Adjourning Alzheimer's

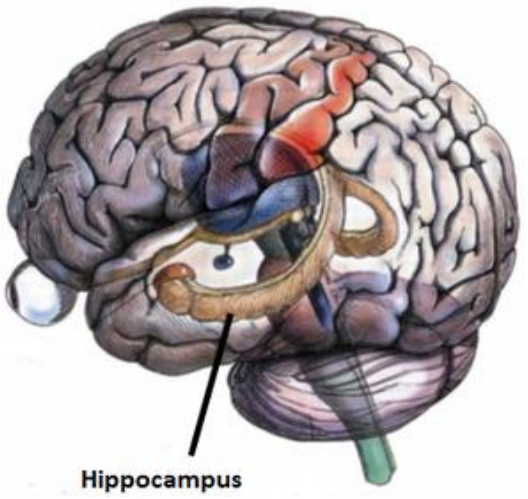
The Edge (Day 57)

Most people know that muscle cells grow with the **physical stress** of exercise. The greater the stress, the more the muscle cells grow - to a point. There is an **optimal zone of physical stress**, heavier than what the muscle cells can comfortably lift, but not so heavy so as to result in significant injury. This optimal zone of muscle growth and remodelling exists in a narrow region between physical capability (weight a person routinely lifts) and impossibility (weight far past their capabilities).

Neurons also grow with stress, but not physical stress; neurons respond to the **experiential stress** of new, challenging experiences. Whenever a person has an experience outside their comfort zone, they learn something new, during which new neuron projections or even new hippocampal neurons are created. Just like in muscle cells, there is an **optimal zone for learning**; the learning experience should be unfamiliar and therefore somewhat discomfiting, but not so foreign so as to result in utter confusion, or mental trauma. Like muscles, this optimal zone of brain growth and remodelling also exists in the region between that which is overly familiar, and that which is utterly confusing.

Thus, both muscle cells and neurons optimally grow and remodel when a person finds **the edge**, the place where you push yourself, the region between the order of routine and the chaos of taking things too far; in muscle cells it is physical, in neurons it is experiential. Finding a muscle's edge enhances a person's strength, but finding the brain's edge enhances a person's mind.

Enhances the memories that form **you**.



Neurogenesis occurs in the human hippocampus throughout a person's life.

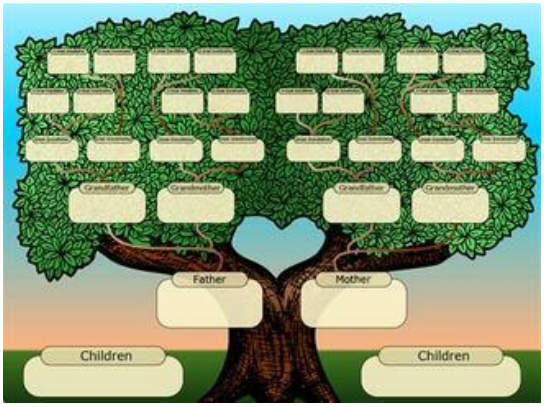
In addition to new neurons projections and new neurons, neurons can be altered a third way, one that is not so much a process of creation as it is a process of **revealing** what is already there.

We all contain a **genetic code**, the entirety of our sequence of genes, within each of our nucleated cells. These genes provide a template for the expression of proteins, molecules that build the cells and ultimately, build us. The genetic code is fixed and cannot be altered; thus, many scientists believe that a person cannot escape the destiny of their genetic code. Yet this is not so, for in truth we can actually alter which genes remain dormant, or "locked," and which ones become expressed, or "unlocked."

The **ancestral hypothesis** states that our genetic code represents the cumulative biological potential of all the ancestors that preceded us. However, much of that genetic code remains locked in life, the genes never expressed, most of our ancestral biological potential never actualized. If we could unlock those genes, we could each **realize our full potential** as the current manifestation of a long line of ancestors. Yet the only way to unlock these genes is to challenge ourselves by seeking new experiences that lie between familiarity and confusion, experiences that call for new genes to reveal themselves, turning more of the potential you "on" so as to reveal aspects of "you" that you never knew existed.

