SCIENCE in SOCIETY REVIEW

The Triple Helix, Inc.

THE TRIPLE HELIX

FALL 2015

Welcome to the 2016 edition of the Science in Society Review!

While the 2015-2016 school year has been one of exciting changes within the Triple Helix, the Science in Society Review continues its legacy as the core of our chapter, operating as our central forum for science in society.

Our articles are intended to elicit critical thoughts and discussion on the links between science and other fields, including business, law, and ethics. As society moves and changes, it is important for people to take a step back and take a holistic approach in understanding science. By reading this journal, you are joining our mission in understanding the dynamic relationship between science and society. It is our hope that these articles will challenge you to critically think about science in an interdisciplinary context and ponder where science should progress as we move forward.

If you enjoy your experience reading this journal, we cordially invite you to join the Triple Helix.

–Sean Yamakawa and Yamini Vyas
Co-presidents of the Triple Helix (JHU chapter)

STAFF

Published by The Triple Helix

CONTENTS

ABOUT

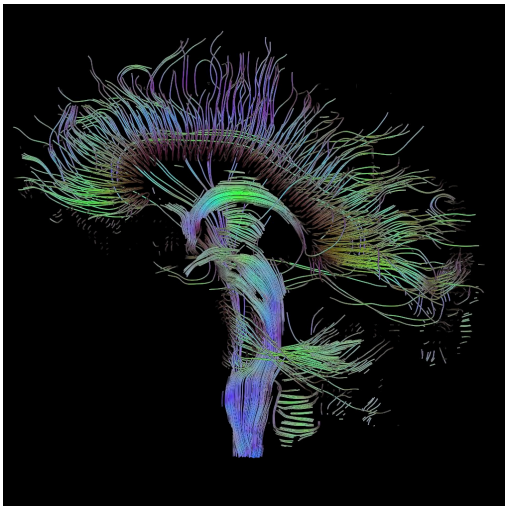
The Triple Helix is an international network of undergraduate students that focuses on the dynamic relationship between science, society, and law. We aim to promote education and critical thinking about current developments in science and the implications of these issues within a broader societal framework. The flagship journal of the Triple Helix is the Science in Society Review, which features articles that tackle scientific issues from any interdisciplinary lens including business, law, and ethics. Starting in the fall of 2016, the Triple Helix will also be responsible for the publication of the Hopkins Undergraduate Research Journal (HURJ). In addition to these publications, the Triple Helix also hosts discussions, lectures, and conferences throughout the semester, so there is always something to look forward to! If you have any questions or comments about The Triple Helix at Johns Hopkins, please contact jhu@thetriplehelix.org.

The Perpetually Changing Organ

An in-depth exploration of the mechanisms and implications of neuroplasticity

Scientists originally believed that the adult brain was hardwired, much like a machine, and that its neural networks were fixed and unchangeable. This was based on the false presumption that the human brain is composed of highly specialized regions that cannot "cross-function," or work in substitute of each other. Scientists, however, did understand that the brain was incredibly plastic during early childhood, and processes such as synaptic pruning (the degradation of excess neural networks) highlighted the concept of neuroplasticity in early brain development. However, they believed that this plasticity came to an abrupt halt once this development was completed. Because of this strong notion that highly specialized brain regions were not interchangeable in function, researchers and physicians alike assumed that brain damage was permanent; such patients had no chance of regaining the functions of the damaged regions. Over the last few decades, however, scientists had a conceptual breakthrough that completely changed our perception of the brain.

The brain can reconstruct and rewire its neural pathways, even when the original pathways no longer work due to some type of damage or block. To effectively explain the concept of neuroplasticity, Dr. Norman Doidge, a physician-researcher who explores this phenomenon, parallels the brain to a ski slope in The Brain that Changes Itself (2007). In skiing, many different paths down the slopes are created. The more often a path is used, the deeper it becomes. Say, however, that one of the ski paths becomes blocked by a fallen tree. The skier will then have to create a new path around the tree, by venturing off the original path, to reach the same destination. The human brain works in a similar way: there are a series of favorable neural pathways that it uses for specific behaviors and actions, akin to the major ski paths that most skiers use. If these neural pathways get blocked for any number of reasons, the brain can reorganize itself and create a new neural path that reaches the same destination in the brain, thereby allowing it to continue normal functioning. The more a neural pathway is used in the brain, the stronger the connections between the neurons in the network, thereby making it much easier for the neurons to fire and work together. This analogy highlights the adaptability of the brain, but does not illustrate the ready moldability of it. The brain does not just change when there is damage, it changes much more frequently and with a greater ease. Specifically, the brain's neural pathways can potentially change with our experiences, thoughts, and everyday actions.

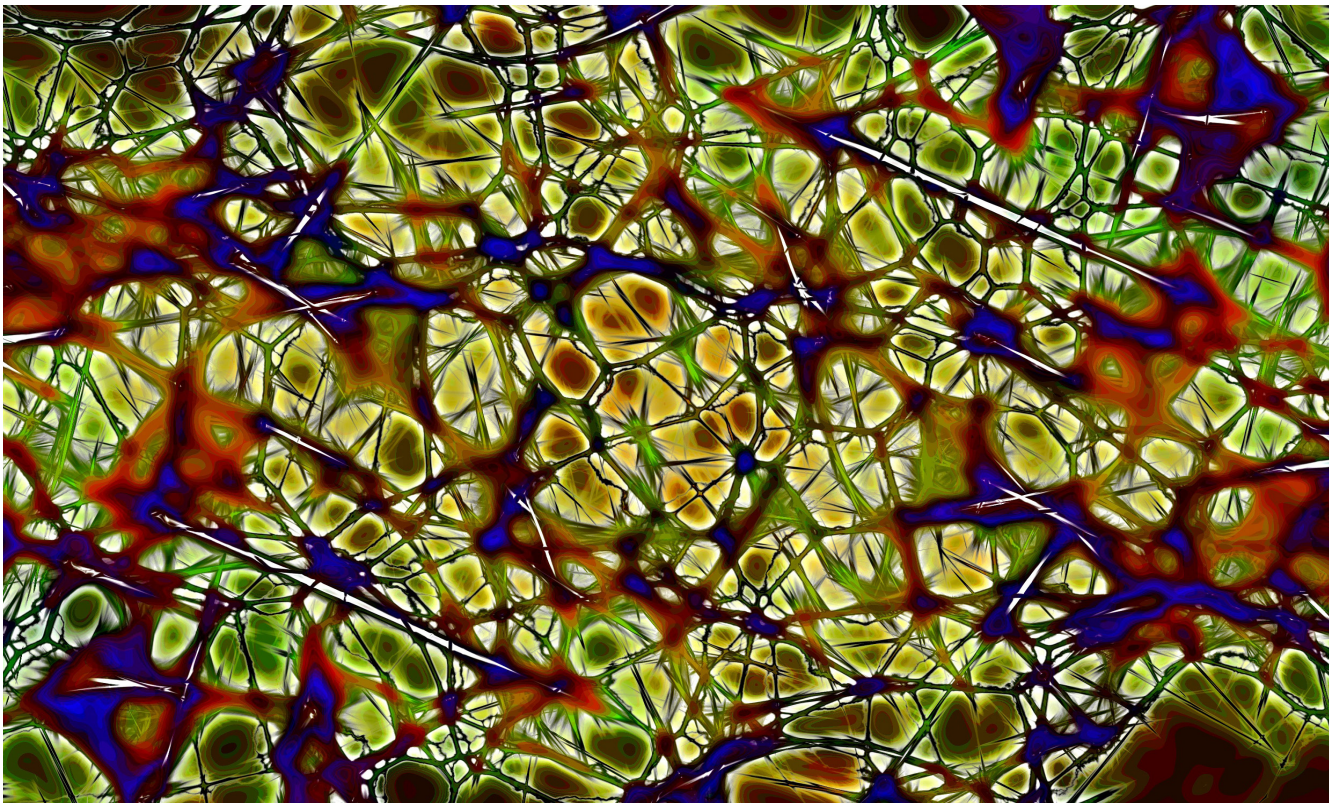


An image of neural pathways in the brain taken using diffusion tensor imaging

The Neural Mechanisms Behind Brain Plasticity

When two neurons transmit their impulses at the same time, we say that these neurons fire together. This concept leads us to one of greatest theories in neuroscience, the Hebbian theory, which states that neurons that fire together, wire together. This simply means that as neurons fire together, they become stronger in transmitting information to each other (i.e. the connections between their synapses get stronger). Through this simple principle, scientists have come to realize that pathways in the brain can be formed and/or reinforced through classical conditioning. Through this conditioning, one stimulus is paired with another to produce the same physiological response. This can be illustrated through the experiments of Ivan Pavlov on his dogs, who noticed that his dogs salivate when they see food. For his experiment, Pavlov rang a bell before giving the dogs food. The stimulus of the ringing bell was paired to the stimulus of the food and the dogs' salivation. Over time, this connection between the

Published by The Triple Helix



Neural networks in the human brain

ringing bell and the presentation of food was strengthened in the dogs' brain. The neurons that fired with the ringing bell in the dogs' brains were paired with the neurons responsible for salivating at the sight of food; these neurons "wired" together because they kept firing together. Eventually, the dogs began salivating just by hearing the bell itself! This conditioning highlights the changeable nature of the neural connections in our brain.

So what allows these changes in our neurons? Although there are a variety of biological and neurological factors, astrocytes play a major role in altering the pathways of the brain [6]. Specifically, astrocytes involved in tripartite synapses (synapses in which there is a an astrocyte that modifies the connection between the two neurons) have the ability to modify the connections between neurons. They are also responsible for lateral signaling, a process that allows for even more connections to be formed between neural pathways. They can dissolve and help create connections between neurons, allowing for the brain to be readily moldable to any number of experiences and issues that come its way. Scientists are still unsure of how these astrocytes are activated to change such connections with experience. Once these neural connections are created, these pathways are reinforced by neurotransmitters, or brain chemicals, that are released when one neuron passes an action potential (nerve impulse) to another neuron. These neurotransmitters are released by the axon, or "sending end," of one neuron, and are absorbed by the dendrites, or "receiving end," of the next neuron. Through this chemical transmission, neurons are able to communicate with one another.

Medical Applications and Implications

Neuroplasticity has applications in a variety of areas – ranging from brain therapeutics to sports training, military training, education, and virtually anything that results from changes in the brain. Moreover, as the following subsections will illustrate, recognizing the brain's ability to reconstruct its neural pathways creates endless opportunities to cure brain diseases and disorders. Now that scientists and physicians know that the brain can readily transform itself, they can potentially cure an incredible amount of neurological disorders and dysfunctions, ranging from brain damage due to stroke or even certain neurological hereditary diseases. In the following two subsections, the paper will examine two case studies, presented in The Brain that Changes Itself, that exemplify the use of neuroplasticity in modern medicine.

Case Study 1 – Michelle Mack

Michelle Mack was born with only half of her brain; the left hemisphere of her brain had never developed because of a catastrophic event in the womb. The brain uses the left hemisphere for speech processing and development, so what happened to Michelle's language capabilities since she lacked these areas? The answer, surprisingly, is nothing. Michelle can speak normally; people cannot tell that she is missing a whole half of her brain! In this case, Michelle's brain has rewired itself to work in speech processing with only the functional half,

portraying the awe-inspiring way that the brain adapts its networks to function in the desired manner.

Case Study 2 – Cheryl Schiltz

Cheryl Shiltz had a hysterectomy and received a medication which unfortunately ended up poisoning her vestibular apparatus (the balance system), making her feel as if she was perpetually falling into an abyss. However, neuroscientist Paul Bach y Rita created an invention, using Cheryl to test it, that would potentially cure Cheryl and others like her of their disorders. The invention, placed on her head with an electrical tab on her tongue, would create signals that worked around the dysfunctional sensory pathways of the vestibular apparatus. Because Cheryl's vestibular pathways were damaged, the invention used the pathways linked to the tongue to provide Cheryl's brain with her orientation in space. Now, the tongue is obviously not used for balance purposes. However, the signals from the tongue were able to carve new pathways in the brain, bypassing the damaged vestibular pathways, to reach the vestibular processing area of the brain. After using this machine multiple times, there was a residual effect when Cheryl took off the device; she was still able to maintain her balance! With increased use of the device, the residual effect had become so great that Cheryl no longer needed the invention. In essence, the new neural pathways had been reinforced well enough to function without the aid of the device. Bach y Rita calls this concept sensory substitution, in which the touch of the tongue was used in place of the vestibular apparatus. His invention laid the foundations of the sensory substitution devices that we have today.

" We may eventually be able to utilize its full power to treat all neurological issues and perhaps even 'enhance' our own brains "

Sensory Substitution Devices

Sensory Substitution Devices (SSDs), are medical devices that utilize the concept of neuroplasticity to solve various sensory disorders and conditions. Researchers at the Hebrew University of Jerusalem used SSDs to allow blind participants to read using 'sound' (signals through the auditory pathways) while also creating 'mental images' from pictures on smartphones, converting the picture into electric signals that make their way to the visual cortex [1]. In essence, this process transforms the stimuli of one sense (one that is impaired) into another stimuli (one that is functional). Using this concept of sensory substitution, just as was used for Cheryl, we can improve the lives of those who are sensually impaired.

Applications for Daily Lives

Knowing about neuroplasticity is not just useful for those who have brain disorders or who are undergoing some type of training, but is also applicable to all people in a broader sense. Specifically, it can help one prevent age-related cognitive decline, simply through constant "exercise" of the brain. By reinforcing the neural pathways involved in critical thinking and analysis, it is possible to make a ninety-year-old think like a middle-aged man once again. But there is a negative side to neuroplasticity: it makes our brain susceptible to change even when we do not want it to be. This is especially true in the case of bad habits. The more a bad habit is committed, the more the neural pathway for that bad habit is reinforced. Once these neural networks are established, they tend to outcompete other ones, making it increasingly hard to rid oneself of the bad habit. The lesson: the longer a person waits to stop a bad habit, the harder it will be. Overall, as scientists continue to understand more about this incredible feature of the brain, we may eventually be able to utilize its full power to treat all neurological issues and perhaps even "enhance" our own brains.

– Ansh Bhamar

Edited by Samantha Getsin

Ansh is a student researcher at the Gallagher Lab at JHU particularly interested in neural plasticity and neurodegenerative diseases..

