How different examples of brain plasticity inform our understanding of the workings of the brain.

Zhanna Kryukova
Saunderites
Biology
PAB

"The softest, freest, most pliable and changeful living substance is the brain – the hardest and most iron-bound as well."
- Charlotte Perkins Gilman

Introduction.

Merriam-Webster defines 'plasticity' as "*the quality of being able to be made into different shapes*". Brain plasticity or *neuroplasticity* is the ability of the neural pathways, synapses and neurotransmitter mechanisms in the human brain to change as a result of the environmental influence, thinking processes or injury. Simply put, it is how the brain adapts due to experience. Brain plasticity is ongoing throughout one's life, although the speed, degree or type can vary depending on age, behaviour and genetics. Brain plasticity is what allows us to learn and memorise information by strengthening the synaptic connections and creating new ones (structural plasticity). It also enables recovery from brain damage or injury by changing the area of the brain responsible for carrying out certain functions from the damaged site to a healthy site (functional plasticity).[1]

In my essay, I am going to explore several examples of plasticity of the brain, theories of the mechanisms behind them and what it can mean for further research into brain processes and rehabilitation.

Hebbian theory or Hebb's rule.

The secret behind the working of the brain is the connections between neurons - synapses. Brain activity depends on quality and efficacy of the process of signal transmission along the synapses. As we age and develop so does the neuronal network in the brain. One of the primary ways of affecting the abundance and efficacy of synaptic connections is through learning. Donald Hebb was the one to propose the theory of how learning affects the brain circuits. Hebb believed that every time a signal travels from a neuron to a neuron, their synaptic connection strengthens. So the more the presynaptic cell stimulates the postsynaptic cell, the stronger the link.[2] To quote Carla Shatz, '*Cells that fire together, wire together*'.

Before extended research into the brain structure was carried out in the 1980s, it was widely believed that once the brain had developed in early childhood, it was not subject to any more changes. Now we know that the brain does become somewhat less plastic as we age, and few new connections are formed. However, it can still 'rewire' itself through the changes in strength of connections between the neurons, which depends on their *positive stimulation.* [3]

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[1] http://faculty.washington.edu/chudler/plast.html

[2] R. Hernandez. "*Hebb's theory: From synapse to consciousness*" (Society for Neuroscience, 1995) vol.21 p.246

[3] A. Bronstone "*Brain plasticity and functional losses in the aged: scientific bases for a novel intervention"* (Reprogramming the Brain, 2006) p.88

I think the concept of Hebbian learning ties to what human society perceives as intelligence. People coming from a healthy, stimulating environment in which there are plenty opportunities for creative thinking are more likely to have a well-developed neuronal network. Whereas individuals without those opportunities may find their synaptic transmissions lacking in speed. Similarly, the decline in cognitive functions in older people may be connected to the fact that they challenge themselves less.[4] Much like with physical exercise that stimulates the body's metabolism, active brain engagement positively affects neuronal metabolism. Mikhail Lomonosov, a famous Russian scientist, used to say, '*Mathematics should be studied if only for that it puts the mind in order*.' Even though he lived centuries before serious research into neuroplasticity commenced, his remark was not far from the truth: challenging problem-solving activities do, quite literally, organise and shape our brain.

From here we can conclude that natural decline in mental functions accompanying the ageing process that is widely believed to be inevitable can, in fact, be if not reversed then slowed down.

However, it is not only positive brain stimulation that alters the neuronal map. Injury, stress, chemicals, sensory deprivation, habits, etc. can bring about changes in the brain. However, the majority of principles of synaptic plasticity are based on Hebbian theory.

Sensory deprivation and cross-modal plasticity.

Consider the first example. Many sources claim that blind people have much sharper hearing than sighted individuals. Is it because now, they focus more when listening? Is it due to having more practice in using their hearing? Does their sight no longer distract them? Alternatively, could it be that their brain had found a way of modifying itself to compensate for the lost sense?

A group of German scientists conducted the research to look into this question.[5] They sped up regular human speech and observed brain activity in blind and sighted people listening to the recording. Human hearing is commonly limited to 10 syllables per second; however, blind individuals could understand what was said even at the speed of 25 syllables per second. They ran and fMRI (a scan of the brain that registers changes in blood flow to certain areas). The results were surprising. It showed that a blind person's brain processed these sounds both in the hearing region and in the visual cortex of the brain, the one that only responds to light in sighted people.

