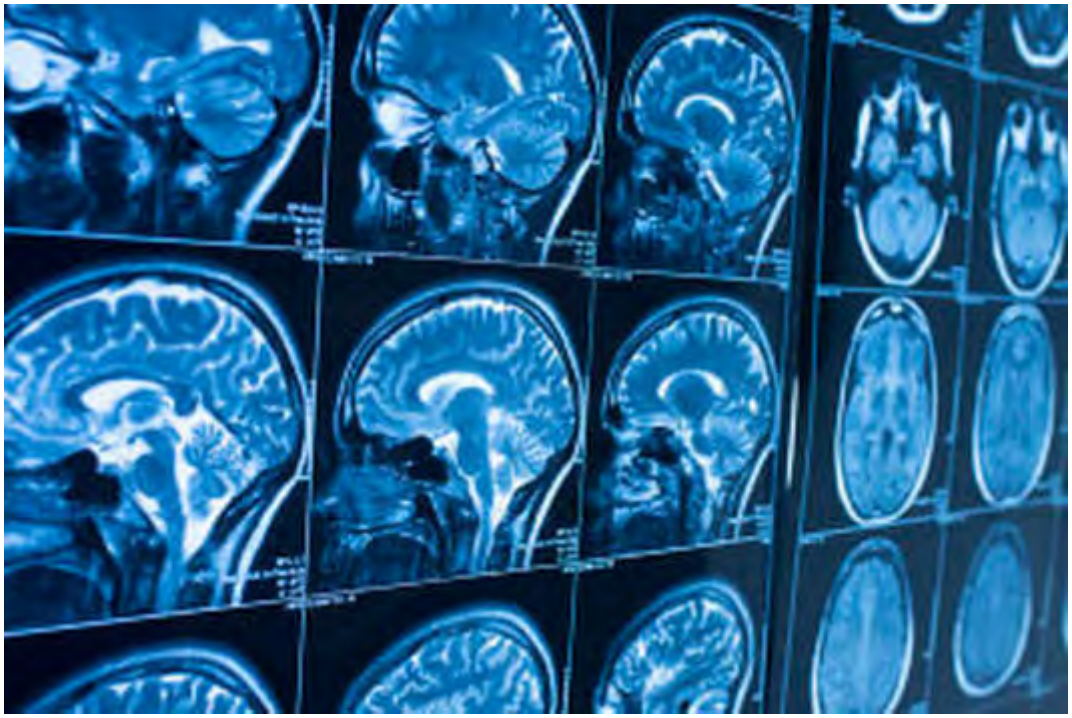

Image Source: https://news.harvard.edu/gazette/story/2019/04/harvard-unveils-new-technique-60-times-faster-than-traditional-fmri/

What led to the study?

With an ageing population comes an inevitable increase in the prevalence of age-associated neurodegenerative diseases, such as amyotrophic lateral sclerosis (ALS), which is characterized by the degeneration of upper and lower motor neurons within the brain and spinal cord. With a prognosis of 2–5 years from onset to fatality, it is crucial to identify the underlying mechanisms of ALS and use these insights to develop effective therapies for patients.

What are the main goals?

ellular changes in phenotypes caused by ageing are prerequisites

for ALS

2. Identify overlaps between age and ALS-associated hallmarks, and investigate whether overlaps would implicate cell type-specific ageing as a key contributor to ALS development

3. Discover high fidelity models to better recapitulate age-related human diseases and identify potential therapeutics

How did the researchers do it?

Researchers hypothesised that the slow degeneration of motor neurons at the neuromuscular junction (NMJ) lead to neuronal degeneration and the subsequent motor symptoms. Hence, in this study, the researchers aim to discuss how motor neurons, skeletal muscle, astrocytes and Schwaan cells relate to normal ageing as well as ALS.

What was discovered?

Characteristic phenotypic changes relating to normal ageing and ALS had been discovered in motor neurons, skeletal muscle, astrocytes and Schwaan cells. There are both similarities and differences in the phenotypic changes observed.

Potential novel treatment

A strong need to integrate in vivo and in vitro, animal and human models of ALS and ageing to achieve an optimal approach for validating key findings and for discovering best evidence to link normal ageing and ALS. Furthermore, the use of more relevant models would allow for the discovery of therapeutic treatments.

Reference: *Pandya, V. A., Patani, R. (2019). Decoding the relationship between ageing and amyotrophic Brain, 143(4), 1057–1072. https://doi.org/10.1093/brain/awz360*

Page Authors:

Loh Jia Hui & Ho Hui Tong

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TETANUS TOXIN (HC-TETX), A POTENTIAL PHARMACOLOGICAL ALTERNATIVE THAT CAN PREVENT OR DELAY NEURONAL DETERIORATION DUE TO AGING AND DISEASE

9/16/2021 0 Comments

Source: https://pixabay.com/photos/fence-wooden-fence-wood-boards-3565867/

What led to the study?

