The Mozart Effect
Does music make you smarter?

The Large Hadron Collider: Politics, Pride, and Priorities in Particle Physics

Mirror Neurons: Potential answers or empty promises?
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A global forum for science in society

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Message from the Chapter President

Dear Reader,

Kofi Annan, in his Commencement address at Harvard University in June of 2004, set forth not a request, but a demand. He urged graduates of American universities to “live up to your country’s best traditions of global commitment and global leadership” in the context of an increasingly interdependent and globalized world. Four months later, a new force emerged on college campuses across America. The Triple Helix was formed in October 2004 at Cornell as a small collection of students dedicated to the critical analysis of the impact of science on society. This organization quickly spread from one coast to the other, and from the United States to countries across the globe. Since then, it has provided an opportunity for undergraduates to formally explore the intersection of science, society, and law. It has exemplified some of our country’s best traditions of scientific inquiry and the free exchange of ideas to facilitate communication among young academics across the United States and the world. This organization has convinced me that undergraduates are taking the former United Nations Secretary General’s words seriously.

As I approach graduation and relinquish the presidency of The Triple Helix at Brown University, it is my hope that this unique organization has meant for others as much as it has for me. I hope that future generations of this organization will continue to see themselves not simply as a collection of writers, editors, and organizers, but rather a community committed to advancing the global understanding of science in society. Most importantly, I hope that The Triple Helix will continue to embrace its unique role in the global leadership of undergraduate scholarship in order to help create the leaders of tomorrow.

Kofi Annan closed his address succinctly: “To my fellow graduates of 2004, wherever you may be this afternoon, go out to the great world and make a difference.” I present the same challenge to the graduates of 2009 and to The Triple Helix in all of its successful years to come. Thank you for the privilege to have served as president these past two years, and thank you to all of those who have helped make this sixth edition possible.

Sincerely,
Samuel W Terman
President, The Triple Helix at Brown University

TTH @ Society for Neuroscience

In November of 2008, five members of Brown’s TTH chapter had the opportunity to attend the thirty-eighth annual Society for Neuroscience conference in Washington, D.C., along with over 30,000 other attendees. Over the course of the five days, Brown students explored a myriad of symposia, lectures, workshops, and 14,000 poster presentations with the goal of gaining as much exposure as possible to such a diverse range of neuroscience topics.

Of great interest were the events that specifically drew connections between neuroscience and society. Several students attended a talk by renowned choreographer Mark Morris, who discussed the correlations between dancers’ perception and their movement in time and space, and others learned about initiatives to engage the public in neuroscience, including Brain Awareness Week and the International Brain Bee.

Founded in 1969, the Society for Neuroscience is the world’s largest non-profit organization devoted to furthering research in the study of the brain and nervous system. Each year, the annual conference invites researchers, educators, doctors, students, and other brain enthusiasts to discuss their newest findings and exchange emerging ideas within this relatively young field of science.

Special thanks to Brown’s Department of Neuroscience and Office of Student Life for their generous support.

MariaLisa Itzoe, Managing Editor 2009 - 2010
Kam Sripada, Editor in Chief 2008 - 2009
Message from the CEO

Dear Reader,

This is a time of change. National leadership, economic approaches, scientific advancements are all changing at locations around the globe. The Triple Helix is no different. Our broad mission and international presence offer a variety of directions for future initiatives, and before we move forward, it is important to confidently frame our vision by taking a moment to reexamine the mission and meaning of a “triple helix.”

The first triple helix was introduced to the world not in 2004 but in 1953, as Linus Pauling’s suggested model for the structure of DNA. It was a complete and utter failure. To add to Pauling’s embarrassment, the fundamental chemical error that lead to his loss of the Nobel Prize was discovered using a college textbook, General Chemistry, which Pauling himself had famously authored.