Neuroplasticity explains this phenomenon. Loss of sight causes the neurons in the visual cortex to be "rewired" to process auditory signals instead of visual signals. This way the brain compensates for the loss of vision. Instead of having an extensive portion of the brain go to waste, new connections

[4] A. Bronstone *"Brain plasticity and functional losses in the aged: scientific bases for a novel intervention"* (Reprogramming the Brain, 2006) p.90

[5] I. Hertrich, S. Dietrich, A. Moos, J. Trouvain and H. Ackermann "*Enhanced speech perception capabilities in a blind listener are associated with activation of fusiform gyrus and primary visual cortex*" (Neurocase: The Neural Basis of Cognition, 2009) vol.15 p.163-170

between neurons are formed to give blind people an advantage in the form of heightened hearing. This rewiring is possible because of cross-modality: interactions of visual and auditory circuits in the brain. These two senses are not separate; in fact, they mostly work together (i.e. when we register someone's lip movements it helps us better understand what they are saying). The link allows for the existing connections between the two regions to become strengthened over time.

Then Hebbian theory steps in. Neurons in auditory and visual areas were previously connected but only barely so and did not make a significant difference to how we process audio information. After losing their sight, blind people had to make the most of their remaining senses, causing a persistent stimulation of those connected neurons. Interestingly, the age when the person experienced loss of sight plays the critical role in whether they will be able to use their visual cortex to hear. People born blind cannot do it because their visual cortex was never stimulated and so, has not been "activated"; there are no existing connections to strengthen. Additionally, people who lost sight in their early twenties and onwards are also unlikely to acquire heightened hearing because they had passed the time when most of the brain "wiring" took place. Their visual experience does not influence the natural formation of these connections as much as it does in a developing brain of younger people, which can redirect them to process sounds.

Another related example is **human echolocation** - the ability of some people to perceive their surroundings by detecting echoes that bounce off of objects. Although common amongst animals (bats, dolphins and whales), echolocation is something only blind humans managed to master.

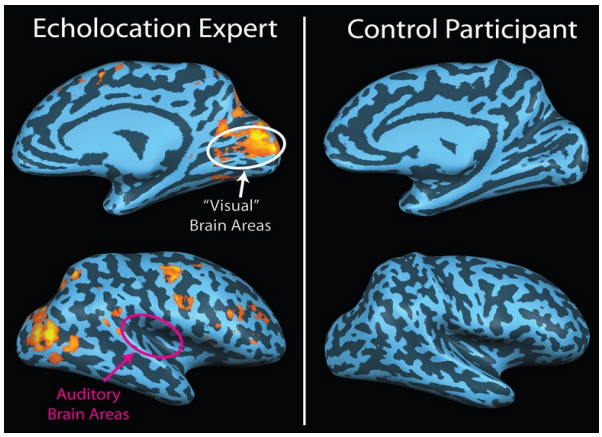

Fig. 1

A Canadian study[6] produced the pictures (fig. 1) that show brain activity when listening to echoes in sighted person and a person able to echolocate. Remarkably, brain activity was only detected in the visual cortex, with nothing unusual happening in the auditory region, which proves that only blind people can echolocate successfully.
The mechanism behind this ability is the same as in the previous study: parts of the visual cortex have adapted to process auditory information as a result of persistent stimulation.
These studies prove that an enhancement in other senses in blind people is not a result of developed improvement over time, but is, in fact, underlain by changes in the brain circuitry. Moreover, we now know that human brain can reorganise itself to compensate for *sensory deprivation*. It means that our brain has a built-in mechanism to restitute for injuries we may sustain during the course of our lives that aims at maximising our chances of survival.

[6] Thaler, L. Arnott, S.R. & Goodale, M.A. "*Neural correlates of natural human echolocation in early and late blind echolocation experts*". (PloS ONE, 2011) vol.6.

However, it is not always the case that brain plasticity brings about positive change. In her book, Dr. Susan Greenfield describes a case of a boy who was blind in one eye. As it turned out, when he was a baby he had his eye covered up to treat a minor infection. Unfortunately, since it happened very early on in life while all vital connections were being established in the brain, this brief episode of sensory deprivation was misinterpreted as a lack of an eye. As a result, the brain quickly rewired itself to use up the space to establish more connections to the working eye instead.

To sum up, cross-modal neuroplasticity usually follows some form of sensory deprivation, and brain starts rewiring itself to employ areas that are no longer active to extend the ability of the remaining senses. The existence of direct synaptic connections between these areas is what makes the process possible because no new connections are formed; only existing ones become stronger. Hebbian learning may give rise to advantageous traits. However, not all changes can be beneficial since they can be mistakenly triggered in the early stages of development.