References

1. Abboud, S., Maidenbaum, S., Dehaene, S., & Amedi, A. (2015). A number-form area in the blind. Nature Communications, 6026-6035. doi:10.1038/ncomms7026
2. Azevedo, F., Carvalho, L., Grinberg, L., Farfel, J., Ferretti, R., Leite, R., . . . Herculano-Houzel, S. (2009). Equal Numbers Of Neuronal And Nonneuronal Cells Make The Human Brain An Isometrically Scaled-up Primate Brain. The Journal of Comparative Neurology, 513(5), 532-541. doi:10.1002/cne.21974
3. Dembosky, A. (2015, August 10). Will Doctors Soon Be Prescribing Video Games For Mental Health? Retrieved November 2, 2015.
4. Doidge, N. (2007). The brain that changes itself: Stories of personal triumph from the frontiers of brain science. New York, New York: Viking.
5. National Institutes of Health. (2012, December 3). Neuroplastcity. Retrieved November 2, 2015, from https://www.nichd.nih.gov/about/overview/50th/discoveries/Pages/neuroplasticity.aspx
6. Pirttimaki, T., & Parri, H. (2013). Astrocyte Plasticity: Implications for Synaptic and Neuronal Activity. The Neuroscientist, 19(6), 604-615. doi:10.1177/1073858413504999

Published by The Triple Helix

HIV Policy Changes from the WHO Promises More Effective Prevention

WHO declares more aggressive HIV treatments will increase survival rate over

Since its initial reported case in 1981 HIV has spread globally to become one of the deadliest and most widespread infectious diseases in recent history, with an estimated 36.9 million carriers and 2 million newly reported cases by the end of 2014 [2]. Its prevalence throughout the world has prompted many governing bodies and public health organizations to draft their own resolutions and policies to address how the disease should be treated.

Among the most prominent is the World Health Organization, the United Nations' official public health agency. The organization periodically releases revisions in its recommendations for treatment and prevention of HIV; the most recent of these revisions was announced earlier this year on September 30th [2]. The new policy includes provisions for more immediate care for anyone who receives a positive diagnosis, as well as those deemed to be at a "substantial risk" of contraction. These changes have been made in light of new research suggesting that such adjustments in the implementation of treatment may prove more effective in combating the spread and lethality of HIV compared to previous beliefs and the policies currently implemented by many governments [1]. Backlash can be expected from numerous public health officials representing their respective countries as these proposals might be deemed infeasible due to cost or logistics. However, a sizable body of data suggesting benefits to this new approach of treatment, as well as the recent improvements in the effectiveness of the treatments offered, suggest that implementation of the WHO's new recommendations may provide a more potent strategy in tackling HIV [1].

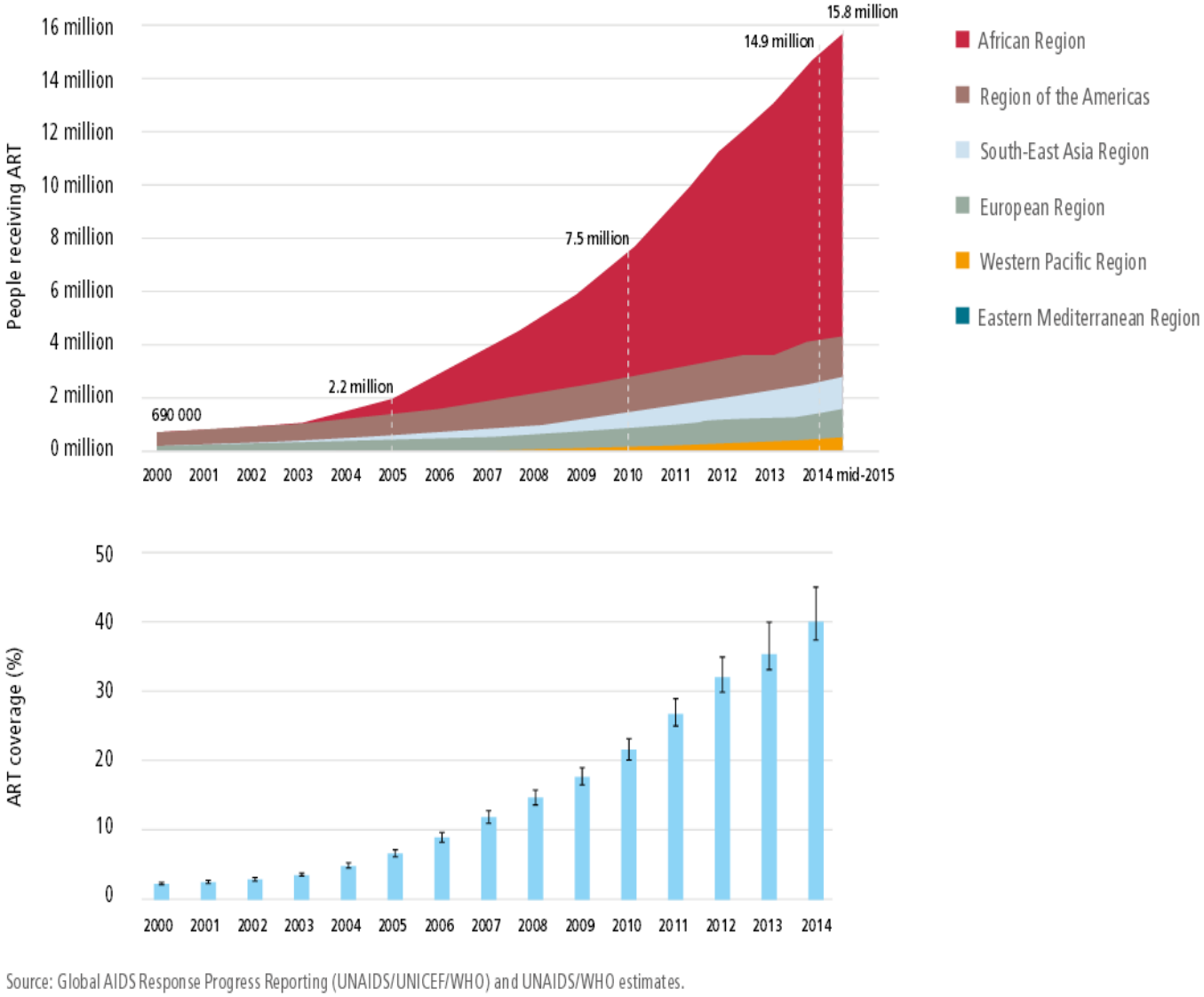
Background

HIV's lethality stems from its immunosuppressing effects following initial entry into the body. The virus carries proteins on the surface of its envelope that can recognize and bind to CD4, a protein found on the membrane of various immune cells. The primary carriers of CD4 are T lymphocytes, which release cytokines upon activation in order to initiate the immune response; macrophages, responsible for the digestion of foreign and potentially harmful bodies such as viruses; and dendritic cells that activate T-helper lymphocytes and magnify the inflammatory response. Once bound to the host cell, the viral DNA will integrate itself into regions of the host's genome that experience particularly high rates of transcription. This ensures that a large number of virus copies will be produced prior to the onset of lysis, in which the host cell is killed after its cell membrane ruptures and cytosolic components are exposed while copies of the original virus are released for further infection. The key aspect to note is the fact that HIV is reliant on the detection of CD4 in order to recognize a potential host as this protein is found exclusively on the membranes of the immune cells mentioned above. The result is the drastic compromise in immune system function characteristic of those infected with HIV, leaving patients vulnerable to a wide range of infections that are now life threatening when they would otherwise pose negligible risk.

Equally concerning as the danger posed by the virus itself is the relative ease in which it can be transmitted from a patient to a healthy individual. HIV survives in certain body fluids of a carrier and will thus be present in any sample of those fluids that contacts an exposure in a potential carrier. This includes contact with infected blood, either through direct exposed contact or indirect means such as the sharing of needles, and transmission through unprotected sex. Also problematic is the fact that the virus itself does not manifest any superficial symptoms, meaning that it may go unnoticed for up to ten years during which it can proliferate within the carrier [3].

Detection, Treatment, and Preventative Measures

Current methods of addressing and combating the epidemic involve preventing both the threat posed by HIV within the body and its spread. Researchers were able to take advantage of the virus' targeting of CD4 cells by developing a test capable of detecting cells carrying this protein in the bloodstream [4]. This tool provides physicians with not only a way to confirm the onset of the disease but also a metric to track its progression. It has been used by a number of organizations worldwide, including the WHO, to determine qualification to begin antiretroviral therapy (ART) to those infected and pre-exposure prophylaxis (PrEP) to those deemed to be



Corresponding line and bar graphs displaying increased global administration of ART between 2000 and 2014, according to WHO figures. These rates are expected to increase even further with the application of their new HIV policy.

at "high risk".

ART consists of administering a minimum of three drugs, each with a different effect meant to combat the proliferation of the virus within an infected patient's body. The combination of different drugs—namely non-nucleoside reverse transcriptase inhibitors (NNRTI's), nucleoside reverse transcriptase inhibitors (NRTI's) and integrase strand transfer inhibitors (INSTI's)—which prevent replication, maturation, and binding of the virus to the host, respectively [5], serves to minimize both the production of new viruses and their ability to infect other immune cells. For those who test negative for HIV but are considered to be at a higher risk of infection, such as spouses and family members of patients, an alternative treatment is provided in the form of PrEP. This consists of a single pill, most commonly a combination of two drugs called tenofovir and emtricitabine, taken daily to reduce the risk of disease transmission in tandem with other preventative measures [5].

While medical treatment can be an effective tool to minimize the spread of HIV in susceptible populations, preventative measures are often the preferred approaches employed in such communities in the hope that they may reduce the need for medical resources. Education in particular is frequently favored as a means of spreading awareness regarding how the virus is transmitted and how to prevent infection; research suggests that education may in fact be the greatest effector of the rates of HIV prevalence between communities, even more than other commonly cited factors such as socioeconomic status [6]. Other prevention methods, including increased

Published by The Triple Helix

access to safe sex resources and improved sanitation, also correlate to lower rates of transmission.

Disparities in Prevalence and Mortality Rates

A thorough strategy to prevent or minimize an HIV outbreak would employ a combination of both preventative measures and medical treatment through means listed above, and indeed previous WHO guidelines as well as governments with affected populations have suggested or implemented such strategies. Often these involve the creation of official task forces to offer screening tests and aid, funding clinics to provide treatment for those diagnosed, and promoting methods of prevention such as proper sanitation and safe sex through abstinence and the use of condoms [7]. Yet despite the apparent parallels between the plans of these governments, glaring disparities in overall prevalence and mortality rates remain. One possible explanation is a simple lack of resources required to effectively carry out such plans; HIV prevalence is highest in areas that tend to have fewer medical resources to treat those already infected as well as educational resources to spread awareness of the disease. Sub-Saharan Africa in particular has been devastated by the virus, with 25.8 million residents currently infected and about 70% of newly reported global cases originating in this region [2]. In contrast, the more affluent community of San Francisco has reported a steady decrease in new cases and lethality over the last two decades thanks to improved access to PrEP [8]. Another possibility is the difference in how available resources are allocated, in which they may be restricted by bureaucratic inefficiency or used for less effective methods. For example, a significant decline in prevalence was observed in Tanzania between 1994 and 2005 following the implementation of programs that stressed HIV counseling and education [9]. In comparison, rates of prevalence actually increased during this same period in Malawi in large part due to difficulty in establishing a comprehensive, multi-sectoral strategy [9].

Looking Forward: Eradicating the Epidemic

To reflect changes in our understanding of the epidemic, the World Health Organization updates its own official recommendations for international HIV policy on a yearly basis. However, the new recommendations from September were significant in that they proposed the most aggressive administration of medicinal treatment suggested by any official body. The key difference between the WHO guidelines originally released in 2013 and the new revisions is the recommended point in infection to begin treatment. The former recommended administering ART to individuals whose CD4 counts had reached or dipped below 500 cells/mm3; this has been revised in 2015 to include all patients, regardless of their current cell count, who appear to suffer from immune system compromise without necessarily falling below an arbitrary concentration. This proposal would hypothetically diminish the reproduction of HIV at an early stage to minimize its impact on the immune system of infected patients. Close acquaintances of these patients would also be eligible to receive PrEP treatment to further reduce the likelihood of transmission; the widened availability for both treatments would be extended to all demographics [1].

Although evidence from well-conducted studies carried out by the organization back up these recommendations, they will likely receive criticism from some government and healthcare officials as being infeasible due to cost. Yet as evidenced from the WHO's report, as well as the trend observed in San Francisco, this new strategy holds a great deal of promise in its effectiveness in combating HIV and may prove to be the critical component in changing the outcome of our efforts to eradicate the epidemic.

– Daniel Schwartzbaum
Edited by Joe Hakim

Daniel is a sophomore Molecular and Cellular Biology major and is interested in writing about recent developments in microbiology and medicine.

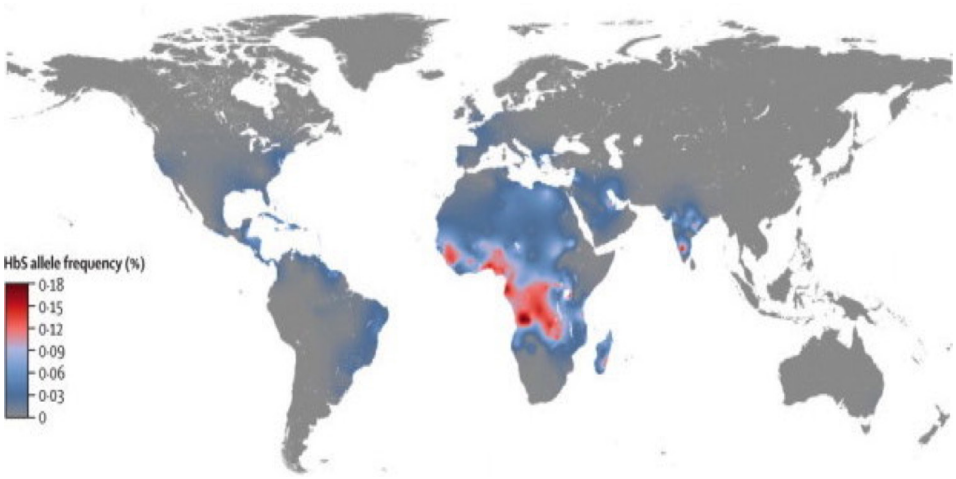
References

1. Guideline on When to Start Antiretroviral Therapy and on Pre-exposure Prophylaxis for HIV. Publication. Geneva, Switzerland: World Health Organization, 2015. Print.
2. HIV/AIDS. (2015, November 1). Retrieved December 2, 2015, from http://www.who.int/mediacentre/factsheets/fs360/en/
3. Stages of HIV Infection. (2015, August 27). Retrieved December 2, 2015, from https://www.aids.gov/hiv-aids-basics/just-diagnosed-with-hiv-aids/hiv-in-your-body/stages-of-hiv/
4. CD4 Count. (2015, September 9). Retrieved December 2, 2015, from https://www.aids.gov/hiv-aids-basics/just-diagnosed-with-hiv-aids/understand-your-test-results/cd4-count/
5. What to Start: Selecting a First HIV Regimen | HIV/AIDS Fact Sheets | Education Materials | AIDSinfo. (2015, April 29). Retrieved December 2, 2015, from https://aidsinfo.nih.gov/education-materials/fact-sheets/21/53/what-to-start--selecting-a-first-hiv-regimen
6. Gillespie, S., Kadiyala, S., & Greener, R. (2007, November 1). Is poverty or wealth driving HIV transmission? : AIDS. Retrieved December 2, 2015, from http://journals.lww.com/aidsonline/Fulltext/2007/11007/Is_poverty_or_wealth_driving_HIV_transmission_.2.aspx

The Role of Context in Health Education

A demonstration of how the context of a disease can vary across multiple communities

Many global diseases, such as tuberculosis and HIV/AIDS, occur throughout multiple continents with various cultures assigning different values to diseases based on their own traditional beliefs and history. As a result, health care educators, such as the World Health Organization and American School Health Association, face obstacles when they attempt to educate the public on certain diseases, but their teaching material is misinterpreted or conflicts with previous assumed knowledge or traditional beliefs. For example, people are more likely to misunderstand a health message on more difficult or abstract topics like disease theory or bacteria than one presenting a concrete familiar topic (Hubley 238). Additionally, harmful traditional beliefs have proven extremely difficult to change, so health educators must address these beliefs in their teachings to avoid conflict (Hubley 235). The different cultural responses to sickle cell disease provide one example of the traditional beliefs that educators must account for when communicating with the public. Addressing the local perception of a disease is an integral component of health education.