At first glance, this seems a poor story to represent one of the 20th century’s most brilliant scientists or to inspire a young, enterprising organization. However, Pauling’s interdisciplinary research career and passionate social engagement allowed him to succeed as few scientists of citizens ever do, earning him two Nobel Prizes in the process. The story of his triple helix’s failure is crucial in reminding us that not only even Pauling occasionally failed, and fail in a profound and public manner, but that he pushed forward.

At the core of TTH’s mission is a desire to span fields, push boundaries, tackle scientific puzzles and social problems, forge new ways of thinking, and expand the horizons of analysis. These are crucial, difficult challenges, and, like Pauling, sometimes we fail. But, even if not every article we write or event we host or initiative we undertake succeeds as we imagine it may, we still push forward.

This is a time of change. Manisha Bhattacharya and TTH leadership around the world have transformed what began five years ago as a regular local journal into a truly global forum for science in society. Pauling was a force of change in his time and we have the potential to be so in ours. With the launch of our Electronic Publishing Division, our International Division of Science Policy, and our Career Development Resources, there are even more exciting days ahead. I hope you will join us as readers, members, and supporters as we continue, in the face of changes and challenges, to expand, to move, to push forward.

Sincerely,
Julia Piper
Incoming CEO, The Triple Helix, Inc.
In 1994, a New York Times reporter Alex Ross, was researching for his latest article, about the use of Wolfgang Amadeus Mozart's music in studying the connection between music and the brain. When the story was finally published, one line stood out: “researchers at the Center for the Neurobiology of Learning and Memory at the University of California, Irvine, have determined that listening to Mozart actually makes you smarter”[1].

This one line caused such a sensation that it has warranted its own name, the “Mozart effect,” whereby listening to Mozart's music, rather than to any other genre or classical composer, is believed to result in an increase in a person's IQ.

But can we really make ourselves smarter simply by turning the radio dial from AC/DC to Mozart? The answer, unfortunately, is no. The study Ross was referring to, “Music and Spatial Task Performance” (Rauscher, Shaw, and Ky 1993), was based only on results from college undergraduates who were given intelligence tests after listening to either Mozart, relaxation tapes, or nothing. The problem with that study, notwithstanding the limited variety of its test subjects, was that the results only lasted 10 to 15 minutes [2]. Instead of permanently increasing the subjects’ intelligence, the intelligence tests given to the subjects only showed increased results for a short period of time, before returning to the same results as before their exposure to Mozart's music. The study also only proved an impact between Mozart’s music and spatial intelligence – intelligence that pertains to understanding patterns, visualization of figures, and comprehension of sequences over time [2]. In other words, not only did the effects last a very short amount of time but they did not affect the general intelligence; there was no basis in that study for such a generalized statement as the one Alex Ross made.

Despite the misguided public perception that arose from Ross' article, there is some truth behind the music and brain connection that the “Mozart effect” phenomenon implies. Since the New York Times article was published, scientists have, to some degree, replicated the study, and found possible causes for its results. Most importantly, though the “Mozart effect” might not create the long term benefits implied by Ross, these studies relating music to the brain have allowed for the discernment of a sort of “pseudo Mozart effect” in younger children. In these studies researchers discovered that, although children did not necessarily become smarter from listening to Mozart, younger children did experience a long term increase in spatial intelligence through involvement in music lessons [3]. Though the “Mozart effect” is both appealing, and false, because it suggests that someone only has to listen to Mozart's music to become permanently smarter, it also leads us to those much desired results. Only instead of merely sitting back and listening, we have to actively participate.