Phantom limbs and pain.

Now I will turn to the "dark side of neuroplasticity"[7]. Phantom limb is a persistent feeling that an amputated or missing limb is still a part of one's body. It can go away or reappear, people can experience painful, twitching or itching sensations in the phantom limb that they are unable to stop. Scientists believe this to be due to the fact that there is still leftover representation of the amputated organ in the brain. So even though the limb is no longer attached to the body, part of the somatosensory cortex responsible for it still exists, projecting the sensation of the limb past the new body boundaries.

Most of the amputees also experience chronic pain in the limb that seems to be unaffected by painkillers. The sensation is usually that of fingers or toes cramping up or being curled unnaturally. The research on the topic is ongoing, and several different theories exist.

The original theory suggests that the pain is due to severed nerve endings in the amputated limb that become irritated[8]. Those nerve endings send nonsensical signals to the brain that interprets them as pain. However, it would not explain the curling sensation or why the pain was unaffected by repeated surgery: one way of treatment that involved cutting off further several inches of the limb.

Two other theories have opposing views. One argues that the pain originates in the PNS. Since the cut-off nerves are not attached to a limb anymore, this confuses the brain, indicating that there is something wrong with the limb. The natural response to it is pain. The basis for the other theory is *maladaptive neuroplasticity*; it argues that the pain is in the brain (CNS). In his book Norman Doidge describes a case led by Dr. Ramachandran: he worked with a young man Tom, who had an amputated arm, and a persistent aggravating itchy feeling in his missing limb. Dr. R. blindfolded him and then touched parts of Tom's upper body with a Q-tip. It turned out that when the Q-tip touched parts of

[7] Norman Doidge, *"The Brain that Changes Itself".*

[8] Livingston, K.E., "*The phantom limb syndrome - a discussion of the role of major peripheral nerve neuromas*", (Journal of Neurosurgery, 1945) vol.2, p.251-255

Tom's face, he could also feel it in parts of his amputated arm. Solely scratching his cheek relieved the itching.

This phenomenon is referred to as synaesthesia. Synaesthesia is a condition where people have two senses tied together, and a stimulus aimed at eliciting one sensation will also produce an additional one.[9] After the limb has been amputated, the whole area of the brain that managed it is left without the "recipient" of the sensory information. Instead, the signals are sent to another part of the body, in Tom's case - to his cheek. This is achieved by the brain circuitry remapping itself: much like in the event of blindness, existing neural connections between the arm and face brain areas are strengthened. However, during the alteration process nerve endings can get tangled or not connect properly, and so any abnormality results in pain.

Another theory proposed by Dr. Ramachandran related to "dark" plasticity suggests that yet again, Hebbian learning is to blame. In many cases, arms and legs were severely injured, and the owner endured severe pain prior to amputation. Because the pain was so persistent, connections between neurons conveying that feeling of pain got strengthened through Hebbian learning, carving this response into the brain circuitry. As a result, even when the limb was gone, the brain, having learned that the limb hurts, continues to send painful signals.

Fig. 2

So how can phantom pain in the nonexistent organs be treated? There are several conventional methods including painkillers, antidepressants, anaesthetics prior and after the surgery.[10] However, whether they work depends on an individual case. If we are to look at solving this problem using the research carried out in the sphere of neuroplasticity, there is a novel approach, investigated by Dr. Ramachandran in the year 2000.

It uses a tool as simple as a mirror. It is a box with a mirror partition with two cut-outs: one for the stump, one for the healthy arm. The person undergoing treatment can only see the reflection of the healthy arm in the place of the amputated one (fig. 2[11]). This creates an illusion that the limb was "resurrected". The patient moves his existing hand and imagines the same movements in the amputated limb, and in many cases this procedure succeeds in alleviating the pain. The method behind it is pairing up the proprioception with the visual feedback to try to alter the brain map.

