Neurodifferentiation

Neurodifferentiation states that the brain can only heal itself if it continually strives to increase the complexity of its circuitry. This statement implies that 'striving' i.e. exercising mental effort is a prerequisite to brain healing. Why is it necessary? How does mental effort or 'striving' contribute to the healing of an injured or malfunctioning brain?

To answer this question, let us first define what neural differentiation is. Neural differentiation, from the term 'differentiate' which means to make something different in some way, is the process of neurons branching out to connect to other neurons so as to establish more elaborate and specialized connections. Highly differentiated circuits have a repertoire of more functions to serve physical, technical or mental demands. For example, compared to a person who has never held a musical instrument, you can say that an expert musician such as Yo-Yo Ma has a highly specialized and *differentiated* neural circuitry. It is his differentiated neural circuits, molded through years of practice, which are the source of his skill and talent. Neural connections that are more differentiated take up more space in the brain and thus have larger brain maps. A brain scan study has revealed that the left hand brain map of expert violinists are enlarged compared to control subjects.

However, we do not need to cite talented musicians or skilled athletes as examples of neurodifferentiation (although there mere presence prompts us to ask the question "what really makes skill or talent?"). Even the ubiquity of being able to live a normal life is already a substantial neurological feat in and of itself. Basic life skills such as movement, memory, speech or communication and comprehension are built upon years of learning ever since one's developmental years. These basic life skills have a biological basis. They are differentiated neural circuits that govern everything we do and allow us to function normally in the world. The downside is that one does not know *how* these skills were acquired and thus is oblivious to the true nature of the plastic brain. There isn't any urgent need to know since they are living a normal and uninterrupted life. Not knowing how these skills were acquired would incapacitate one for a long time whenever a neurological disease or condition may strike. The neurological basis of their life skills would be attacked and they would be debilitated. It would not be known to them that healing is readily available if they knew how to tap into the plastic capability of their brain. Unfortunately, whenever a condition or disease that takes away these basic life skills does occur, that would be the only time they would be driven to discover the neuroplastic aspect of the brain, if their skepticism does not keep them from searching for a way. Conditions such as stroke, aphasia, dyslexia and dystonia or diseases like Parkinson, Alzheimer and Huntington completely impede one's ability to function normally in the world. Thus, as more circuits are damaged and become *de-differentiated*, years of learning and skill become inaccessible and basic function seems to have been lost. Therefore, one can conclude that a differentiated circuitry is the neurological basis of every bodily function. The more one has differentiated circuits, the more one has function, skill and expertise. Otherwise, one is devoid of any sort of use.

This answers the first part of the question posed earlier. We now know that a well differentiated circuitry is the neurological basis of normal function as well as skill and expertise. Hence, we can say that possessing well-differentiated neural networks is necessary for a healthy, normally functioning brain. After all, the prevalent result or aftermath of all brain diseases or conditions is loss of some function of some kind in various degrees. Therefore, the next question is how does one attain a differentiated neural circuitry? Whether it's a specialized skill like knowing how to play an instrument or basic like locomotion and movement, how *exactly* are skills formed in the brain? If skills are brain maps, i.e. bundles of neural circuits that occupy cortical territory, then what exactly causes its genesis from a single neural connection to a complex circuitry of more than a million connections? More connections mean more neurons branching out, creating synapses, and thus differentiating. Therefore, what is it exactly that triggers neurons to branch out and differentiate? What specific action begins this process of plasticity or branching out?

Ever since neuroscientists stumbled upon neuroplasticity and discovered it as a basic feature of the brain that is available for everyone even up until their adult lives (see Chapter 3), Michael Merzenich, a renowned neuroscientist, has found that one of the catalysts that trigger plastic changes to happen is **focused attention.** Researchers on a study of rats paired random input stimuli (auditory tones) with activation of the nucleus basalis, which is the brain region of attention tasked with identifying important stimuli from our environment, showed that cortical reorganization occurred specifically on the paired sound inputs (Kilgard & Merzenich, 1998). Since the nucleus basalis is the center for attention and focus, this study suggests that when we put our full concentration and attention into something (stimulus or stimuli) the brain initiates the process of neuroplasticity and thus learning.

There is direct evidence that shows dendritic branching occurring in the neurons of rats that were subjected to environmental complexity and learning (Holloway, 1966).

Another catalyst that triggers plastic changes to happen is **cognitive struggle**. When we're engaged in something novel, like first learning how to drive a car or speak a second language, we experience acute feelings of mental unease at moments of the skill acquisition process where learning is the hardest such as remembering the sequence of steps on how to successfully get the car moving smoothly or the correct syntax or grammar of saying "You have a nice house" in Spanish. We feel mentally "constipated" and struggle for a few seconds to make sure we get it right. These moments of mental effort are actually the necessary prerequisites for plastic changes to occur in the brain. Without cognitive struggle, nothing can happen at a neurobiological level. In alignment with cognitive struggle, studies on environmental enrichment have shown that BDNF or Brain Derived Neurotrophic Factor, an important protein that helps strengthen plastic changes in the brain, is released.

In neuronal cell cultures, where the effects of neurotrophins could be isolated, BDNF has been found to increase dendritic branching as much as 36%-90% in certain specific cortical layers of the developing visual cortex in ferrets (McAllister, et al. 1995)

Researchers found that the balance of excitatory and inhibitory neurotransmitters between neurons affects the production of neurotrophins such as BDNF (Zafra, et al. 1991). Since the balance of excitation and inhibition is mainly dictated by synaptic activity, it can be said that BDNF expression is activity-dependent. This finding shows more of the many benefits of cognitive struggle.

BDNF has also been found to increase GABA and neuronal inhibition in synaptic plasticity (Huang, et al. 1999). In order to isolate the effects of BDNF, researchers genetically modified young mice to have accelerated levels of BDNF during their early stages of development. What they found is that these transgenic mice had increased visual acuity, accelerated maturation of GABA which helps neuronal inhibition and an earlier termination of the critical period of their visual cortex. All of these findings taken together further corroborate BDNF's physiological function that it serves to strengthen plastic changes in the brain. It is interesting to note that focal dystonia patients are found to have deficient GABA levels. Thus, BDNF could help mitigate deficient GABA levels pathological to focal dystonia.

Research has also revealed that repeatedly fired neuronal connections receive more BDNF than weaker and less repeatedly fired circuits (Huang, et al. 1999). This is one of the molecular mechanisms underlying the synaptic principle of "use it or lose it."