Distribution of the sickle cell trait (HbS allele) (Piel et al. 144)

The second annual Walk a Mile for Sickle Cell event in Atlanta, Georgia.

Sickle-cell disease (SCD) is a recessive hereditary blood disorder that must be inherited from both the father and the mother. If the child only receives one copy of the gene, he or she is a carrier for the sickle cell trait, but is not affected. Each year, around 312,000 babies are born with the disease worldwide (Piel et al. 142). Sufferers of SCD report a low quality of life in both Western nations and developing countries. One of the factors associated with their low quality of life is the stigma attached to the disease: varying superstitions and stereotypes surrounding SCD within communities within Ghana, Kenya, and the United States negatively impact the lives of those affected. Although many nonprofits work to reduce the physical symptoms of SCD, they have not yet reduced widespread cultural stigmas. In order to improve the quality of life of those with SCD, stigma surrounding the disease must be addressed at a contextual level, since its origins vary drastically between cultures.

In the Ghanaian metropolis of Kumasi, many folk beliefs negatively affect the lives of parents and children with SCD. SCD is sometimes considered a "bought" disease that an enemy purchased to bring hardship to the family. This explanation blames the disease on an external source and may cause the parents to view their child as a burden. Without treatment, 98% of children with SCD do not live past the age of five (Dennis-Antwi et al. 466). As a result, parents perceive their children as passing through life very briefly,

Published by The Triple Helix

A free testing event in a remote area of Ghana.

and consequently not worth caring for. This belief results in a self-fulfilling prophecy due to negligence: as one father described, "even in his time of ill health, I often did not pay much attention to him because I was convinced he would die anyway," (Dennis-Antwi et al. 472). Folk beliefs, in addition to the cost of healthcare, cause many children with SCD to not receive treatment. However, folk beliefs provide a way for parents to "make sense" of the disease. Though these beliefs seem to be fading with extended life expectancy of children with SCD (due to bonding with parents), they remain prevalent throughout the community. Health educators must therefore address these beliefs to help parents reconcile with the scientific causes of SCD.

The relationship between health education and folk beliefs is more complex in the Mijikenda community of Kenya. The parents of children with SCD report believing a mix of medical and supernatural explanations, which can easily shift over time. Unlike the folk beliefs of Kumasi, the Mijikenda folk beliefs are based on heredity. The Mijikenda society is patrilineal, meaning that social and political identities are passed through the male line, which results in different parental roles for men and women. Specifically, mothers bear responsibility for childcare and any health problems in the child. When a child is born with SCD, the mothers are accused of either solely carrying the disease in their family or, if her family shows no evidence for SCD, being unfaithful to their husbands (Marsh et al. 349-352). Since the beliefs of the Mijikenda more closely resemble the genetic cause of SCD, health education may integrate into the community more easily. However, since folk beliefs also include beliefs about maternal heredity, educators must be cautious to not unintentionally assign more hereditary blame to mothers. The perceptions of disease cannot be generalized across different communities. Instead, health educators must assess the perception of a disease on a local basis and incorporate traditional beliefs into their teachings.

In the US, the history of racism plays a larger role in the perception of SCD. In the media, individuals with SCD are almost always portrayed with darker complexions, leading to the disease being exclusively associated with African Americans and labeled as a "Black disease" (Bediako and Moffitt 424-425). However, the sickle cell trait occurs throughout the Arabian Peninsula, India, and the Mediterranean coastline (Piel et al. 142-151). A study in the Qatif region of Saudi Arabia found that 2.35% of infants were born with SCD, compared to only 1.8% of infants in Kumasi, Ghana (Nasserullah et al. 289-292; Dennis-Antwi et al. 466). But because SCD is perceived as a "Black disease," some non-African Americans may

be resistant to screening. For example, when the NCAA began testing athletes for the sickle cell trait, a white student-athlete remarked, "'Everyone who's had ninth grade bio[logy] knows the origins of sickle cell. My ancestors come from Europe - no malaria there,'" (Bediako and Moffitt 426). In reality, the sickle cell trait can be found in the many of the European countries bordering the Mediterranean. Because SCD is seen as only affecting African Americans, many non-African Americans do not feel the need to be tested. Additionally, since SCD is closely associated with "blackness", the disease can be associated with negative views of African Americans. One study found that nurses often showed red-flag behaviors with SCD patients and stereotyped them as drug abusers (Jenerette et al. 180). Anecdotal evidence also suggests that healthcare workers often withhold pain medication from patients with SCD (Bediako and Moffitt 426). While the US may lack folk beliefs about SCD, racial stereotypes still influence the perception and treatment of SCD patients. Health educators must specifically address these views to separate SCD from an exclusive African American association.

"Without treatment, 98% of children with SCD do not live past age 5."

Sickle cell disease is a global issue. To increase awareness and improve treatment, health educators must integrate traditional beliefs of SCD into their programs. In Kumasi, Ghana, folk beliefs treat SCD an attack against the family. In the Mijikenda community of Kenya, traditional beliefs blame the mother for SCD. The popularity of these beliefs seems to be decreasing due to Western influence, although 70-80% of Africans are estimated to still use traditional medicine as a form of primary health care ("Traditional Medicine"). In the US, unscientific beliefs are also present, such as the perception of SCD as a "Black" disease and stereotypes against SCD patients. These three different forms of belief will each require a different approach by health educators. In Ghana, educators would want to stress the scientific basis of SCD and its hereditary nature, but avoid demeaning traditional beliefs. In Kenya, they would instead want to emphasize how both parents give a copy of the sickle cell trait to their affected child to reduce maternal blame. In the US, health educators will need to clarify that SCD can affect multiple races and directly address stereotypes of the disease. Community education (primary and secondary education, pamphlets, support groups, etc.) and genetic counseling will need to address traditional beliefs on a contextual basis. Other diseases, such as HIV and malaria, are also present across multiple continents and will require a similar approach. Health education in any community would be incomplete without addressing the local perceptions of disease.

– India Reiss
Edited by Shriya Awasthi

India is a sophomore Molecular and Cellular Biology major who works in the Johnston lab in the Biology department where she studies the effect of different photoreceptor ratios on color vision in fruit flies.

References

1. Bediako, Shawn M., and Kimberly R. Moffitt. "Race and Social Attitudes about Sickle Cell Disease." Ethnicity & Health 16.4-5 (2011): 423-29. Print.
2. Dennis-Antwi, Jemima A., Lorraine Culley, David R. Hiles, and Simon M. Dyson. "'I Can Die Today, I Can Die To morrow': Lay Perceptions of Sickle Cell Disease in Kumasi, Ghana at a Point of Transition." Ethnicity & Health 16.4-5 (2011): 465-81. Print.
3. Hubley, J.h. "Barriers to Health Education in Developing Countries." Health Education Research Health Educ Res 1.4 (1986): 233-45. Print.
4. Jenerette, Coretta M., Bosny J. Pierre-Louis, Nadine Matthie, and Yasmeen Girardeau. "Nurses' Attitudes Toward Pa tients with Sickle Cell Disease: A Worksite Comparison." Pain Management Nursing 16.3 (2015): 173-81. Print.
5. Marsh, Vicki M., Dorcas M. Kamuya, and Sassy S. Molyneux. "'All Her Children Are Born That Way': Gendered Experiences of Stigma in Families Affected by Sickle Cell Disorder in Rural Kenya." Ethnicity & Health 16.4-5 (2011): 343-59. Print.
6. Nasserullah, Z., A. Al Jame, H. Abu Srair, G. Al Qatari, S. Al Naim, A. Al Aqib, and M. Mokhtar. "Neonatal Screening for Sickle Cell Disease, Glucose-6-phosphate Dehydrogenase Deficiency and A-thalassemia in Qatif and Al Hasa." An nals of Saudi Medicine 18.4 (1998): 289-92. Print.
7. Piel, Frédéric B, Anand P Patil, Rosalind E Howes, Oscar A Nyangiri, Peter W Gething, Mewahyu Dewi, William H Temperley, Thomas N Williams, David J Weatherall, and Simon I Hay. "Global Epidemiology of Sickle Haemoglobin in Neonates: A Contemporary Geostatistical Model-based Map and Population Estimates." The Lancet 381.9861 (2013): 142-51. Print.
8. "Traditional Medicine." World Health Organization. Web. 11 Nov. 2015.

Published by The Triple Helix

Falling from HEAVEN

An exploration of the history, reasoning, and practicality behind the HEAVEN procedure: a proposal for head transplantation

In 2013, an Italian surgeon named Sergio Canavero outlined a procedure he called "HEAVEN". HEAVEN stands for the "head anastomosis venture" project, and in his outline, Canavero lays out the steps he deems necessary to fully graft a person's head onto another, emphasizing spinal connection, which he believes is the greatest barrier of this procedure. He makes clear the two main steps to the entire HEAVEN procedure: hypothermia and GEMINI, the process of spine anastomosis. The subjects undergoing the surgery are defined by "body-recipient" and "donor", and the body-recipient's head is connected to the donor's body.

Much of Canavero's analysis is based upon historical cases, most notably that of a rhesus monkey, done in 1970 by Robert White. The monkey was induced into a hypothermic state as a sedation before its head was severed at the C4-C5 level of the vertebrae. Soft tissue, surrounding muscle, the trachea, and the esophagus were slowly divided from the area around the vertebrae. Spinal shock, manifested as a loss of sensation resulting from the trauma of separation, was relieved by a cervical laminectomy. In the laminectomy, the lamina and spinous processes, two protuberances from a single vertebrae, are removed, allowing the spinal column to move backwards and acquire more space [1]. The next few steps in the procedure were involved in cauterizing the vertebral sinus and eliminating the vertebral arteries. Only then are the vertebral bodies severed from each other, and the head and donor body are subsequently held together by metal plates. The monkey was conscious for 3 to 4 hours, and survived for 36. Vladimir Demikhov, a Russian scientist, was a major influence to White with his two-headed dog surgical procedure. In the 1950's, Demikhov transplanted a puppy's head onto another dog. Canavero has decided to pioneer the movement of these experimental topics into practical application in humans.

The Procedure

Hypothermia

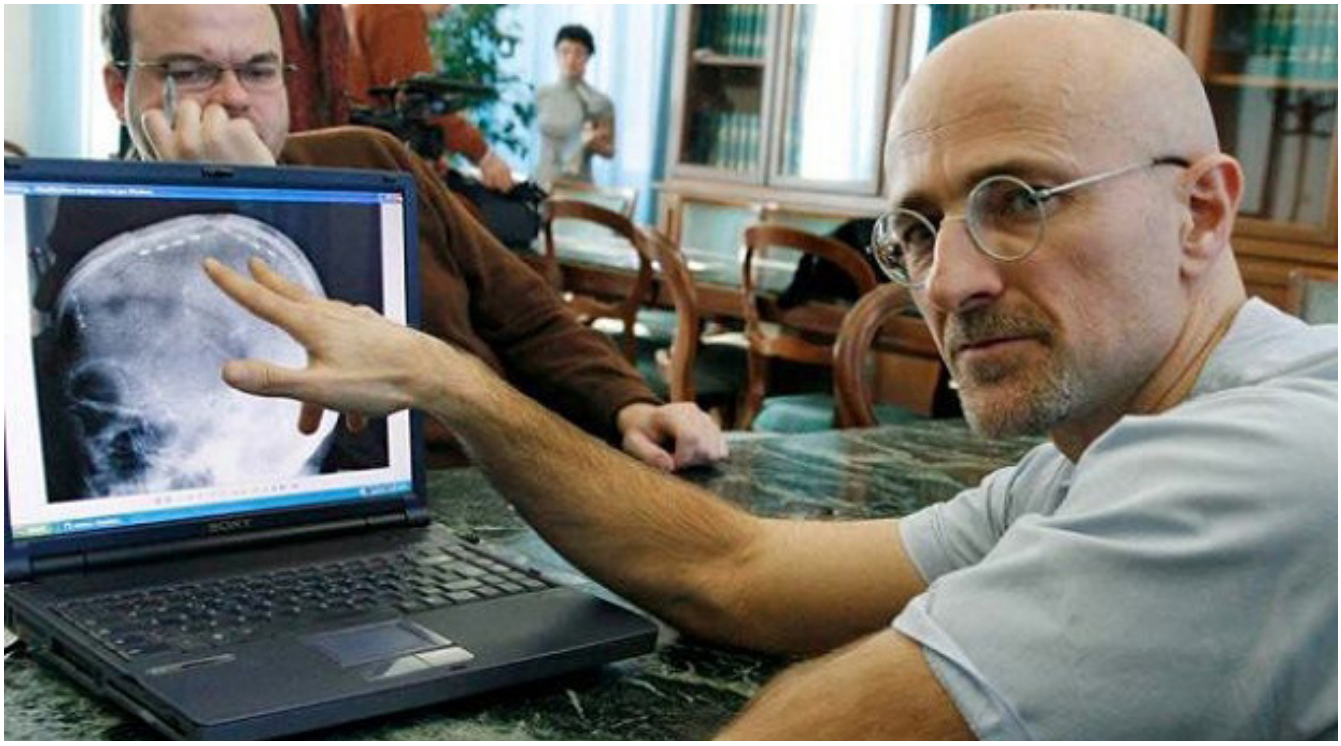
HEAVEN begins with the hypothermia protocol. By cooling the body-recipient's head to a low temperature, the head can then be severed from the body at a reduced risk of damage from circulatory arrest. Cooled to a temperature of 15 C, the brain now has a metabolic rate that is 10% of the normal rate [1]. A conclusion is drawn: profound hypothermia will enable surgeons to have more time to reattach the head, as global ischemia, a condition that arises from lack of oxygen or blood flow to the brain, will be held off. The metabolic demand of the brain is lowered, so the risk of global ischemia correspondingly decreases. The body-recipient's head will be drained of blood and immersed in Ringer's lactate, a solution that is usually injected intravenously to restore fluid and electrolyte balances, to bypass blood clotting, as blood at such low temperatures is coagulopathic, and does not pose clotting issues.

In the protocol, after the patient is placed under anesthesia and the appropriate intubation protocols are finished, a thermistor, a temperature-sensitive resistor, is placed in the temporalis muscle, which corresponds to the side of the head. Vertebral arteries are terminated by temporary occlusion, meaning that blood flow within the arteries is halted temporarily. The left femoral artery and the carotid arteries are placed through cannulation, and the cannulas are connected to a Brown-Harrison high-efficiency heat-exchanger.