A related study, carried out by Moseley and Brugger[12], confirms that body image changes can be done with just the power of one's mind, and do not even need a mirror. The amputees were instructed

[9] Banissy, M.J. "*Prevalence, Characteristics, and a Neurocognitive Model of Mirror Touch Synaesthesia*", (Experimental Brain Research, 2009)

[10] B. Subedi, G. T. Grossberg, "*Phantom Limb Pain: Mechanisms and Treatment Approaches*", (Pain Research and Treatment, 2011)

[11] Image source *http://endthepainprojectupdate.blogspot.com/2009/11/blog-post.html*

[12] L. Moseley, P. Brugger, "*Interdependence of movement and anatomy persists when amputees learn a physiologically impossible movement of their phantom limb*", (PNAS, 2009)

to try to bend their phantom arm into shapes impossible to accomplish with a real limb. More than a half of patients reported success. This means that they managed to reshape neural representations of their arm on the spot, without any visual feedback.

Interestingly, phantom limb sensations are not unique to amputees. During my time in San Francisco this summer I have visited the Exploratorium - interactive science museum. There is a station where a person puts their hand on a table right underneath a plank with a metal hand lying on it (fig. 3). Their real hand is invisible to them, "replaced" by the metal one, placed half a foot higher. The second person strokes both hands simultaneously so that the first person feels the touch in his real hand but sees only the metal one. I have done the experiment myself. Indeed, after around 30 seconds, the sensation, first "located" under the plank, slowly migrated up so that I was convinced it was the metal hand that felt the strokes. Furthermore, after additional two minutes, when my friend hit the metal hand, I instinctively jerked my hand away.

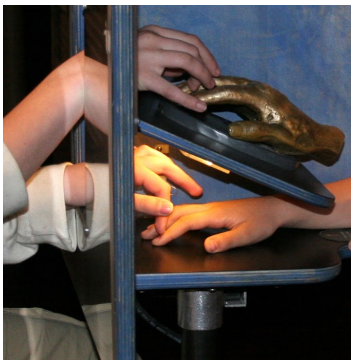

Fig. 3

The importance of this research is that it allows us to expand our knowledge on the subject of neuroplasticity and to what extent we can control and manipulate on-the-spot changes. As highlighted by Moseley's experiment, neuronal connections are so malleable, that they can be altered, if briefly and temporarily, by the sheer power of thought. The case of the induced phantom limb illustrates how we can easily reshape our body image by tactile stimulation paired with vision.

It is important to point out that phantom limbs are not entirely detrimental. This projection of body image is what allows the successful use of prosthetics: without the proprioception in the prosthetic, walking would have been an exercise in stumbling. This phenomenon makes me wonder whether there is an evolutionary reason for the brain to keep the missing limb on its sensory map and trying to preserve original body dimensions even after injury.

Even though maladaptive neuroplasticity is the original cause of the phantom limb pain, the very same lability of the brain can be used to reverse the effects and return the brain to normal.

Synaesthesia.

As mentioned above, synaesthesia occurs when two senses that are normally separate are triggered at once by one stimulus. Synaesthesia is not limited to phantom limbs; there are different forms of it. For example, there are people who, upon hearing a sound will also experience a taste, or see a colour. More typical examples of synaesthesia include seeing letters and numbers in different colours, with a distinct colour associated with each symbol, called grapheme-colour. [13]

[13] http://www.nhs.uk/Conditions/synaesthesia/Pages/Introduction.aspx

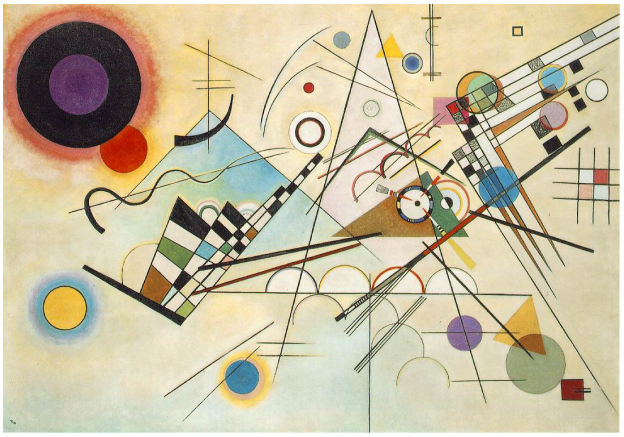

Fig. 4

Russian painter Wassily Kandinsky (who is considered to be one of the founders of the abstract art) used to go to concerts and "write down" the music by painting what he heard. He called his works "Compositions" (fig. 4: 'Composition VIII'). It is now believed that he had a form of synaesthesia where he perceived sounds as shapes and colours. The peculiar way in which the neurons in his brain connected gifted him with a unique insight into art. So is synaesthesia a disorder? Or is it a gift?