So what might be a cause of the so-called “Mozart effect”? One of the theories proposed by Rauscher in response to the original study was that Mozart's complex style of music somehow “warmed up” the neurotransmitters in the brain that influence spatial reasoning, our ability to perceive and interpret patterns [2]. Another possibility proposed is that the “Mozart effect” is no more than a representation of the fact that all of Rauscher’s test subjects enjoyed Mozart's music more than they enjoyed the relaxation tapes or silence. When people are happy, such as when they are listening to something they enjoy, they tend to perform better on tests, though this theory does not fully explain why spatial intelligence would be affected more so than general intelligence. One study, “The Mozart Effect: An Artifact of Preference” (Nantais and Schellenberg 1999), was designed to test this hypothesis, by exposing the test subjects to the music of Mozart, the music of Schubert (another classical composer), and a narrated Stephen King novel. The results showed that people who preferred what they were listening to, as opposed to the other options, experienced an equal increase...
in performance on intelligence tests no matter which of the three options they were listening to. People who preferred Stephen King over classical music showed a similar temporary increase in spatial intelligence, while they were listening to the narrated King novel, to Rauscher’s test subjects. [4] In other words, the “Mozart effect” seems to be no more than the fact that when people are in a good mood, such as while listening to something enjoyable, they perform better on tests overall, including intelligence tests.

Now that we know how the “Mozart effect” came about, what about the previously mentioned success of music lessons? Even though merely listening to music is no way to make yourself smarter, there is another kind of “pseudo Mozart effect” that has come to light because of the research designed to prove the phenomenon fake. Along with listening to music, scientists also studied the influence of involvement in music lessons, especially on children. The discoveries here have been much more substantial and consistent than the original Mozart effect. The results have been the discovery very young children (about 4 to 7 years old) do receive a long term benefit from music lessons – a slight increase in not just spatial, but general intelligence [3].

Why does this occur? And why does it just occur in young children? The two are interconnected. Firstly, music lessons are similar to school lessons, and so, by way of their commitments to academics and music, the children become more studious, allowing them to increase their intelligence more so than child who only attends school [3]. Secondly, music lessons increase the children's skills in memorization, concentration, and attention, all of which in turn improve test performance. Finally, there is the additional theory that since musical tunes are abstract patterns that must be listened to instead of observed, when children understand them they also better understand patterns more generally (which we know is part of spatial intelligence).

So though adults and children alike can’t become smarter simply from turning on the radio, there is something to be said about involving children in music from an early age. However, because of the misperception of the Mozart Effect, some political policies on musical education in school have failed to capitalize on the discoveries made concerning the “pseudo Mozart effect.” Most notably, in 1998, Georgia governor Zell Miller proposed a program to give every child in Georgia a tape or CD of classical music to encourage children to listen more to classical music and receive, what he thought would be, a long term increase in spatial intelligence. In response to his decision, Frances Rauscher, one of the scientists of the original Mozart effect study, recommended that parents spend their money on music lessons rather than CDs, if they really wished their children to receive a long term benefit, in line with her findings [5].

In other words, the “Mozart effect” seems to be no more than the fact that when people are in a good mood, such as while listening to something enjoyable, they perform better on tests overall, including intelligence tests.

In reality, the Mozart effect, whether short or long term, is no quick route towards higher intelligence. There are academically excellent students who both have and haven’t been involved in musical programs from a young age. Yet there is something to be said for those who commit to learning an instrument or participate in choir. They receive the benefit of being committed to an activity that not only requires attention, memorization, and motor skills, but also performance skills and rhythm comprehension. Is it a surprise then that those children involved in such from an early age go on to be more successful in the other areas of their life than other children? Learning to make music requires commitment to bettering all of our skill sets, allowing us to better ourselves while enjoying the music we are creating. The “pseudo Mozart effect” is simply an additional bonus.

Sarah Benjamin is an undergraduate at Carnegie Mellon University

References:
Resistance to HIV-1 and the Potential of Viral Hemorrhagic Fevers in Current Research

Aviel Ettin

Since the first AIDS cases were reported in 1981, various individuals have been found to possess immunity to HIV-1 despite repeated exposure [1]. These cases of HIV-1 immunity were originally and for the most part geographically limited to two distinct areas in the world: Scandinavia and Kenya [2, 3]. Both these areas have a long-standing historical prevalence of viral hemorrhagic fevers, which have been suggested as the cause of the immunity in Scandinavia [4]. Consequently, a more evolutionary perspective with regard to the causes of this illness may expose the nature of the disease and provide researchers with a better vantage point to try and curtail it. It may be the research that demonstrates why some people do not get HIV that helps doctors treat those who do.