GEMINI

The purpose of GEMINI is to separate the spinal cord into two parts with as little damage to the organ as possible. Canavero adamantly stresses the importance of sharply severing the spinal cords. In a study done in 2013 on the differences between spinal cord injuries and lesions by sharp instruments, the force involved in creating a lesion in the spinal cord was found to be less than that involved in blunt trauma. In the study, sharp instruments were used to create lesions, which are characterized by opening of the dura and penetration of part of the spinal cord. He suggests using a diamond snare-blade or a nanoknife to create the lesion [2]. Severance of the spinal cord and reattachment will inevitably impact the motor skills of the body-recipient. Although voluntary movement has often been attributed to the direct connection between the primary motor cortex in the brain and the spinal cord, the majority of the neurons that are attributed to movement are found in indirect pathways between the motor cortex and the spinal interneuronal sys-

Published by The Triple Helix



Italian surgeon, Sergio Canavaro, believes he can successfully conduct a head transplant.

tems, which is defined as the gray matter within the spinal cord. Canavero cites a study in which it has been shown that a patient suffering from tetraplegia, losing sensation and mobility in all four limbs, made a full recovery, even there was atrophy of white matter and in the pyramidal tracts. In a study on gray matter atrophy in the spinal cord and its correlation with multiple sclerosis, it was found that gray matter area and disability was inversely related, obtaining a negative correlation [16]. The study compared the area of white and gray matter derived from images with multiple sclerosis with the results of another study that obtained postmortem measurements of white and gray matter areas in spinal cords without any disease. They found that while there was 33% decrease in overall spinal cord area and a 22% decrease in white matter, there was a 63% decrease in gray matter.

Decreased motor ability seemed to be correlated with a loss of gray matter. An objective of the GEMINI procedure is therefore to regrow the severed axons and dendrites within the gray matter at short distances. In order to accomplish this, a variety of substances, such as poly-ethylene glycol (PEG), will be used to fuse together the severed neural connections or repair neurons that have been damaged in the severing process [2]. Axonal fusion has been done in the past, and there have been developments of scaffold materials as regeneration stimulation as well as devices that could participate in surgical microsplicing and subsequent repair of those severed axons. The whole purpose of these developments is to find a way to allow axons to regenerate to a point where they reestablish the synaptic connections that were lost.

Canavero presents two procedures that he wants to implement. The first involves using a PEG solution and flowing it over the lesion site for two minutes before it is flushed out. The second involves using a "semi-interpenetrating network of PEG and photo-cross-linkable chitosan (a type of bioplastic)" to create an adhesive [2]. The prediction is that there will be no gaps between fused axons, and that the axons will fuse with each other in a particular way that guarantees correct electrical activity and pathways.

After neural fusion, the healing and regeneration process is complemented with electrical stimulation for faster results. The theory behind this electrical stimulation process has its basis in the fact that the networks next to a spinal lesion may lose their excitability qualities if insufficient stimulation is given to the cells. A 2014 study on spinal excitability and its effect on voluntary movements found that patients who had suffered complete paralysis and regained voluntary movement through epidural stimulation required different levels of stimulation to move. The resting excitability state of the spine differed among the individuals in the study as well. Mobility increased after daily stimulation and training, indicating that functional connectivity had been at least partially restored [19].

The patient undergoing the head transplant will then be kept in an induced coma for three to four weeks before the necessary rehabilitation steps begin. This allows the regeneration and fusion of the two severed parts of the spinal cord to proceed undisturbed and increase chances of an absolute recovery.

Published by The Triple Helix

Possible Complications

Although Canavero does give a detailed description of his procedure, there are still many aspects that he is glossing over, especially the molecular aspects of the recovery process. His procedure seems to reflect a broader, macroscopic side of healing, with emphasis on the physical nature of fusion. He does not take into account the many cellular factors that may prevent him from attaining the optimal level of recovery he wishes to achieve.

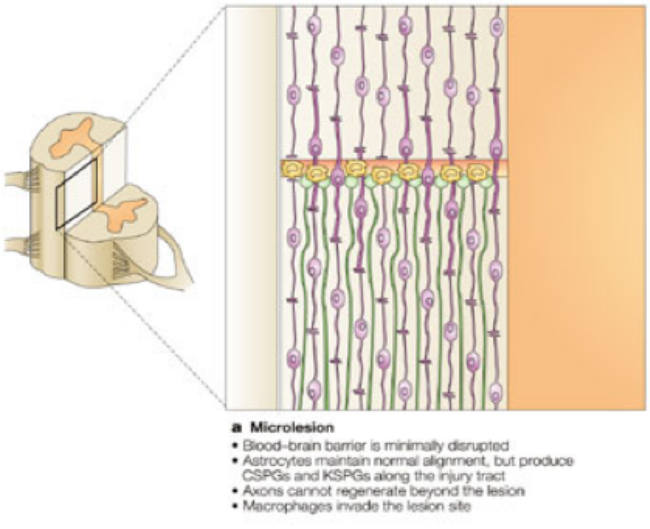
There are complications in axonal regeneration within neurons in the central nervous system. A study was done in 2004 on glial scars, which forms in lesions. When opening of the meninges, such as the dura mater, is involved in the lesion, astroglia, which are neural cells that usually regulate brain homeostasis and causes neuroinflammatory responses, mix with connective tissue that are now in contact with each other. The inflammatory response that astroglia is involved in is called reactive gliosis. Observation of non-regenerating nerve fibers and the presence of entangled and reactive astroglia around those ends give the indication that this reactive gliosis response prevents full regeneration [9]. In a microlesion, astrocytes may prevent the axons from regeneration by forming a barrier. Chondroitin sulfate proteoglycans are generated by the scar tissue, and are involved in inhibiting axon regeneration. In normal neural development as well, CSPG's guide the growth of axons, serving in the notochord to inhibit extension of axons. Absence of CSPG's in the notochord causes the motor nerves and neurons in the dorsal root ganglion, which is composed of a collection of nerve cell bodies and is part of the gray matter of the spinal cord [9]. Other growth-inhibiting proteins, such as SEMA3 and ephrin-B2, are involved. These factors could potentially pose a barrier to adequate recovery. Axon regeneration is different in adults as well. There seems to be a loss in instrinstic neural regeneration as a person ages [17].

Therapeutic hypothermia has been gathering attention in the past few years. It has been used in cardiac surgery and neurological procedures to control the intracranial pressure. For every 1 C decrease in body temperature, the cerebral metabolic rate decreases by 6-7%. In most procedures, therapeutic hypothermia only cools the body to 32-34 C, which is the recommended temperature range [13]. It is not clear which hypothermia-inducing procedure Canavero plans to use.

Hypothermia has been shown to have adverse effects on platelet function [14]. Canavero does mention the compromised ability of blood to clot at low temperatures, as demonstrated in when the body-recipient's head is cooled in Ringer's lactate in order to not experience blood clotting. Hypothermia prevents platelets from aggregating, as well as lowering the platelet count. A study done with a mock hypothermia circulation of the blood, similar to the one Canavero is describing, suggests that the reasons for lower platelet count include binding to the walls of the circulation system, shear stress, and platelet destruction. After 24 hours of circulation, the platelet count was shown to attain a very low level. Tests were done to see how well platelet function recovers after rewarming, and the conclusion was that recovery of platelet function does not begin immediately after the body starts the rewarming process. Recovery is not uniform [14]. This study was done with mild hypothermia, cooling from 37 C to 32 C, so the effect of cooling to 15 C or below may provide adverse effects to a greater extent.

Studies with platelet-rich plasma, or PRP, have been shown to induce axon regeneration in the central nervous system, and can be involved in cases of spinal cord trauma. The composition of PRP involves many platelet-derived wound healing factors. PRP is able to bind to the fibrin between the nerve gaps and induce axon regeneration, and it may even be able to interact directly with severed axons to promote regeneration [18]. These studies indicate that platelets and platelet-derived factors play a role in the regeneration process. Compromise of the system, as in induced hypothermia, may affect the ability of the axons to regenerate. True, PEG may be able to fuse the axons together, but how much of the neuron's chemical balance will be restored? The neuron may still be able to fire because of some restoration of gradient across the cell, but balance would definitely not be attained, especially since PEG restoration is a quick process. If some of the body's own healing factors are compromised, it may cause the regeneration process to be slower or relatively ineffective.

Canavero's support for PEG fusion is based on a study done by G.D. Bittner in 2012. The study looks into the effects of microsutures and PEG on neural regeneration



The effect of CSPG's on microlesions in the spine.

in sciatic nerves in rats. The sciatic nerve is a peripheral nerve that begins in the lower back and runs down the back of each leg. Peripheral nerves have been found to regenerate differently from neurons in the central nervous system. Many regeneration-associated genes are found in peripheral nerves, and axons regenerate relatively quickly when compared to CNS neurons [20]. Environment is important in the regeneration process, and the environment of the CNS neurons does not provide an optimal capacity for supporting neuron growth. Support is also garnered from other studies on the PEG procedure. A study by Riyi Shi in 2013 involves two segments of the spinal cord being aligned, and PEG is flowed over the lesion site for two minutes, as defined in GEMINI. In another study, different molecular weights of PEG were found to relate to the extent of repair. Although these studies do support the use of PEG as a membrane fusing sealant for neurons, they were mostly performed on white matter lesions.

The singularity of each body also has to be taken into account. Too much of the body's systems are regulated by the brain, from modulation by the hypothalamus to signaling from the pons and medulla. Everyone's body has their own rhythm and own set pace; for example, people have different rates of metabolism and different blood pressures. Even if the head transplant were to work, by connecting a different brain to a body that it is unaccustomed to regulating, it may do more harm to both the body and brain than good. They would both try to adjust with or reject one another to establish an equilibrium across the bodily functions, and if that is not achieved, then there is no knowing what will happen.

There seems to be, overall, shaky support for Canavero's procedure, and there are still many questions that need to be answered. Despite all this, a surgery has already been set for 2017, and, as Dr. Hunt Batjer, a president-elect of the American Association for Neurological Surgeons, speculates, the patient may face something that is "worse than death".

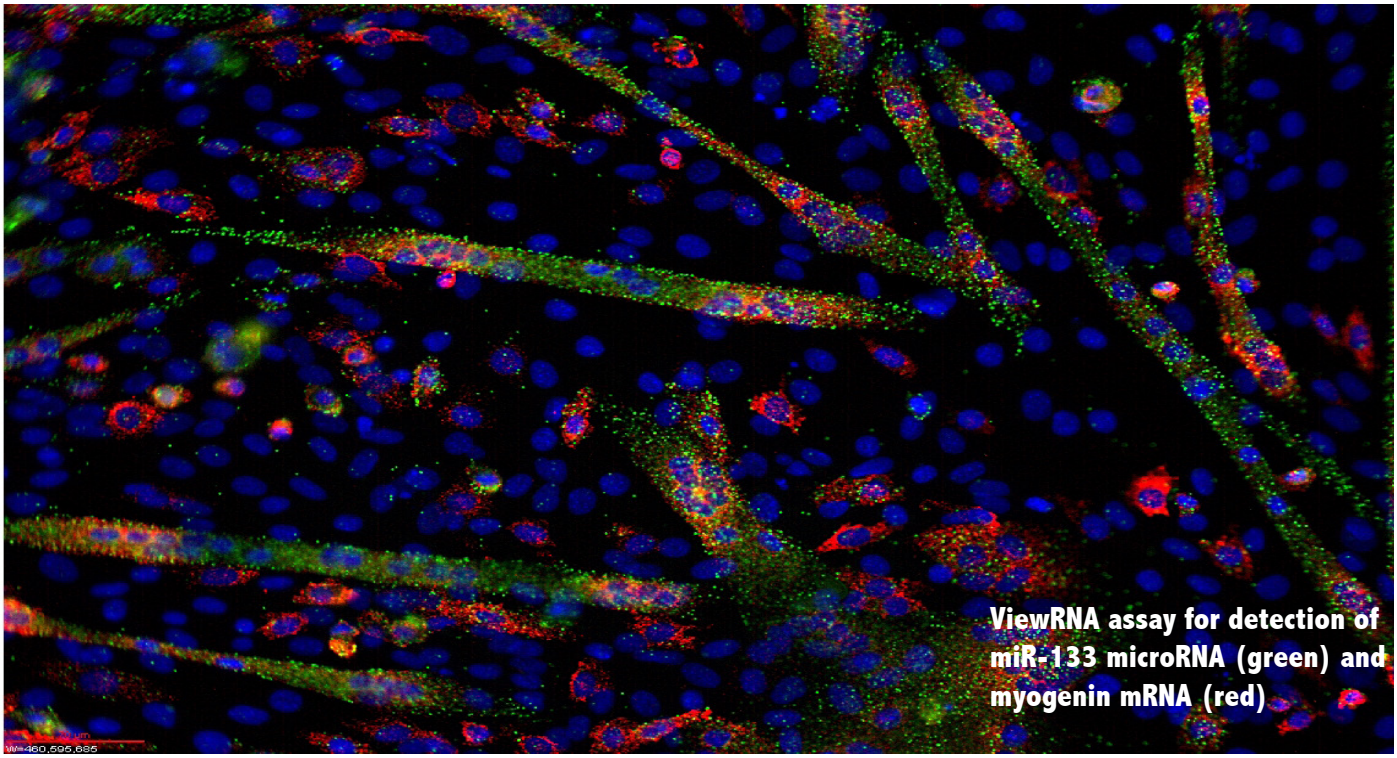
– Tiffany Huang
Edited by Adam Wolin

Tiffany is a freshman Molecular and Cellular Biology and Biophysics double major who is interested in writing about surgery and protein biology.