According to the NHS website, at least 4% of the UK population experience synaesthesia. For the most part, people feel positive about it ("Synaesthesia helps me remember things well, and helps me find passages in text quickly."[14]). They perceive it as something that sets them apart and can even be an advantage in learning and memorising. Others report their condition interfering with everyday lives, causing distractions. There is, however, no substantial evidence for links between synaesthesia and neurological or psychological disorders. Nonetheless, synaesthesia may not be a cause, but a sign of a defect in the brain. There were several cases in which stroke led to synaesthesia.

On the other hand, recent research can imply that synaesthesia is not a disorder, but a natural ability that most people lose with age, but some retain[15]. A group of scientists conducted research on children aged between two and nine months. Researchers showed pictures to infants: the backgrounds were in different colours (red, green, blue and yellow) and had either circles or triangles drawn on in black. If babies did not have synaesthesia, they would observe all the pictures for the same amount of time, regardless of shapes drawn. However, if they saw shapes in a particular colour, they would look at some of the images longer. For example, if one of them always saw circles in green, then that infant would look at a picture of circles on a green background longer, than on one of any other colour. Observations confirmed the theory. The hypothesis behind the experiment states that everyone is born a synaesthete, but due to the changes in the brain cortex as we age, synaptic connections responsible for synaesthesia fall apart. If this is true, it is yet another proof of the immense changes that take place in the brain during our lives.

Synaesthesia can be the result of "overwiring" in the brain causing neuronal connections that should not typically be there. While it may be a result of brain injury and the brain trying to restore lost connections, more often than not it is not linked to any disorder, and should not be considered as such. I think it would be worthwhile to investigate whether adult synaesthetes have their condition as a leftover ability from when they were infants, i.e. their senses, once tied together, failed to separate sufficiently. Synaesthesia illustrates that examples of neuroplasticity cannot all be divided into "useful" or "disadvantaging".

[14] http://drholly.typepad.com/synesthesia_interview/

[15] K.Wagner, K.R.Dobkins, "*Synaesthetic Associations Decrease During Infancy*" (Psychological Science, 2011)

Behavioural damage due to stroke. Self-directed neuroplasticity.

Lastly, I am going to discuss one of the most pressing questions in modern neuromedicine: stroke consequences and recovery. As mentioned before, synaesthesia can be one of the consequences of stroke. This is due to the fact that when neurons in the damaged network are trying to reconnect, newly organised circuitry sometimes causes a linkage between two senses. However, far more grave consequences of stroke occur because neuronal connections are not restored properly. I am going to focus on changes in human behaviour and how neuroplasticity can be involved in treatment.

Stroke is a medical condition caused by interrupted blood supply (leading to loss of oxygen and nutrients) to the brain that damages neuronal connections due to cell necrosis.[16] One of the most common effects of stroke is a noticeable change in behaviour. People become irritable, impatient, apathetic or aggressive because of changes in the brain circuitry.

As established earlier in my essay, neuronal connections are the defining characteristic of brain activity. So when they are disrupted, it can lead to memory loss, paralysis, speech difficulties, etc. Immediately after injury, structural neuroplasticity kicks in. There is a very small window of opportunity for interrupted synaptic connections to be restored. Even though the process of recovery can go on for years, it is crucial for action to be taken in the first three months when brain plasticity is most active[17].

The brain is the organ of behaviour. Throughout our lives, our typical behaviour remains relatively constant. As our brain changes due to age, so does our behaviour. Following the same principle, drastic detrimental changes in brain structure will bring about sudden changes in behaviour. (Phineas Gage is a famous example - a man with an immense damage to his frontal lobe that completely altered his personality). So the opposite is also true: "positive" changes will restore behaviour. Therefore, rehabilitation techniques should be aimed at restoring neuronal connections. As illustrated by previous examples, nearly any activity can modify the brain. However, to be effective, the changes must persist.