In the Scandinavian region, approximately 10 percent of the population exhibits a deletion of a specific gene that prevents immune cells from developing CCR5 receptors, disabling HIV-1 virus entry into the cell [5]. This mutation is variously associated with the Black Death in Europe, smallpox, or a history of viral hemorrhagic fevers [6, 7].

Furthermore, in Kenya there are populations of sex workers who, even after repeated contact to the virus, remain resistant to infection [8]. While this group of sex workers does not show the deletion found in the Scandinavian individuals, the presence of hemorrhagic fevers in this area could prove to be an underlying link between these two groups and provide sufficient selective pressure to drive this resistance in both populations.

Scandinavian Hypotheses: CCR5-Δ32

The frequency of the CCR5-Δ32—a deletion mutation found on chromosome 3—varies widely among European populations. Rates range as high as 0.166 percent in Russia and 0.143 percent in Sweden and lower in southern Europe, with frequencies of 0.050 percent in Spain and 0.041 percent in Greece [2]. These data support an original theory that some historic event of enormous selective mortality—an epidemic of sorts—resulted in positive selection pressure for the geographic distribution of this 32bp deletion [9]. It was originally speculated that the Bubonic Plague, Yersinia pestis, which claimed the lives of 25 to 33 percent of Europeans during the Black Death from 1356 to 1352, provided this selective pressure.

Alison Galvani, a professor of epidemiology at Yale University, hypothesized that the Bubonic Plague could not have driven the frequencies of this mutation to over 10 percent in such a short time span and that the ΔCCR5 alleles originated from a mutation event that occurred far earlier [6]. Through the use of a population genetic framework that takes into account the temporal pattern and age-dependent nature of specific diseases, Galvani speculated that smallpox was a more likely cause. In contrast to the Bubonic Plague, which tapered out around 1750, smallpox has only recently been eradicated. Therefore, the cumulative toll of human fatalities caused by smallpox over this greater time span reduced reproductive potential by affecting the young disproportionately. As a result, only those who possessed the mutation were able to survive and pass on their respective genes.

More recently, Christopher Duncan and Susan Scott, professors at the School of Biological Sciences in Liverpool, England, claimed that this selective pressure originated from viral hemorrhagic fevers [4]. Cases of viral hemorrhagic fevers manifested themselves in the plagues of the Nile valley and Mesopotamia (700 to 450 BC), the plague of Athens (430 BC), the plague of Justinian (541 to 700 AD) and the plagues of the early Islamic empire (627 to 744 AD) [7]. Based on the changing demographics of Europe from 1000 to 1800 AD, recurring cases...
of hemorrhagic fever over the next three centuries then steadily raised the frequency of the CCR5-Δ32 mutation in Europe to present-day values—even more so than smallpox could. Although the plague peaked during the Great Plague of London in 1665, Duncan claims that the “hemorrhagic plague did not disappear completely, but continued in Sweden, Copenhagen, Russia, Poland and Hungary in 1800.” This appears to coincide with and perhaps provide an explanation for the specific geographic distribution of the mutation across Europe.

Kenyan Hypothesis: Cytotoxic T-lymphocytes
In contrast to these models, a group of Kenyan sex workers lacking the CCR5-Δ32 mutation were persistently free of any sign of HIV infection despite being exposed to the virus at least once per week for as long as five years. The women rarely used condoms with clients and had a high incidence of other sexually transmitted diseases. Various theories for this resistance have been proposed, the most popular of which suggests that protection against sexually acquired HIV infection can be attributed to virus-specific cytotoxic T-lymphocytes (CTL)—white blood cells capable of inducing death in infected somatic or tumor cells [3]. Dr. Sarah Rowland-Jones of the Molecular Immunology Group at Radcliffe Hospital in Oxford, England, claimed that, “The most probable explanation for the finding of HIV-specific CTL, able to kill virus-infected cells in apparently uninfected but repeatedly HIV-exposed women, is that they have been immunized by exposure to HIV” [10]. A study by Kaul et al., at the Departments of Medical Microbiology in the University of Nairobi, Kenya, confirmed this observation, explaining that CTL in the cervical mononuclear cells of the genital mucosa of the sex workers prevented the heterosexual transmission of HIV infection [11]. This hypothesis was further supported by the discovery that purified Immunoglobulin A from HIV resistant sex workers is able to inhibit HIV infection of susceptible cells in vitro [12,13].