References

1. Canavero S. HEAVEN: The head anastomosis venture Project outline for the first human head transplantation with spinal linkage (GEMINI) Surg Neurol Int. 2013;4S335-42.
2. Canavero S. The "Gemini" spinal cord fusion protocol: Reloaded. Surg Neurol Int. 2015;6:18.
3. De Georgia M, Deogaonkar A, Merrill TL. Methods to induce hypothermia. In: Mayer SA, Sessler DI, editors. Therapeutic hypo thermia. New York: Marcel Dekker;2005;293–322.
4. Tokutomi T, Morimoto K, Miyagi T, Yamaguchi S, Ishikawa K, Shigemori M. Optimal temperature for the management of severe traumatic brain injury: effect of hypothermia on intracranial pressure, systemic and intracranial hemodynamics, and metabolism. Neurosurgery. 2003;52:102–11.
5. White RJ. Cerebral hypothermia and circulatory arrest. Review and commentary. Mayo Clin Proc. 1978;53:450–8.
6. Bittner GD, Ballinger ML, Raymond MA. Reconnection of severed nerve axons with polyethylene glycol. Brain Res. 1986;367:351–5.
7. Bittner GD, Keating CP, Kane JR, Britt JM, Spaeth CS, Fan JD, et al. Rapid, effective, and long-lasting behavioral recovery produced by microsutures, methylene blue, and polyethylene glycol after completely cutting rat sciatic nerves. J Neurosci Res. 2012;90:967–80.
8. Sharma K, Selzer ME, Li S. Scar-mediated inhibition and CSPG receptors in the CNS. Experimental neurology. 2012;237(2):370–8.
9. Silver J, Miller JH. 2004. Regeneration beyond the glial scar. Nat Rev Neurosci 5:146–156.
10. Schlaeger R, Papinutto N, Panara V, et al. Spinal cord gray matter atrophy correlates with multiple sclerosis disability. Ann Neurol 2014;76:568–580.
11. Sledge J, Graham WA, Westmoreland S, Sejdic E, Miller A, Hoggatt A et al. Spinal cord injury models in non human primates: are lesions created by sharp instruments relevant to human injuries? Med Hypotheses 2013; 81: 747–748.
12. Alstermark, B., and Isa, T. Circuits for skilled reaching and grasping. Annu. Rev. Neurosci. 2012; 35: 559–578.
13. Alzaga AG, Cerdan M, Varon J. Therapeutic hypothermia. Resuscitation. 2009;80:573-579.
14. Van Poucke, S., Stevens, K., Kicken, C., Simons, A., Marcus, A. and Lancé, M. Platelet Function During Hypothermia in Experi mental Mock Circulation. Artificial Organs. 2015
15. Narayanan V, Kanury M, Jenks J. Heat Exchanger Analysis Modified to Account for a Heat Source. ASME/JSME 2007 Thermal Engineering Heat Transfer Summer Conference, Volume 1.
16. Schlaeger R, Papinutto N, Panara V, et al. Spinal cord gray matter atrophy correlates with multiple sclerosis disability. Ann Neurol 2014;76:568–580.
17. Pasterkamp, R. J., Giger, R. J., Ruitenberg, M.-J., Holtmaat, A. J., De Wit, J., De Winter, F. Expression of the gene encoding the chemeorepellent semaphorin III is induced in the fibroblast component of neural scar tissue formed following injuries of adult but not neonatal CNS. Mol. Cell. Neurosci. 1999;13:143–166.
18. Kuffler, Damien P. Platelet-rich plasma promotes axon regeneration, wound healing, and pain reduction: fact or fiction. Molecular Neurobiology. 2015;52:990-1014.
19. Angeli CA, Edgerton VR, Gerasimenko YP, Harkema SJ. Altering spinal cord excitability enables voluntary movements after chronic complete paralysis in humans. Brain. 2014;137:1394–409.
20. Huebner EA, Strittmatter SM. Axon Regeneration in the Peripheral and Central Nervous Systems. Results and problems in cell differentiation. 2009;48:339-351.
21. Rad, I., Khodayari, K., Alijanvand, S. H., and Mobasheri, H. (2015) Interaction of polyethylene glycol (PEG) with the mem brane-binding domains following spinal cord injury (SCI): Introduction of a mechanism for SCI repair J. Drug Targeting 23, 79– 88

Published by The Triple Helix



The Microscopic Answer to a Macroscopic Problem

Finding the cure to cancer is the Holy Grail in medical research today. And this cure may be found in a family of short non-coding RNA segments known as microRNAs (miRNAs). MiRNAs only contain 20-24 nucleotides; however miRNAs play a vital role in many biological pathways including apoptosis, proliferation, differentiation, migration and metastasis. Since miRNAs are involved in a multitude of biological processes, it is safe to assume that these non-coding pieces of RNA have a number of different duties. At the post-transcriptional level in protein production, miRNAs are able to control gene expression by binding to the 3'-untranslated region of target RNAs. They can also affect the relationship between the effector and target mRNAs, which can alter the way certain proteins or molecules are produced and whether the subsequent processes carried out are favorable or harmful for us (e.g. lead to cancer).

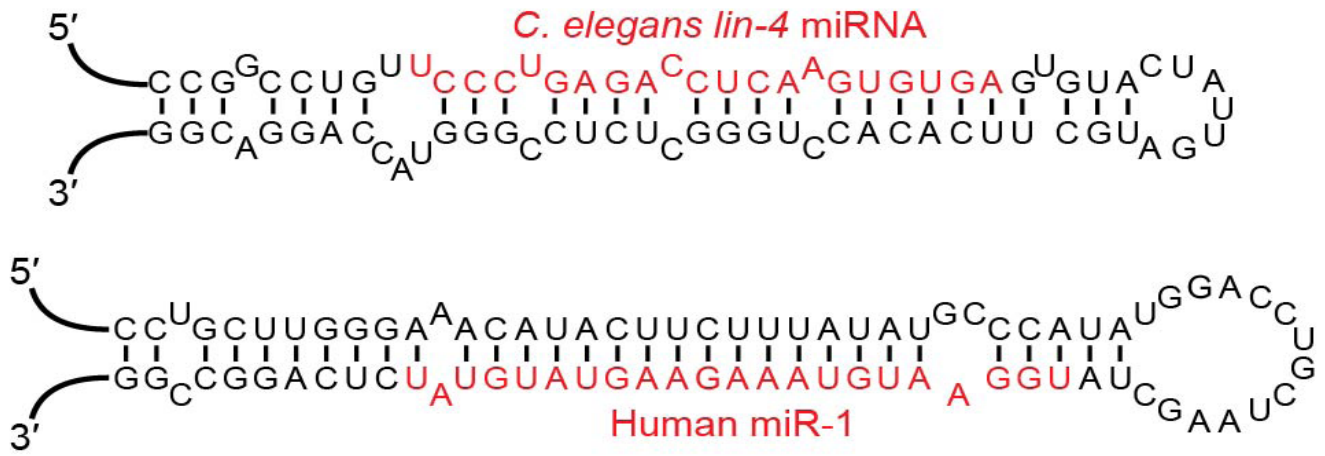
Due to their versatility, miRNAs have been the subject of research for a plethora of diseases. For instance, miRNAs have been known to be involved in neurodegenerative diseases, neurodevelopmental diseases, inflammatory diseases, viral diseases and cardiovascular diseases, in addition to cancer. The importance of microRNAs in cancer prevention and cure is captured in its past discovery, present research and future breakthroughs.

History

The first miRNA, miRNA lin-4, was discovered in the laboratories of Victor Ambros and Gary Ruvkun in 1993. While working in the Hortitz's lab with the nematode C. elegan, Ambros and Ruvkun discovered a link between the lin-4 and lin-14 genes. In the December 1993 edition of Cell they both published their findings: they had successfully identified lin-4 as a small non-protein transcript that regulates lin-14 at its 3'-untranslated region. This was a game changer: Ambros and Ruvkun introduced the world to a new non-protein coding transcript that regulates what up to that point was a previously unheard of mechanism at the cellular level. Knowing that such a mechanism existed essentially revealed a previously unknown biological molecule and pathway that in the future could potentially be manipulated to cure diseases such as cancer.

The second miRNA, known as Let-7, was discovered in 2000. Let-7 was was the first gene discovered of its type found in numerous species, including humans.

With this new knowledge of the existence of non-coding



The picture above illustrates the shape of C. elegans Let-4 miRNA and Human miR-1.

RNA and their essential roles in gene expression, researchers have since been able to progress in their search for and analysis of further miRNAs – of which thousands have been found and documented. There is even a repository, known as the miRbase, which keeps track of all the miRNAs discovered so far. Processes such as deep sequencing and oligonucleotide miRNA microarrays have been used to analyze and better understand the known miRNAs. Furthermore, quantitative real time polymerase chain reaction, bead-flow cytometry and high-throughput Klenow enzyme assay are used to understand the role of miRNAs in diseases and tumor production.

MiRNAs and Cancer

The link between miRNAs and cancer was first discovered in 2002. Deletion of the chromosome that contained the miRNAs known as miR-15 and miR-16 was found to play a large role in chronic lymphocytic leukemia. Since then, miRNAs have been linked to almost all types of cancers, including breast, liver, lung and gastric cancer. The type and role of miRNAs in each of these cancers varies by the type of cancer; however, miRNAs generally act as tumor suppressors or oncogenes, suggesting the beneficially of miRNAs in cancer prevention.

There are multiple avenues down which cancer research with miRNAs can take. First, researchers can continue to search for miRNAs in various other forms of cancer and study their roles in the mechanisms for that particular cancer. Second, researchers can start synthesizing therapies that utilize the knowledge that miRNAs exist. These therapies can be used in accordance with pre-existing chemotherapies to make them more efficient or can be developed to work on their own. They can also be used as predictors of drug efficacy and non-invasive biomarkers. Without a doubt, the potential that miRNAs bring to the world of cancer research is limitless. Indubitably, microRNAs are versatile biological molecules that have recently been incredibly pervasive in the world of cancer. Consequently, these small bits of non-coding RNA yield a promising future for cancer research.

– Kasthuri Nair
Edited by Pankhuri Jia

Kasthuri is currently a part of Admissions Representative, the co-director of External Events for Johns Hopkins Dance Marathon, and a Research Assistant at an Ovarian and Breast Cancer Pathology Lab at the Johns Hopkins Medical School.

References

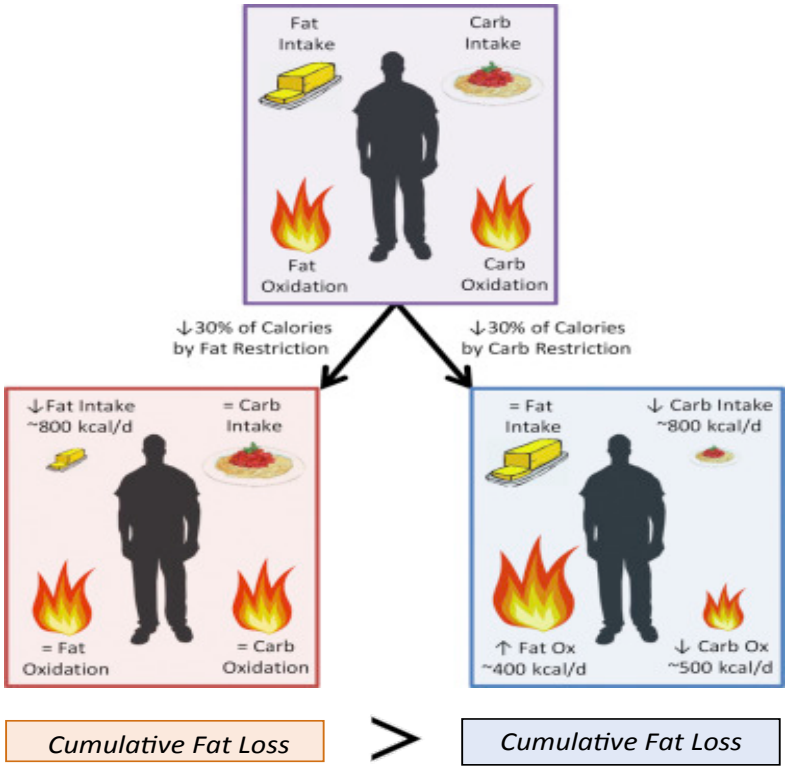
1. History of Medicine Timeline. http://www.datesandevents.org/events-timelines/10-history-of-medicine-timeline.htm. Accessed December 6, 2015.
2. Jansson MD, Lund AH. MicroRNA and cancer. Mol Oncol. 2012;6: 590-610.
3. Almeida MI, Reis RM, Calin GA. MicroRNA history: Discovery, recent applications and next frontiers. Mutat Res. 2011;717:1-28.
4. Hayes J, Peruzzi PP, Lawler S. MicroRNAs in cancer: biomarkers, functions and therapy. Trends Mol Med. 2014;20:460-469.
5. van Schooneveld E, Wildiers H, Vergote I, Vermeulen PB, Dirix LY, Van Laere SJ. Dysregulation of microRNAs in breast cancer and their potential role as prognostic and predictive biomarkers in patient management. Breast Cancer Res. 2015;17: 21.

Published by The Triple Helix

Why Cutting Carbs Just Doesn't Cut It

Targeted restriction of dietary fats results in greater body fat loss than carbohydrate restriction in obese individuals

From Atkins 40, to Weight Watchers, to Nutrisystem, the low-carbohydrate diet has inspired countless weight-loss programs that sensationalize modern popular culture with promises of a 'slimmer and healthier new you'. In spite of the recent popularity of the low-carb diet, the low-fat diet achieved an era of popular currency towards the close of the twentieth century. As such, weight loss regimens have traditionally offered dietary restriction of either carbohydrates or fat [1,2]. However, the question of which diet is superior has provoked controversy within the scientific community and general populace alike. An understanding of the effects of varying macronutrient content in the human diet will not only improve approaches toward healthy nutrition but will also contribute to the development of practical obesity interventions.



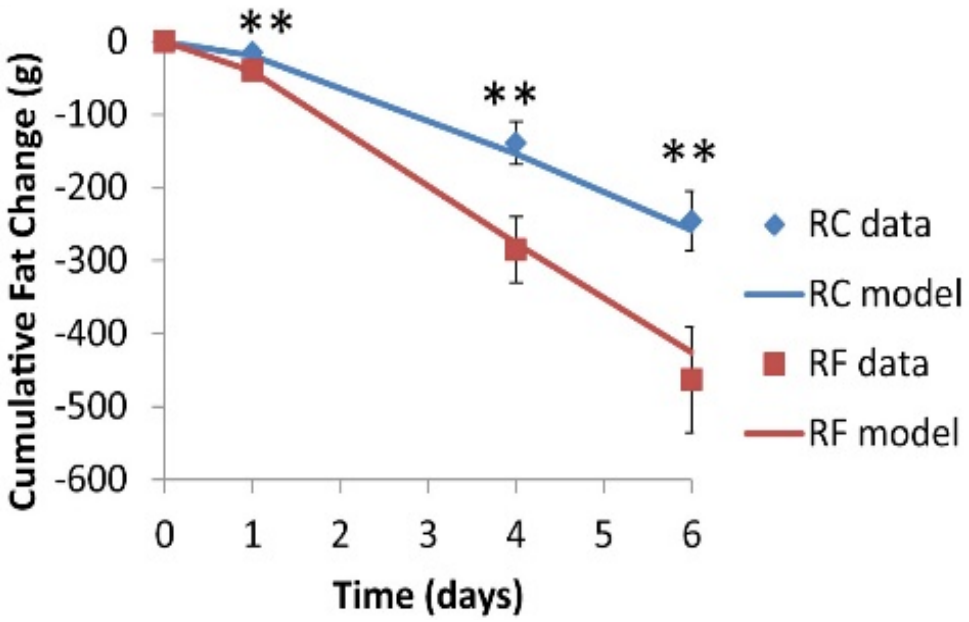
Dietary fat restriction results in more body fat loss than carbohydrate restriction in obese adults. Adapted from (Hall et al., 2015)

As the prevalence of obesity steadily rises and scientific research struggles to identify treatments, optimizing diet control appears to be at least a temporary, practical means of mitigating obesity. Prevailing theories on insulinogenic reduction of carbohydrates posit that the low-carb diet is required for body fat loss [3]. However, recent studies suggest that this overwhelming confidence in the low-carb diet may be unfounded. Dietary fat restriction has been shown to result in more body fat loss than carbohydrate restriction in obese people, an indication that the "low-carb" diet is not required for fat loss [1].