So far some neuroplasticity-based techniques of treatment were used[18], however, I think it is *self-directed* neuroplasticity that could be the answer to speeding up the healing process. Self-directed neuroplasticity is based on the idea that we can consciously control how our brain structures itself. Dr. Rick Hanson formulates it this way, '*You can use your mind to change your brain to change your mind for the better*' ("mind" in this context implies the self-aware and conscious part of a person). In other words, we can influence our neuronal connections with our thoughts, which will in turn influence what we think like[19]. It is somewhat like teaching your brain healthy habits. One specific example of successful self-directed neuroplasticity is meditation. It involves concentration and attention aimed at focusing on a specific thought or goal. Principles of Hebbian learning back the theory up scientifically. Research

[16] http://www.nhs.uk/Conditions/Stroke/Pages/Introduction.aspx
[17] Murphy, Timothy H., and Dale Corbett. "*Plasticity during Stroke Recovery: From Synapse to Behaviour*." (Nature Reviews Neuroscience, 2009) p.861-72
[18] J.A. Kleim, T.A. Jones, *"Principles of Experience-Dependent Neural Plasticity: Implications for Rehabilitation After Brain Damage*" (Journal of Speech, Language, and Hearing Research 2008) vol. 51
[19] https://www.rickhanson.net/

also provides objective evidence in the form of MRI scans that show an increase in cortical thickness and gyrification (folding)[20]. Moreover, the areas affected are frontal and pre-frontal lobes – parts of the brain linked to attention, creativity, concentration and original thought. The study was carried out on healthy people, but it does not mean that the same principles cannot apply to stroke patients. In fact, restoration of frontal lobe would help treat behavioural issues that manifest as apathy, loss of concentration and aggressiveness.

According to World Health Organisation, over 15 million people worldwide experience stroke every year. Of those 15 million, five million do not survive and another five are left disabled. Stroke is the third leading cause of death in the world[21].

Behavioural changes in patients gravely affect their daily lives and their relationships with relatives. Depression and apathy can slow down the process of recovery and because the recovery is slowed down, it is hard to reverse personality changes; the patient is left in a vicious circle. Impacts of personality change can include loss of trust from friends and family, memory loss, difficulties with planning and thought processing and risk of increased aggression. Because of memory loss some patients have trouble connecting their past self with their present self and feel conflicted when they remember something they did in the past, thinking of it as done by another person.

Successful research on the topic of self-directed neuroplasticity will provide patients with accessible information and non-costly methods of self-treatment that can help more people and will spread awareness about the subject.

Conclusions and research objectives.

The sphere of neuroplasticity is a relatively new one with endless opportunities for further investigation. How strong can two neurons be connected? To what extent can the brain change? Can we speed up the process? What type of brain activity optimises Hebbian learning?

Exploration of principles of cross-modality can make echolocation as a practice and form of treatment more widespread and accessible, which is of great significance to blind people. Besides making their day-to-day lives more comfortable and reducing daily risks, their new abilities, such as heightened hearing, may make them sought out by employers for their unique skills. Other questions that can be addressed are, for instance, what other senses can potentially become linked? Or could it be that cross-modal plasticity can be achieved without the destructive consequences of sensory deprivation?

Synaesthesia is also an exciting new field. Research done in infants proves that all our senses were connected and maybe still are to some extent. It also raises a question whether it was evolutionarily beneficial that they separated and whether there existed an organism that did have its

[20] Lazar, Sara W., Catherine E. Kerr, et al. "*Meditation Experience Is Associated with Increased Cortical Thickness.*" (NeuroReport, 2005) p.897-1893

[21] http://www.who.int/mediacentre/news/releases/2014/world-health-statistics-2014/en/

senses interconnected. The ultimate question remains: is synaesthesia an advantage, a disorder or an atavism?

Phantom limbs illustrate that our brain will maintain proprioception and keep the body image "stored" even if the physical body lacks parts. I wonder if it could be because proprioception is of immense importance to locomotion and, indirectly, our survival.

Self-directed neuroplasticity nowadays is still perceived as something rather fictitious as opposed to scientific. However, brain scans and MRIs unambiguously show that it has a direct impact on our brain. Moreover, these methods are not limited to stroke patients, but can be employed by healthy people as well to maximise their cognitive potential. In addition, understanding how neuroplasticity works in a healthy brain can help applying its principles in medicine.

Lastly, I cannot overstate the relevance and priority of investigation into brain damage. Stroke is one of the leading causes of death worldwide. Survivors suffer from multiple neurological conditions that can leave them incapacitated for the rest of their lives, can affect their sense of self, memory and relationships, not to mention the impact it has on family and friends. I believe principles of brain plasticity can be explored further to develop an optimum program for self-treatment.

Neuroplasticity is a largely perplexing process that is not fully understood yet. I believe that it is an area of great potential. By looking at different examples of neuroplasticity, we can begin to understand how it works in different contexts and how it all ties together. Further investigation of the field may uncover amazing opportunities for people. The research is especially germane nowadays, when we are close to defeating diseases of the body but are far less successful in treating disorders of the mind.

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