With a series of evidence showing the emergence of a resistance to HIV-1 in Kenya, an interesting observation can be made about the prevalence of two common and concentrated diseases found in the area: Ebola and Yellow Fever. Ebola, from the family Filoviridae, and Yellow Fever, from the family Flaviviridae, are both viral hemorrhagic fevers. Since viral hemorrhagic fever is now attributed to the development of the CCR5-Δ32 mutation and therefore resistance to HIV-1 in Scandinavia, perhaps viral hemorrhagic fevers are the connection between these two resistance phenotypes.

Medical Implications
From the Scandinavian hypothesis, it seems that examining the positive role that genetic mutations play in conferring resistance against HIV may provide future promise that therapies based on interfering with the CCR5 receptor could have a positive influence on the treatment of HIV. Based on evidence found in the Kenyan hypothesis, understanding how individuals with a high degree of HIV exposure avoid persistent infection seems paramount to the design of an HIV vaccine. But by looking at the pathophysiology of the presence of viral hemorrhagic fevers in both these cases may provide the necessary link needed to eradicate HIV-1 in its entirety. ■

Aviel Ettin is an undergraduate at Brown University.

References:
Direct-to-Consumer Genetic Testing: The Wild West of Clinical Laboratory Services

Christie Ciarlo

What do earwax type, bitter taste perception, and alcohol flush reaction have in common? All these characteristics are determined by a single nucleotide substitution in a gene, and they are all currently offered as subjects of personalized genetic testing. Just order a kit online, spit into a tube, and send it back. The service seems harmless enough, but when we consider that such trivial characteristics are not the only ones available for personal testing, it becomes apparent that larger issues are at stake. Direct-to-consumer (DTC) testing for genetic diseases and markers of disease susceptibility raise a multitude of issues in both public health and privacy protection. In general, the results of genetic testing have the potential to affect people’s decisions about maintaining their health, and these decisions may be based on faulty results or an incomplete understanding of their meaning. Furthermore, though eliminating the medical middleman seems on the surface to be a triumph of personal privacy protection, it in fact creates new routes for exposing an individual’s genetic information to private corporations, law enforcement agencies, and even the general public. These issues have been publicly under consideration for at least five years, but DTC genetic testing is still subject to poorly defined regulation. That, or it is banned altogether.

Technology and Regulation
Direct-to-consumer refers to a situation in which a healthcare provider does not act as an intermediary between the patient and the laboratory service. It generally costs several hundred US dollars but can reach several thousand. Most of these tests can be ordered online, and the kits can be sent to virtually any country in the world. Companies may test for anything from a single nucleotide polymorphism to variations in a set of genes known to be associated with disease. Genetic tests currently offered cover a variety of traits with varying degrees of scientifically established connections to certain diseases. Tests may aim to evaluate disease risk, diagnose disease, aid in evaluation of disease treatment, or determine the probability of passing on genetic problems to children.

Currently in the United States, DTC genetic testing is regulated at both the state and federal levels, and it has been banned in about half of US states, as well as France and Switzerland [1]. Current regulatory statutes have proved to be ineffective in ensuring the accuracy of DTC genetic testing results. Genetic testing, like all other clinical testing, is subject to the Clinical Laboratory Improvement Amendments (CLIA), which were passed by Congress in 1988 in order “to ensure the accuracy, reliability, and timeliness of patient test results regardless of where the test was performed” [2]. CLIA applies to “any facility which performs laboratory testing on specimens derived from humans for the purpose of providing information for the diagnosis, prevention, treatment of disease, or impairment of, or assessment of health.”