Background

The discussion of whether the low-carb or low-fat diet is superior warrants a brief review of the fundamental concepts in energy metabolism. Food intake is primarily quantified in terms of the caloric content of food consumed; therefore, weight loss is often considered from a calorie-centric perspective [2]. The well-known "calories-in minus calories-out" theory posits that an individual accumulates fat and therefore gains weight when more calories are consumed than are expended. This simple conclusion stems from an underlying concept in studies of energy metabolism—the first law of thermodynamics—which establishes that energy is neither lost nor gained but rather conserved. That is, the calories that are consumed but not expended are stored as fat in the body [3].

However, to discuss weight-loss only in terms of caloric intake would be severely undercutting the true complexity of the phenomenon. The body's fuel sources come in three primary forms: fats, carbohydrates, and proteins. Therefore, not every calorie consumed is equivalent and calories can theoretically be distinguished from one another. When food is consumed, fat is directly stored in adipose tissue upon digestion. Conversely, digestion of carbohydrates increases levels of glucose in the blood which cells immediately use for fuel, or is stored as gly-



RF and RC diets both result in body fat loss, with significantly greater cumulative reductions for RF diet (Hall et al., 2015)

cogen in the muscle and liver. The liver goes on to convert a certain percentage of the glycogen into fat which is later stored in fat cells. However, this 'repository' of stored fat in adipose tissue is not inert: fat exists in an inactive, stored form as the triglyceride and an active form as the fatty acid, and conversion of these fat stores into energy occurs by lipolysis, in which triglycerides are broken down and converted into adenosine triphosphate (ATP) [3,4,5].

Theory on Reducing Insulinogenic Carbohydrates

In his theory on the reduction of insulinogenic carbohydrates, Gary Taubes argues that "any diet that succeeds does so because the dieter restricts fattening carbohydrates...Those who lose fat on a diet do so because of what they are not eating—the fattening carbohydrates" [3]. Taubes purports that weight-loss is often approached from the traditional calorie-centric; however the types of calories lost is the more important factor. He concludes that weight loss is often misattributed to cutting calories when it should be attributed to cutting carbohydrates. Because carbohydrates comprise about sixty percent of a standard diet, when caloric intake is reduced, the carbohydrate count is also inevitably reduced thereby reducing insulin secretion and fat storage. The crux of his argument is that restricting carbohydrates is the only way to lose body fat [3].

Confounding Variables in Previous Studies

Previous studies attempting to identify the independent effects of a low-carb diet or a low-fat diet have been plagued by confounding variables. Experimental challenges arise because the effects of fat restriction and carbohydrate restriction are not mutually exclusive: just as calorie restriction inevitably results in carbohydrate reduction, carbohydrate restriction often results in fat restriction [1]. As such, in studies characterizing the effects of targeted carbohydrate restriction, resulting body fat losses cannot be singularly attributed to reduction in carbohydrates because fat reduction simultaneously occurs. Moreover, these studies require participants to report their food intake making it difficult to exert total control over their diet and introduces some skepticism [1,6]. However, this precludes researchers from determining whether metabolic changes are the result of decreases in carbohydrates or decreases in overall intake.

Recent Study by Kevin Hall, NIDDK, NIH

In a recent study performed at the National Institutes of Diabetes and Digestive and Kidney Diseases (NIDDK), National Institutes of Health, Dr. Kevin Hall provides data contrary to Taubes' claim that targeted carbohydrate restriction is necessary for body fat loss. This notion that a low-carb diet is essential to body fat loss is based on the observation that even low-fat diets reduce carbohydrates which in turn induces fat loss. If Taubes' claims are valid, then one would theoretically expect selective reduction of fat without reduction of carbohydrates to have no effect on body fat.

To test the aforementioned hypothesis, investigators at the NIH Clinical Center conducted an inpatient metabolic balance study which involved selective isocaloric reduction of either carbohydrates or fat. Ten male and nine female participants who were obese with a mean body mass index (BMI) of 35.9 were recruited for the study. Upon randomization, participants stayed in the metabolic ward for two 2-week inpatient periods separated by a 2-4 week washout period. During the inpatient stay in the metabolic ward, subjects maintained constant physical activity. For the first five days, subjects received a eucaloric baseline diet (50% carbohydrates, 35% fat, and 15% protein) of approximately 2740 kcal/day. For the following 6 days, subjects received a diet restricted in energy by 30% by means of either 60% reduction in dietary carbohydrates (Reduced Carbohydrate – RC) or 85% reduction in dietary fat (Reduced Fat – RF). Fol-

Published by The Triple Helix

lowing the washout period, the subjects were given the opposite condition (RC or RF) than what they had received during the first inpatient stay. Although both the RF and RC diets were reduced in calories, they were both of equivalent caloric content. Moreover, the RF diet was selectively designed such that it did not have reduced carbohydrates. The RC diet decreased insulin secretion, as expected, whereas the RF diet did not. The study design therefore ensured that there were no confounding variables and that selective restriction of either carbohydrates (with reduction in insulin secretion) or fat had been achieved.

This rigorous study's primary finding was that, while both RF and RC diets resulted in body fat loss, the RF diet resulted in greater body fat loss than the RC diet by approximately 80% greater cumulative body fat loss. The observation that selective reduction of dietary fat without reduction of carbohydrates under the study conditions is definitive evidence that the low-carb diet is not the only means to reduce body fat. However, it would be naïve to extend this data to the conclusion that a RF diet is conclusively better than a RC diet. Rather, the investigators acknowledge that whereas a very-low fat diet was tested, the RC diet was not as low as a traditional low-carb diet. They concede that further reductions in the carbohydrate content could potentially achieve the same degree of body fat loss. In fact, with varying ratios of carbohydrate and fat in an energy reduced diet, differences in body fat were predicted to be rather marginal in the long-term, suggesting that the body seeks to 'neutralize' differential effects that result from variations in dietary macronutrient content. Furthermore, it is important to note that differences described by Hall et al. are in terms of body fat loss and not weight loss; in fact, the RC diet was shown to result in greater weight loss which is most likely attributable to sodium and water loss. However, considerations of body fat loss are far more important than weight loss in the treatment of obese individuals [1].

"Considerations of body fat loss are far more important than weight loss in the treatment of obese individuals."

Implications

The results of this study have far-reaching implications for not only the study and treatment of obesity but also for how the general public approaches nutrition and healthy dieting. For obese individuals, body fat loss is more important than weight loss. Thus, designing a diet that optimizes body fat loss is central to research on obesity which could potentially benefit from the renewed value given to targeted fat reduction in body fat loss as a result of this study. Furthermore, these findings reject the notion that the low-carbohydrate diet has a metabolic advantage and is required for body fat loss. These new results by no means discredit the benefits of a low-carbohydrate diet nor do they encourage defaulting to a low-fat diet. Rather, they challenge our rigid perception of low-carb diets as the "go-to" for fat reduction. They encourage people to instead choose the diet that they can adhere to and from which they can derive consistent benefits [1].

– Kushi Ranganath
Edited by Albert Huang

Kushi is currently a freshman Public Health and Neuroscience double major and is interested in writing about global health topics such as diabetes, obesity and cardiovascular disease. She is also an avid member of the JHU Woodrow Wilson Debate Team.

References

1. Calorie for Calorie, Dietary Fat Restriction Results in More Body Fat Loss than Carbohydrate Restriction in People with Obesity. Hall, Kevin D. et al. Cell Metabolism, Volume 22, Issue 3, 427 – 436.
2. Ludwig, D.S., and Friedman, M.I. (2014). Increasing adiposity: consequence or cause of overeating? JAMA 311, 2167–2168.
3. Taubes, Gary. Why We Get Fat and What to Do about It. New York: Alfred A. Knopf, 2011. Print.
4. Wertheimer, E., and R Shapiro. 1948. "The Physiology of Adipose Tisue." Physiological Reviews. Oct; 28: 451-64.
5. Westman, E.C., Feinman, R.D., Mavropoulos, J.C., Vernon, M.C., Volek, J.S., Wortman, J.A., Yancy, W.S., and Phinney, S.D. (2007). Low-carbohydrate nutrition and metabolism. Am. J. Clin. Nutr. 86, 276–284.
6. Winkler, J.T. (2005). The fundamental flaw in obesity research. Obes. Rev. 6,199–202.

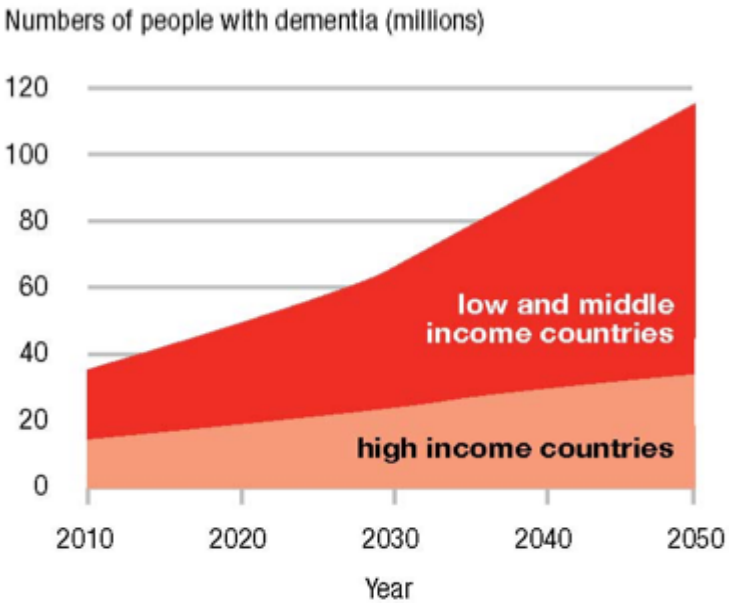
From Denial to Delusion

An attempt to unfold the alzheimer mystery

Dementia is a syndrome that affects memory, interpretation, judgment, and ability to perform familiar tasks. Just like cancer and AIDS in the 1970s, dementia has become embarrassing for families; some avoid discussing it with others, even doctors. With a shift in demographic landscape from the youth to the elderly and increasingly frequent head injuries in professional sports (such as concussions in NFL), dementia will surely become an increasingly vital topic in the coming decades. Even today, it is already one of the major causes of disability among senior citizens.

A common form of dementia, Alzheimer's Disease (AD) is a permanent brain malady that progressively hinders memory and thinking skills. The possibility of developing AD rises with age. Unlike typical age-related declines in cognitive ability, AD develops into severe disability and brain damage.

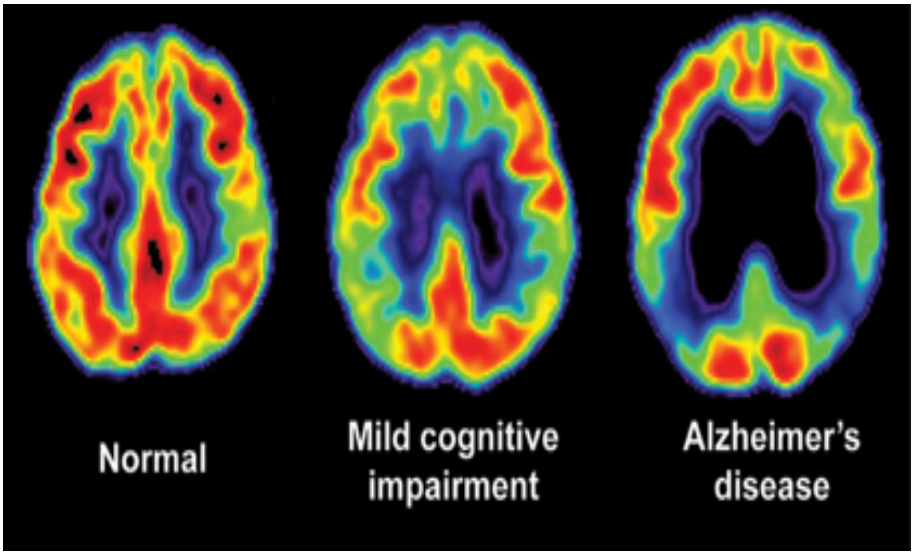
Those with severe AD are unaware of time, place, relatives, and friends. They tend to be incapable of caring for themselves, and also experience bladder and bowel incontinence, changes in muscular function for mobility, increased agitation, and failure to determine geographical location. Death generally follows from aspiration pneumonia or other infections as the brain ventricles expand with the narrowing of cranial nerves (Journal of Internal Medicine).



Illustrated above are the predicted numbers of people with dementia for countries with varied economic status.

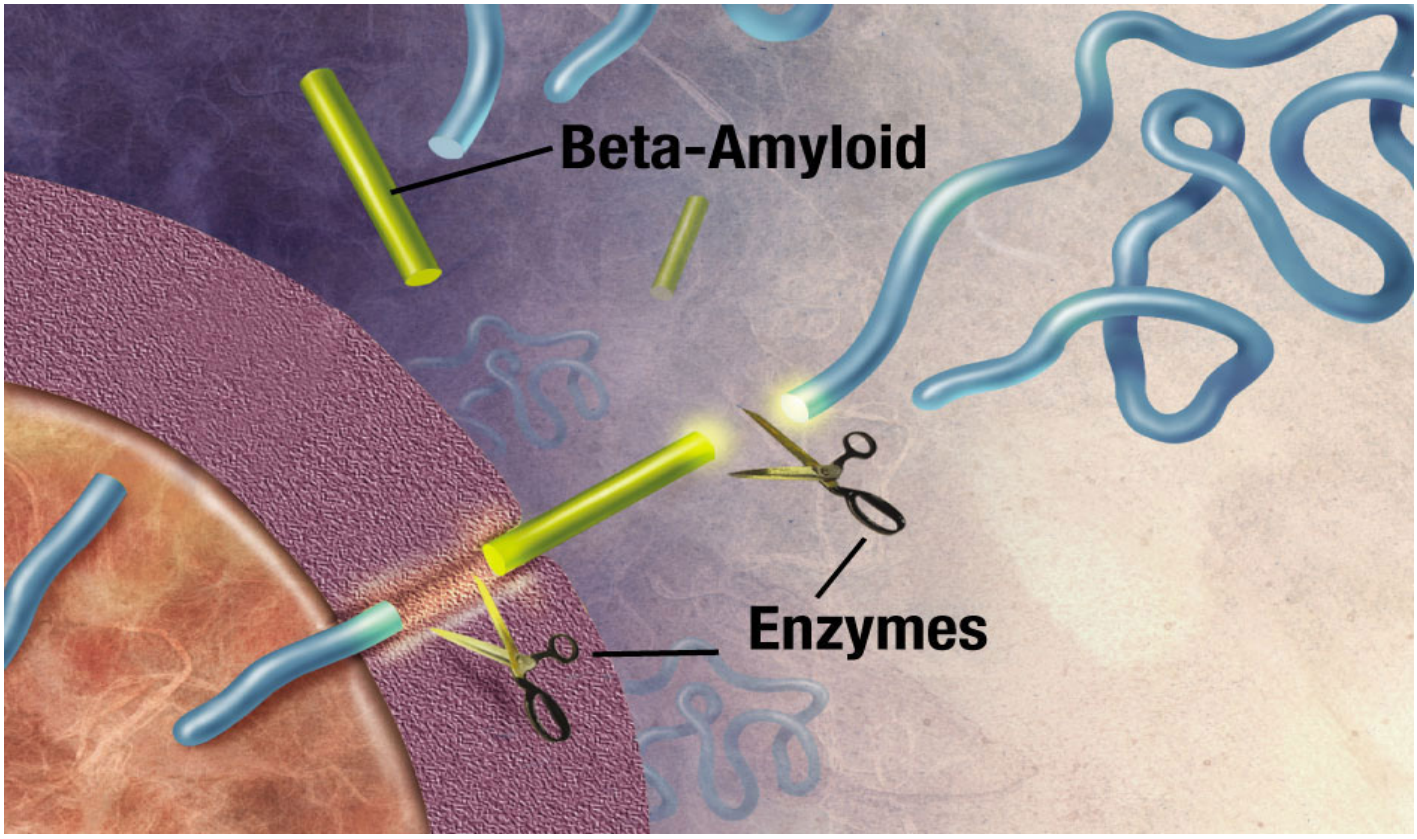
Cellular and Regional Mechanisms

The neuropathology of AD is related to the damage and death of neurons, ultimately leading to atrophy of the brain caused by deposits of the protein fragment beta-amyloid (plaques) and twisted components of tau proteins (tangles). Beta-amyloid proteins are short peptides that are atypical byproducts of the transmembrane amyloid precursor protein (APP). Beta-amyloid monomers are soluble and undertake a conformational change to form a beta sheet-rich tertiary structure, which aggregates to form amyloid fibrils. These fibrils deposit between nerve cells in dense formations known as SP. As a result, amyloid angiopathy occurs: less dense plaques diffuse throughout the walls of carotid blood vessels in the



PET scans of a normal brain with no neurological disease, a brain with slight impairment, and a brain with AD (left to right).