As of 2020, the United Nations reported that there are about 727 million people that are 65 years old and above, this number is expected to double by the mid-century. We have to be prepared to undertake the responsibility of providing effective therapies to the ageing population. It is important that our aged age healthily both physically and mentally. Neuronal ageing is one of the most important

se what are we without our brains and muscles?

As we age, neurons shrink in size and lose their trademark branch-like shape. One of the hallmarks of an ageing neuron is the loss of dendritic spines - little projections that connect to other neurons. When motor neurons are unable to form proper synapses with muscle, it severely affects our ability to move because our muscles can only operate on cues sent by the brain. Ageing also reduce signalling cues for neurons to grow and form synapses.

In recent years, studies have shown that we should focus on therapies that are non-toxic and work to trick our neurons to grow and form synapses, thus delaying the ageing process. In this blog entry, we will show you how a non-toxic segment of the tetanus toxin functions similar to neurotrophic factors. What's more remarkable is that apart from restoring our motor neurons back to their former state, the toxin segment also works to improve memory and learning!

What are the main goals?

The study looked at how effective the tetanus toxin segment was in protecting and restoring neurons in elderly mice (18 months old) by monitoring their mobility while also looking at characteristics of their motor neurons - whether they resembled the morphology of younger neurons.

How did the researchers do it?

10 mice were treated with the tetanus toxin segment, while 10 control mice were administered with saline daily for three days. By the end of 30 days, both groups had their mobilities and neuron morphologies compared.

What was discovered?

gressively with age for both experimental groups, mice treated

with tetanus toxin showed an increase in overall motion function and had better exploratory behaviour when placed in a new environment compared to the control group.
Microscopic examination of the treated mice also showed an improved neuronal architecture when compared to the control mice.

Potential novel treatment?

Hc-TeTx improves brain function under aging conditions, demonstrated by the improved neuroplasticity and morphology of motor neurons, and the enhanced motor function in aged mice.

We do not condone anyone to purposefully cut themselves on infected rusty metals!

Page Authors:

Chua Kevin & Dexter Xiao

Reference

Vazquez-Roque, R., Pacheco-Flores, M., Penagos-Corzo, J., Flores, G., Aguilera, J., & Treviño, S. et al. (2020). The C-terminal fragment of the heavy chain of the tetanus toxin (Hc-TeTx) improves motor activity and neuronal morphology in the limbic system of aged mice. Synapse, 75(6). https://doi.org/10.1002/syn.22193

For the more scientific-minded individuals, feel free to click on read more to learn more about what the researchers found in-depth!

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GENETIC AND PHARMACOLOGICAL INTERVENTIONS IN THE AGING MOTOR NERVOUS SYSTEM SLOW MOTOR AGING AND EXTEND LIFE SPAN IN C. ELEGANS

9/10/2021 0 Comments

Image source: https://www.sibeliusnaturalproducts.com/wp-content/uploads/2019/10/shutterstock_748933015.jpg

What led to the study?

ɔtic release from the motor neurons at neuromuscular junctions

(NMJ) contributes to the age-dependent motor activity decline. This suggest that the boosting of synaptic release could possibly reduce age-dependent motor activity decline

Since SLO-1 (C. elegans ortholog of BK channel) has been reported to dampen synaptic release from motor neurons at NMJs, researchers wanted to test if the knocking out of SLO-1 could result in a slower rate of age-dependent motor activity decline.

What are the main goals?

To identify a molecular target that can be targeted via pharmacological treatments or genetically to reduce the rate of motor aging and promote life span.

How did the researchers do it?

Behavioural and life-span assay were carried for wildtype (normal) C. elegans and slo-1 mutant (knockout of SLO-1) young C. elegans and slo-1 mutant old C. elegans.

Paxilline, pharmacological blockers of SLO-1 were used on normal young and aged C. elegans.

What was discovered?

slo-1 mutant C. elegans in aged, but not young, C. elegans result in a slower rate of motor activity decline and are long lived, meaning that the loss of SLO-1 helps to reduce the rate of motor aging and promote life span.

Paxilline (Pharmacological blockers of SLO-1) also result in the reduction of motor ageing and promote life span in aged, but not young, C. elegans.

Potential novel treatment

With the BK channel being evolutionarily conserved, we could do more research to examine the targeting of mammalian BK channels for potential treatment.

Page Authors:

Soh Qi Hui & Khoo Zhao Chen

Reference

Li, G., Gong, J., Liu, J., Liu, J., Li, H., Hsu, A.-L., Liu, J., & Xu, X. Z. S. (2019). Genetic and pharmacological interventions in the aging motor nervous system slow motor aging and extend life span inc. elegans. *Science Advances*, *5*(1). https://doi.org/10.1126/sciadv.aau5041

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Ageing of Motor Neuron

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