Genetic testing obviously fits into this category, yet critics of DTC genetic testing still argue that it has gone rampantly unregulated. The Centers for Medicare and Medicaid Services (CMS), the agency which enforces CLIA, requires that laboratories meet basic requirements, including a system for verifying the accuracy of test results, as well as following “proficiency testing standards,” which detail requirements that must be met for specific tests. Unfortunately, no official standards have been set for genetic testing, resulting in insufficient quality control due to complications inherent in the self-reporting of errors [3]. Furthermore, in 2006, CMS stated that it did not intend to create standards specifically for genetic testing [4]. The FDA has a hand in regulating only a small fraction of genetic tests, particularly those that are marketed as products rather than laboratory services, and it does not have jurisdiction over the kits sold to customers that are processed “in house” [5].

Public Perception of Genetic Susceptibility
DTC genetic testing has become problematic due to the public misconception of the relationship between genetic information and the realities of disease. In the context of current regulation, genetic tests offered may have little or no scientific validation as predictors or markers of disease. A popular DTC genetic testing company, 23andMe, offers a test for schizophrenia that is based on only one scientific study. Furthermore, the public may be inclined to believe that genetic information is a final, immutable determinant of not only health, but also other physical and psychological traits and functions.

It is easy to see how misconceptions of the meaning of genetic information could lead to unhealthy decisions. Upon finding that he or she does not possess a gene variant associated with a given disease, a person might neglect visiting a doctor even in the presence of symptoms or might neglect...
to carry out preventative measures for that disease. Genetic test results may be particularly misleading because a genetic disorder is often only one of many possible causes of a disease. For example, 5 to 10 percent of American women have a hereditary form of breast cancer linked to alterations in the genes BCR1 and BCR2 [6]. The presence of these alterations suggests a high risk for breast cancer, but the absence of them provides little information. On the other hand, if a test result comes out positive for a risk, a person may become paranoid or inclined to purchase products that may have no actual benefits to his or her health.

Some advertising by companies providing genetic tests reinforces misconceptions about the relevance of genetic factors. In theory, the Federal Trade Commission ensures that advertising is not misleading or deceptive. Currently the agency has not taken any action against specific DTC genetic companies, though in 2006 it released a statement advising consumers to be skeptical about the claims made by such companies. Some companies offer obviously misleading information, such as GeneLink, which scans genetic information and sells customers a "personalized" skincare product to "help compensate for genetic deficiencies."

Some major genetic testing companies are responding to criticisms with improvement in counseling options and descriptions both of what information genetic tests can provide and of the scientifically accepted significance of specific genetic differences. DNA Direct expressly describes how it has worked to meet the guidelines for DTC genetic testing set by the National Society of Genetic Counselors and the American College of Medical Genetics. The company offers consulting services both before and after genetic tests, and it clearly describes what information can be learned from specific tests, as well as what issues one should consider before taking a test [7]. 23andMe provides two categories of reports: clinical reports, which "give you information about conditions and traits for which there are genetic associations supported by multiple, large, peer-reviewed studies" and research reports, which "give you information from research that has not yet gained enough scientific consensus to be included in our Clinical Reports" [8]. Yet the fact that they still offer these tests attests to the lack of concern for medically significant misinterpretation of results.

Not So Confidential

Though some argue that DTC genetic testing provides increased privacy protection for consumers, it may in fact be the opposite. While DTC testing avoids the necessity of having records at clinics where medical professionals can view them, the information obtained by testing companies becomes their property and stays on file in their database. Many testing companies assure their customers that their information will be kept private, with the stipulation that they may be required to release it by law [10]. Furthermore, many companies release genetic information for research purposes, though they state that no personal identifying information will be associated with it.

In 2005, a fifteen year-old boy determined the identity of his father, who was guaranteed anonymity by a sperm bank, using genetic testing and information available online [9]. The father had never supplied his genetic information, but after receiving the results of a DTC genetic test the boy was able to find him. Such an incident attests to the ability of genetic information to invade personal privacy.