Published by The Triple Helix



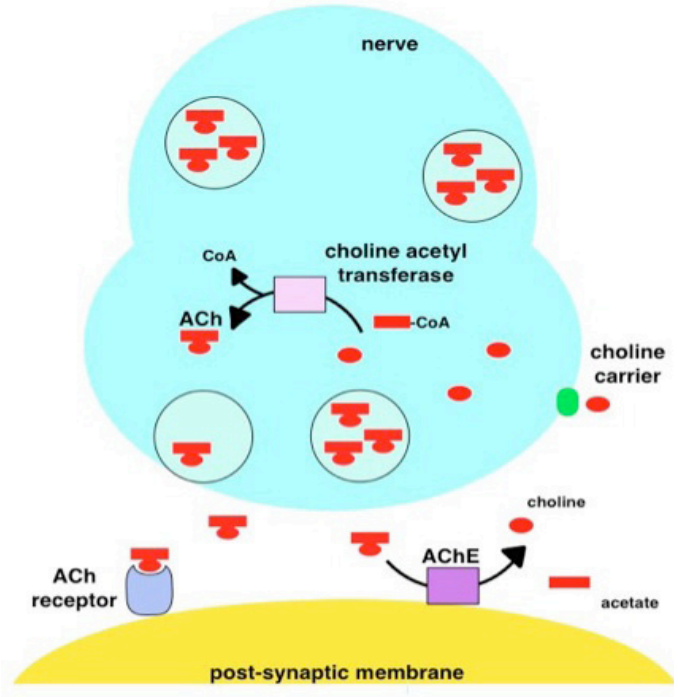
Shown above is an amyloid precursor protein (APP) being severed by enzymes, with beta-amyloid proteins as byproducts

brain, creating effects similar to that of hypertension, with high blood pressure. Similarly but occurring in neurons, tau proteins also aggregate abnormally. In those with AD, excessive phosphorylated tau proteins accumulate as paired filaments and eventually accumulate into clumps inside nerve cells, obstructing continuous blood flow (2). The resulting senile plaques and neurofibrillary tangles prompt the injury and death of neurons by disrupting the synapses critical for survival of cells. Loss of synapses directly leads to the death of neurons, ultimately causing in memory failure, synoptic personality changes, and general atrophy of the brain.

Current Advancements in Treatment

Alzheimer's disease is a complex multifactorial disease that combines heredities and epistasis, which can possibly uncover new pathways. Effective sources to decrease the risk of developing AD include a higher level of education, since it keeps the brain more active, and a Mediterranean diet, because it is rich in sources of vitamin B-12. (4). The familial ADAD can be recognized by mutations in the amyloid precursor protein (APP) and/or presenilins 1 and 2 gene 4). Alterations in the APP and presenilin genes cause further production of beta-amyloid 1-42 proteins. Interestingly, chromosome 21, the same one that causes Down syndrome when extra genetic material is present, codes the APP. A particular part of a brain's APP processing pathways yields beta-amyloid proteins, fragments that are the foremost piece in plaques causing Alzheimer's-related brain changes. Therefore, a duplicate of the APP gene would increase production of beta-amyloid and trigger the series of biological events leading to common symptoms of AD. The point that APP is intensely connected in the pathology of Alzheimer's through two different mechanisms, one concerning a whole extra copy of the normal gene and the other concerning specific minor coding alterations — foretells the need for more resilient, concentrated research on Down syndrome and Alzheimer's. Additionally, the apolipoprotein (APOE) allele is a major genetic risk factor for AD, correlating with a greater number of protein clusters of amyloid plaques in brain tissue. Although the APOE gene does not directly guarantee AD (whereas a mutation in APP or pre-senilin does), it increases the probability of developing it. Individual carrying a mutation in the APOE allele have 3 to 15 times increase risk of developing Alzheimer disease.

Many current treatment methods have greater efficacy when prescribed earlier on, before too much dementia has occurred. Cholinesterase inhibitors, for example, treat the symptomatic aspect by blocking the cholinesterase-an enzyme that breaks down the neurotransmitter acetylcholine (2). This therapeutic source hinders the enzyme acetylcholinesterase, which breaks down



Mechanism: Cholinesterase inhibitors block cholinesterase which in turn halts the breakdown of acetylcholine.

acetylcholine in the synaptic cleft and therefore increases acetylcholine levels in the brain. However, these drugs do not offer a direct solution for AD but compensate for the loss of neurons that communicate via this enzyme, only slowing down cognitive loss. Use of such drugs early on in the diagnosis is necessary to quickly reduce major, permanent damage. Other medicines that help stop or reduce impacts of the disease include drugs that target tau and stabilize microtubules, helping to transport nutrients and assist with general communication between cells. Furthermore, Secretases, sources of enzymes critically responsible for forming beta- amyloid as well as the APP gene, can also be used (3). These therapeutic finding have created new therapies directed at blocking these enzymes, thus stopping or reducing the development of the disease. More research for the development of drugs that can be effective in the later stages of AD is still required. For now, early AD detection is a necessity for reduced dementia.

Concluding Remarks

Alzheimer's disease will spread significantly because of the exponential growth of aging. If no effective treatment is presented, AD will become an even more significant health issue worldwide and cause an even greater economic burden to health care systems. Therefore, there is an urgent need for research in both early diagnoses with specific markers as well as effective therapies and treatments at every level of AD. Currently, only short term symptomatic treatments are available to the patients and a myriad of work still needs to be done. For instance, the correspondence between the pathology in Down's syndrome and that in Alzheimer's shows a promising opportunity for discovery in the many questions about the formation of the beta-amyloid proteins, which cause plaques between nerve cells, and tau proteins, which cause tangles inside cells. These abnormalities have been proven to disrupt communication and the synapses of neurons, thus causing the deterioration of the brain. Consequently, we need further understanding of the neuropathological changes of the disease and its risk factors to offer better treatment options for this illness, which is currently terminal; our future populations and the economic conditions depend on it.

– Teja Polisetty

Edited by Vrshank Subramanian

Teja is currently a freshman Biomedical Engineering and Applied Mathematics double major and is interested in writing about STEM, economics, and the regulation of cells during wound healing.

References

1. Lu, Linda C., and Juergen Bludau. Alzheimer's disease. Santa Barbara, Calif.: Greenwood, 2011. Print.
2. Mann, David. "The Neuropathology of Alzheimer Disease: A Review WithPathogenetic, Aetiological and Therapeutic Considerations." Mechanisms of Ageing and Development : 213-555. MEDLINE. Web.
3. Roberson, Erik D..Alzheimer's disease and frontotemporal dementia methods and protocols. Totowa, N.J.: Humana ;, 2011. Print.
4. Solomon, A. "Advances in the Prevention of Alzheimer's Disease and Dementia."Journal of Internal Medi cine (2014): 1-22. PubMed.gov. Web.
5. Whitfield, David R. et al., "Depression and Synaptic Zinc Regulation in Alzheimer Disease, Dementia with Lewy Bodies, and Parkinson Disease Dementia. "The American Journal of Geriatric Psychiatry (2014): 1-8. PubMed.gov. Web.
6. World Alzheimer's Report 2009. London, Alzheimer's Disease International, 2009.Neurological disorders: public health challenges. WHO, Geneva, 2006.

Published by The Triple Helix

The Lingering Beast

A discourse on Vitamin A deficiency in the developing world and how to prevent it

It's afternoon in sub-Saharan Africa, and groups of children are playing together happily. Dusk arrives as the sun sets, and suddenly some of them run back to their huts while others continue playing games. The children in the huts sit completely still, unmoving until their families come to feed them and guide them around. These children can't see. They suffer from night blindness, one of the first symptoms of nutritional blindness.

Nutritional blindness first manifests with night blindness and then progresses to dry eye, a condition in which the eye cannot produce enough mucus to lubricate itself. Consequently, the cornea – the transparent outer layer of the eye – becomes rough and keratinized, developing corneal ulcers, open sores in the cornea. These ulcers create a hole in the eye, through which the aqueous fluid of the eye's external cavity can leak out. Eventually, in more severe cases, the entire cornea can melt away. This final stage causes permanent blindness and can occur over the course of less than a day (3).

What causes nutritional blindness? The answer is simple: vitamin A deficiency. Vitamin A is required to form rhodopsin, a protein in rods that is used to see in low-contrast surroundings as well as at night. Insufficient vitamin A leads to limited rhodopsin formation, leading to night blindness. Dramatically higher rates of mortality have also been linked to the condition, as studies have shown that the nutrient aids the immune system in fighting infectious diseases (3). In first-world countries, a multitude of vitamin A-rich foods and supplements are readily available. Because vitamins are incorporated easily into our assorted diets, we often take their nutritional value for granted. Thus, in our efforts to ameliorate the living conditions of the developing world, we focus on more prominent diseases and disorders – ones that would affect us and the people around us more commonly, such as AIDS.

Compared to HIV/AIDS, which has a prevalence of 4.7% in sub-Saharan Africa (UNAIDS), vitamin A deficiency prevalence ranges from 20 to 40% on average across

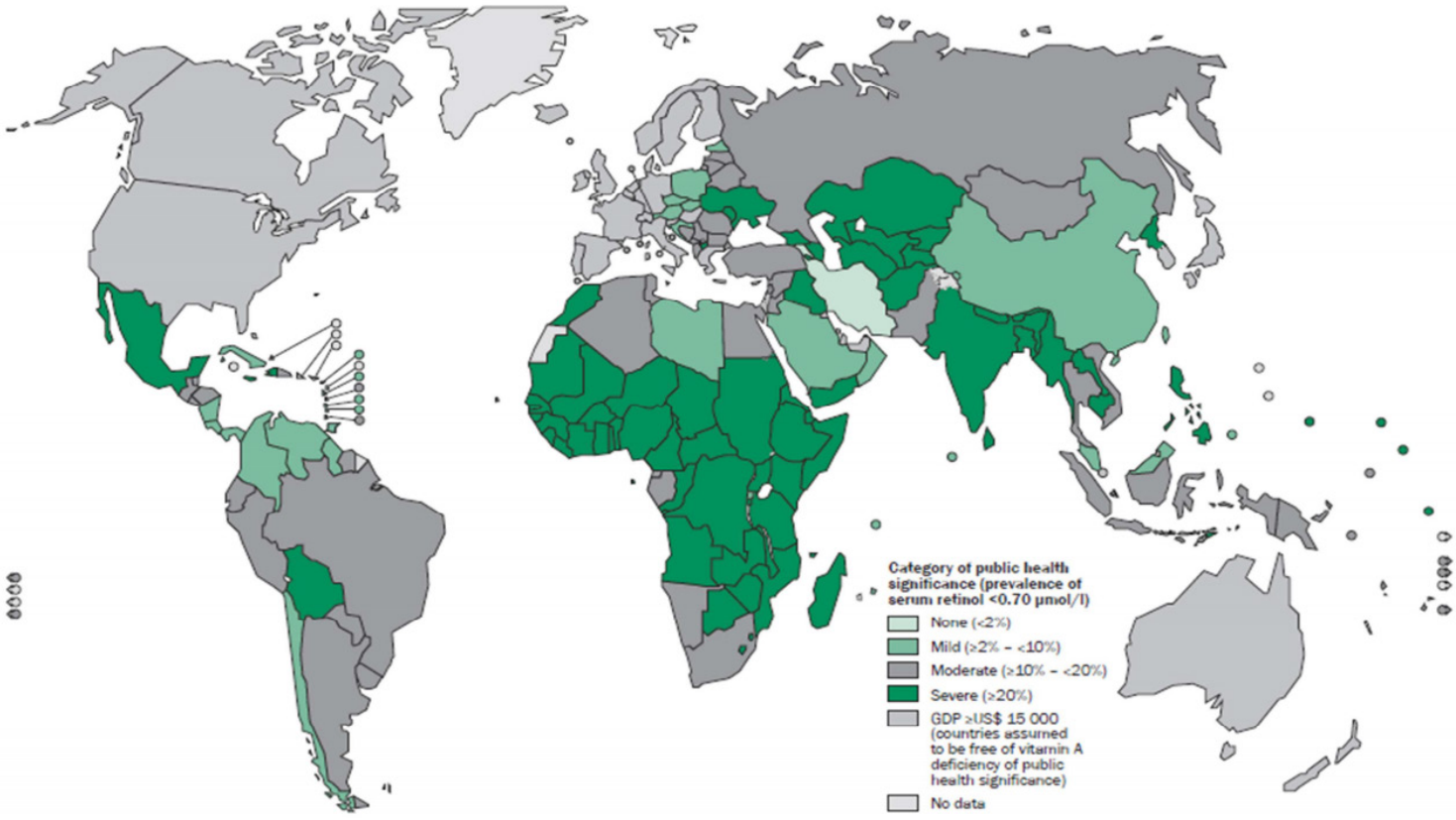
regions in the same area (2). The actual number of people suffering from AIDS may be greater – around 25 million compared to 300,000 for vitamin A deficiency. However, there is currently no cure for AIDS, while a capsule of vitamin A – enough to prevent nutritional blindness in a child for half a year – costs two cents to obtain.

Discovered by Alfred Sommer in 1976, oral intake of these Vitamin A capsules was much more effective in treating the afflicted children than the previously recommended method, injections of fat-soluble vitamin A, as oily vitamin A cannot be absorbed into the body. Per his request, the pharmaceutical company Roche quickly developed a water-miscible form of the vitamin. However, Sommer had proceeded with directly squirting capsules of fat-soluble vitamin A into the mouths of his patients. When he compared the two methods of treatment in a study, he found that the results were the same for each treatment group (3).