The ancestral hypothesis posits that by seeking new, challenging experiences - seeking the edge - you can **rescue your ancestors** from obscurity. You rescue them, by partially becoming them. You rescue yourself, by becoming you. But not the "you" that exists right now.

The "you" that you **could be**.



We each have the capacity to unlock the biological potential of a long line of ancestors, but only if we constantly confront new, challenging experiences.

By seeking the edge, we can potentially **turn on** numerous genes that are currently silenced (and perhaps turn off some that are currently overactive). Repeatedly, scientists tell us we are the sum of our genes (hence the pursuit of gene therapy for diseases), yet this is not so - no, it is more accurate

to state that we are the sum of those genes that are expressed; many are not. The concept of differential gene expression is described by the scientific field of epigenetics.

In the 1940s, British biologist Conrad Hal Waddington introduced the concept of **epigenetics**, which literally means "above genetics." Strictly speaking, epigenetics describes heritable changes in gene expression, through processes such as DNA methylation and histone modification, that do not alter the structure of the genes themselves. Plainly speaking, this means that **the same genetic code can be "read" in different ways** by the body, simply by physically blocking genes so they cannot be expressed into proteins, or unblocking them so they can. Blocked genes remain "locked," unable to express themselves, whereas unblocked genes are "unlocked," able to contribute to the growth and remodelling of the cell, and ultimately the person.

If epigenetics sounds confusing, consider the novel *The Count of Monte Cristo* by French author Alexandre Dumas. The original 1844 story is set in stone. However, various film adaptations are made every one or two decades, the story brought to life by a different director and set of actors every time; each adaptation varies tremendously (watch the 1975 and 2002 versions; I leave it to you to decide which is better). Thus, **how the story is told impacts how it is brought to life as much as - or more than - the story itself**. Epigenetics states that although each person's genetic code is set in stone, through varying and different experiences, that code can be brought to life in vastly different ways. Thus, how the genetic code is read impacts how it is brought to life as much as - or more than - the code itself.

The original story of The Count of Monte Cristo is set in stone, yet each film adaptation varies tremendously. Likewise, a person's genetic code is also fixed, but can be brought to life in vastly different ways.

Let's s look at a simple example that illustrates the power of epigenetics - consider two different cells in the same person, such as a skin cell and a neuron. Both have the same genetic code, but **different genes are locked and unlocked in each**, resulting in two cells with utterly different structures and functions. Exact **same** code. Totally **different** cells.

We are not just the sum of our genes, but **the sum of those genes that are expressed**. By seeking the edge, we can unlock dormant ancestral genes, revealing more of who we can be.

Epigenetics has far-reaching implications, one of which is that it provides a **potential method** for improving Alzheimer's.

Regardless of what the advocates of gene-based therapies often imply, the truth is that in nearly all cases, Alzheimer's does not result from alterations to the genetic code itself, but is a consequence of factors unrelated to the genetic code - that is, metabolic disturbances due to epigenetic factors. This implies that by altering which genes are locked and unlocked, **what a person does may alter their Alzheimer's**. Thus, if we try to lock the genes that contribute to impaired brain insulin signalling, and focus on unlocking the genes that open up alternate pathways of energy metabolism, maybe - just maybe - we can alter the pathological process that is Alzheimer's.

This means seeking therapies that unlock those ancestral parts of "you" that are anti-Alzheimer's, yet provide experiences that place you between familiarity and confusion, between capability and impossibility; therapies that are **challenging yet doable**.

Let us seek the edge. The edge that rescues your ancestors, reawakens the "you" that you could be…not only saving what you already have, but **revealing new aspects of you**, aspects that have never been turned on before.

In 2019, together, **we will seek the edge**.

Matt (Neurologist, Waikato Hospital).

References

(1) Weinhold. 2006. Epigenetics: The Science of Change. Environ Health Perspect 114(3), 160-167.

(2) Sanchez-Mutt and Graff. 2015. Epigenetic Alterations in Alzheimer's Disease. Front Behav Neurosci 9(347), 1-17.