Sommer presented his case for oral vitamin A treatment to WHO, arguing that oral treatments do not require trained health workers nor sterile needles, rendering them much cheaper. Yet WHO countered that the children could spit it out of their mouths and that parents preferred injections. WHO decided to include only a small footnote about using oily vitamin A orally – if there was no water-miscible vitamin injection available. It took ten years for Sommer to convince WHO to finally make oral vitamin A the official recommendation (3).

Treating vitamin A deficiency is one goal, but preventing it is a much more ambitious one. How do so many children become vitamin-A-deficient in the first place? Numerous studies have shown that many people with nutritional blindness actually get enough calories. It turns out that the root of the problem is plants. Although green vegetables are rich in beta-carotene, the precursor of vitamin A, simply feeding children an abundance of plants does not significantly raise their vitamin A levels. Because beta-carotene is fat-soluble, ingesting it in a non-oily food forces the body to use anywhere from ten to twelve times as many molecules to make the conversion compared to eating it in an oily substance (3).
Biofortification improves the ability of plants to produce nutrients. Biofortification, however, is challenging to perform with natural selection. Thus, Profs Ingo Potrykus

Figure 12a: Vitamin A Deficiency (as measured by serum retinol) in Preschool Age Children Globally [55]



Status of vitamin A deficiency throughout the world

Published by The Triple Helix

and Peter Beyer turned to genetic engineering with a plant that is the staple of a plethora of Asian countries – rice. After eight years of research, in 1999, they successfully developed rice plants with beta-carotene in their kernels. Because the grains had a yellow-orange color, they were termed 'golden rice', and the team's initiative came to be known as the Golden Rice Project (3).

Although golden rice is nontoxic and does not contain any added pesticidal properties, the public has been educated by environmental organizations like Greenpeace to be wary of genetically modified organisms (GMO's), which could be potentially health hazardous. Public concern about golden rice being a GMO led to years of legislative red tape before the first test field of golden rice was finally approved of and planted in 2004. Not only was that experiment successful, but researchers at Sygenta, the biotech company that the golden rice team partnered with, had also just produced a new line of golden rice that had 23 times the amount of beta-carotene that was in the first prototype. The future of golden rice looked bright (3). In 2008, Guangwen Tang of Tufts University, together with colleagues from China, conducted a study using golden rice. Four years later, the American Journal of Clinical Nutrition published the findings: golden rice was as effective as spinach and supplements at eliminating vitamin A deficiency. The public blowback was immediate. Greenpeace claimed that the researchers had used the children in the trial without consent, causing Tufts to open up an ethics investigation into the study. This investigation found several discrepancies – for example, some consent forms were only received after the trial had begun. Tufts banned Tang from using human subjects in her trials for two years, and the journal retracted the study in 2014, with the reason that there was insufficient evidence to confirm that consent was properly obtained from all participants (4).
Despite its powerful potential to greatly reduce vitamin A deficiency in children all throughout the developing world, golden rice is still not being grown today. The retraction of Tang's study was a setback for the team, but they are still campaigning to make golden rice acceptable for commercial production. General public opinion is anti-GMO, but many of the claims that the opposition has made have been debunked by various studies that have shown golden rice to not be harmful. While Greenpeace and other anti-GMO organizations continue to run public opinion campaigns against golden rice and consequently block the developing world's access to a potentially lifesaving product, we should remain aware of both sides of the story, and, more importantly, of the overarching problem that still plagues much of the world today. We may have the privilege to not have to worry about nutrient deficiencies, but this should not blind us to the very tangible hurdles that others still have to jump.

– Evelyn Yeh
Edited by Khadijah Crawford

Evelyn is currently a freshman Biomedical Engineering major and is a part of Residential Advisory Board, Charm City Science League, Public Health Student Forum, and Inter-Asian Council. She is also conducting research at the Center of Imaging Science.

References

1. Bloem MW, Wedel M, REgger RJ, Speek AJ, Chusilp K, Saowakontha S, Schreurs WHP. Am. J. Epidemiol. (1989) 129 (6): 1095-1103.
2. Fanzo, Jessica. The Nutritional Challenge in Sub-Saharan Africa. United Nations Development Programme: 2012.
3. Price, Catherine. "Nutritional Blindness." Vitamania: Our Obsessive Quest for Nutritional Perfec tion. New York: Penguin, 2015. Print.
4. Stoksad, Erik. "Golden Rice Paper Retracted after Legal Bid Fails." Science Mag. AAAS, 31 July 2015. Web. 4 Nov. 2015.
5. Tang G, Hu Y, Yin SA, Wang Y, Dallal GE, Grusak MA, Russell RM. beta-Carotene in Golden Rice is as good as beta-carotene in oil at providing vitamin A to children. Am J Clin Nutr 96: 658 – 664, 2012. [retracted study]
6. United Nations Joint Programme on HIV/AIDS (UNAIDS). The Gap Report, 2014.

Instrument of Diseases and Cures

A study on infectious disease and global exchange

The cause of approximately one-third of human deaths worldwide, infectious diseases propagate in manners that depend on environments in which pathogens thrive, consequentially shaping the societies that develop alongside and in spite of them [2]. The resulting microbiological co-evolution indicates not only which bacteria, viruses, and parasites survive best in certain urban/rural environments, but also which environments harbor the greatest number of diseases. Infectious diseases inflict the most damage onto developing nations that suffer from over-population and poor overall health due to insufficient healthcare training and supplies. As twenty-first century society shifted toward a broader, more globalized paradigm, world health thrived from the greater transmission of information but ironically also suffered from the simultaneous exchange of pathogens. Although the increase in globalization allowed infectious diseases to spread to areas not within close geographical proximity of each other, the globalized focus also spread information leading to the development of immunology. However, the economic discrepancy that exists not only between countries of different GDP but also within individual countries impacts the accessibility of treatments by those living in impoverished communities, showing that human rights crises such as poverty ultimately amplify disease.

Globalization refers to the integration of ideas, products, and economies between countries without dependence on their geographic linkages and proximity. Post-Industrial Revolution society enabled the flow of products across the globe which created an international network of economic dependence. Vaccination development is largely fuelled and funded by industry leadership, indicating that the economics of mass production rely on worldwide consumption that provide the capital for developing immunizations [7]. The high economic investment required for the output of vaccinations demands monetary compensation that places developing nations at a significant disadvantage due to their inability to economically compete for the limited supply of immunizations.

The frequency of transmission and contraction of Chagas disease within the poor populations of Latin America demonstrates the relationship between poverty and disease, while the spread of the disease to external populations reflects the role of globalization in transforming issues of the poor into issues faced by the world. Chagas disease, caused by the parasite Trypanasoma cruzi, sees at least six-seven million cases worldwide. Transmitted by the feces of Triatiomine bugs, the disease is highly prevalent in people below the poverty line. After the bug penetrates human skin and defecates next to the opening, the human will proceed to rub the parasite into the opening and become infected. Secondary and indirect infections arise from blood and organ transfusions from infected donors, transmission from mothers to infants in childbirth, and consumption of food contaminated by the parasite [3].

Human migration has allowed the disease to spread from its native Latin America to other continents. Since 1909, objectives in Brasil for dealing with Chagas disease include presenting information about the disease to the international community and dealing with Brasil's "social ills," a term referring to the severe disparity between social groups and the neglect of certain diseases [5]. However, after more than a century, no vaccine has been produced and existing drugs, such as nifurtimox and benznidazole, are not fully effective [5]. Compared to efforts like the Global Alliance for Vaccines and Immunizations (GAVI) that seeks to improve the access of immunization to children in developing nations, international efforts to effectively eliminate the threat of Chagas disease have failed [7]. GAVI focuses on providing vaccines for illnesses like Human Papilloma Virus, diphtheria, tetanus, and pertussis; the fact that these illnesses have also impacted society in developed nations is only an indication of the fact that people with more socioeconomic power determine which diseases receive worldwide attention [7].

Constant flow of people and technology across borders has increased the risk of disease contraction in

Published by The Triple Helix

geographically separate populations. Smallpox, the only known disease to have been effectively eradicated worldwide, was declared eliminated by 1980. Eradication of a disease that had afflicted people around the globe offered long-term economic benefits by ending the need for expensive public health programs and distribution of scarce resources [7]. Despite the minimal threat posed by smallpox to U.S. public health, eradication efforts supported economic interests and eliminated the threat of an outbreak. Similarly, provision of medical aid or enforcement of quarantining countries with outbreaks of specific diseases protects other countries. Therefore, although donations and volunteers represent humanitarian pursuits to aid people in economically poor communities, the investments made by more-economically developed countries (MDCs) also serve to protect their own national wellbeing.

Given that many disease prevention efforts in developing nations have been the result of campaigns led by the World Health Organization, like the Expanded Programme on Immunization (EPI) in 1974, globalized immunity depends on developed nations' success in producing medications [7]. Statistically, developed nations have experienced the greatest benefits of vaccinations and immunizations that have limited or eliminated threats of death from smallpox, polio, rubella, and other diseases. However, the success of vaccines developed by 1970 against some of the world's most common lethal pathogens was accessible to only 5% of the world's children [7]. This demonstrates direct correlation between national economic status and individuals' access to prevention, bringing into question the incentives for globalized public health pursuits to eliminate illness. Immunization campaigns seem to make global efforts to eradicate diseases recognized because of their relevance to the developed world.

The role of economic interests in public health and infectious disease policy demonstrates the irony of globalization by showing that international efforts targeting disease are made possible by the increasingly globalized economic/political sphere of information, which also facilitates the spread of disease alongside the spread of people. Thus, international efforts aim to protect political self-interests as well. When looking at the HIV/AIDS pandemic, the overwhelming threat to global public health wrought by the presence of over forty million people living with HIV infection as of 2005, is met by social stigma, which weaves controversy into public policy [2]. Its risk of infection to people worldwide through sexual contact, drug use, childbirth, and other methods evokes moral condemnation of certain behaviors, but does not limit threats to the homosexual, drug-abusing population as stigmatized thought has previously indicated [2]. The necessity of international attention due to the severity of the pandemic and its resulting loss of life places MDCs in position to lead the campaign against HIV and AIDS. Since the initial outbreak, development of treatments for the virus and subsequent AIDS condition has contributed to better control and prevention of the virus.

However, the priority of economic interests by those in power to produce these treatments has resulted in monopolization and patents of AIDS drugs, leading to gross inflation [2]. In 2000, the US government claimed to the World Trade Organization that Brazil's manufacturing and free distribution of generic antiretroviral drugs to treat HIV/AIDs violated the Trade-Related Intellectual Property Rights (TRIPS) agreement [8]. This complaint verifies the corporate influence involved with the production and distribution of antiretroviral drugs, which are the only option for patients to live with the illness, for any amount of time. The production and distribution of HIV/AIDS drugs by corporations aims for demand of the medications to exceed the available supply, so that the price can be driven upwards, inflating the cost of the drugs. Juxtaposing the government's provision of antiretroviral medication in Brazil with corporations' patents and inflation of the drugs shows that institutions with the resources and opportunity to produce treatments supply them in an economically efficient manner. With knowledge that HIV/AIDS patients require antiretroviral treatment to survive, distributing

them at costs too high for third-world patients means that companies have prioritized profits over human lives. The dependence of distribution of public health information and technological advancements on globalized sharing of ideas has also enabled individual institutions to weigh costs and generate profits from human sickness, revealing the unethical distortion of disease propagation.

The accessibility of information in twenty-first century society allows for knowledge of human rights crises worldwide. Poverty, as discussed with Chagas disease, worsens conditions that promote disease contraction, while also limiting people's methods of dealing with it. Furthermore, chronic or severe diseases amplify poverty. Some diseases render the infected susceptible, not immune or dead, leaving them vulnerable to further infections and limiting their ability to function within society [6]. By requiring more care and investment to support the vulnerable and ill, these communities suffer by failing to match this necessary input with the limitations of their economic output. Most sexually transmitted diseases fit into this category, afflicting people for years without immediately causing death but making individuals susceptible to further illness and often unable to support themselves [6]. Due to density-dependent health factors, sexually transmitted diseases occur more frequently in poor, dense populations.

The globalized attention towards disease also reflects its ability to spread through recently established international connections. While this depends on physical contact, integration across borders and geographically distant areas has emerged due to synthesis of ideas via technology and trade. Thus, the same mechanisms that allow diseases to infect different populations are also responsible for developing treatment and distributing it along these pathways. The inevitable relationship created between countries of different economic statuses raises the ethical question of whether more developed countries with resources to intervene should be considered responsible to do so in cases dealing with all disease outbreaks, or only diseases that could endanger people across borders. Less emphasis is placed on diseases that ravage confined areas and on those that have dwindled in frequency in more economically developed areas, such as tuberculosis.

To curb the disparity in disease rates that complements disparity in socioeconomic structure, the international community must reconsider its role in preventing and ending disease outbreaks. The international community should focus on discussing ethical dilemmas associated with disease control. This includes providing birth control methods to poor communities to limit the growth rate of populations that experience the highest disease contraction rates, or creating stringent policies that will improve quality of life in impoverished communities so that they do not harbor disease vectors. Directed attention from the international community would allow information to circulate faster than the pathogens they describe. This information would ultimately enable inhabitants of impoverished communities to make productive efforts at improving their living conditions, which in turn would contribute to powerful global improvements in public health.

–Allison Keller

Edited by Manjari Sriparna

Allison is currently a freshman Biomedical Engineering major and is an editor for the Américas Journal of Latin American studies, is involved with Salud, the Tutorial Project, and Hopkins Christian Fellowship.

References

1. Apostolopoulos, Y., & Sönmez, S. Demographic and Epidemiological Perspectives of Human Movement. (2007). In Y. Apostolopoulos & S. Sönmez (Eds.), Population Mobility and Infectious Disease (pp. 3-16). New York, NY: Springer.
2. Beyrer, C., Terzian, A., Lowther, S., Zambrano, J. A., Galai, N., & Melchior, M.K. In C. Beyrer & H.F Pizer (Eds.), Public Health & Human Rights (pp. 268-288). Baltimore, MD: The Johns Hopkins University Press, 2007.
3. Chagas disease (American trypanosomiasis). (2015, March). World Health Organization.
4. Farmer, P. (2010). "Landmine Boy" and Stupid Deaths. In H. Saussy (Ed.), Partner to the Poor (pp. 409-426). Berkeley and Los Angeles, CA: University of California.
5. Gadelha, F.R. & Peloso, E.F. (2013). Chagas Disease: Still a Threat to Our World? New York, NY: Nova Biomedical.
6. Gersovitz, M., & Hammer, J.S. (2001). "The Economical Control of Infectious Diseases". World Bank Group. Retrieved from http://elibrary.worldbank.org/doi/abs/10.1596/1813-9450-2607.
7. Lynch, Heather J., & Marcuse, Edgar K. Vaccines and immunization. In K. H. Meyer & H.F. Pizer (Eds.), Social Ecology of Infectious Disease. (pp. 275-299). Burlington, MA; London, UK; & San Diego, CA: Aca demic Press, 2008.
8. Production of Low Cost AIDS Drugs to Continue in Brazil. (2001). Production of Low Cost AIDS Drugs to Continue in Brazil. Reproductive Health Matters, 9 (18), 178. Retrieved

Published by The Triple Helix

Published by The Triple Helix