An issue relevant to genetic disease susceptibility testing is the discrimination by employers and insurance companies based on genetic traits. Such discrimination was banned by the Genetic Information Nondiscrimination Act, which was signed into law in May 2008 [11]. It remains to be seen how effective this law will be in actually preventing discrimination.

Direct-to-consumer genetic testing raises issues in both public health and privacy protection and has produced much controversy over the past several years. The general public may not understand the full meaning and implications of genetic tests, and DTC genetic tests are not regulated for analytical accuracy as other clinical tests are. The unexpected problems produced by DTC genetic testing will continue to be of concern for both lawmakers and the scientific community.

Christie Ciarlo is currently an undergraduate student at Brown University.

References:

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The Hidden Effect of Beta-blockers: 
An Analysis of the Effects of Beta Blockade on Exercise Capacity

Evan Walker

For the millions of Americans suffering from heart failure, obesity, and high blood pressure, beta-blockers are often the drugs of choice. Beta-blockers lower blood pressure and heart rate, keeping the heart from being overworked. The drugs act by decreasing sympathetic “fight or flight” responses in the human body that are usually associated with stress or exercise by binding to and inhibiting the function of cell receptors usually stimulated by epinephrine and norepinephrine. Heart rate is decreased by inhibition of the sympathetic receptor that increases the intrinsic rate of the heart’s pacemaker, while blood pressure is reduced by inhibition of the sympathetic receptor responsible for constricting blood vessels in many visceral organs. By imposing a ceiling on sympathetic stimulation, beta-blockers can counteract hypertension (chronic high blood pressure). However, since many types of beta-blockers are not receptor-specific, they can have side effects involving organs other than the heart such as adipose, or fat, tissue [1]. One important consequence of taking these drugs is a decrease in exercise performance and capacity due to a decrease in sympathetic tone. This is often observed during beta-blocker administration.

The effects of beta-blockers on exercise capacity are of great interest to the medical community. Beta-blockers are often prescribed along with diet and lifestyle changes for hypertensive patients, and the most important lifestyle change a hypertensive individual can make is to exercise more. However, an increase in sympathetic tone is normally what facilitates the physiologic changes that allow the human body to exercise. A drug is detrimental if it inhibits the ability of a patient to make beneficial lifestyle changes, and it has been proven through multiple studies that beta-blockers do indeed decrease aerobic exercise performance and capacity [2]. In an effort to elucidate the mechanism by which this effect occurs, two types of studies have been conducted. In the first design, patients currently taking beta-blockers stopped the medication and researchers looked for an increase in aerobic exercise performance. In the second design, healthy subjects were given beta-blockers and researchers looked for a decrease in their aerobic exercise capacity.

Cardiovascular Implications For Exercises
One study of the first design, conducted in France in 2006, involved hypertensive patients who had already been taking beta-blockers for roughly 50 months [3]. The experiment involved exercise testing both before and after discontinuation of beta-blocker therapy. A significant increase in aerobic exercise capacity, demonstrated by an increase in the amount of distance walked in six minutes, was observed: the mean distance increased from 338 meters to 417 meters [3]. The discontinuation of beta-blocker therapy caused a slight increase in resting heart rate, a 25% increase in exercise heart rate, and a 50% increase in chronotropic response, or heart rate acceleration during exercise. These are all results of sympathetic un-inhibition. The drastic increase in overall heart rate translated to a large increase in maximal cardiac output. Researchers attribute the patients’ increase in exercise capacity to this increase in cardiac output, which itself is a result of increasing sympathetic tone [3]. An increase in cardiac output translates to an increase in oxygen delivery to the skeletal muscles and organs working during exercise, which results in an increased ability to perform aerobic exercise.

A Canadian study in 2007 produced similar results. Ten men with type 2 diabetes, a disease commonly associated with obesity and hypertension, were administered a beta-blocker for five consecutive days. Aerobic exercise capacity was assessed with a cycle ergometer before and after beta-blocker therapy. As expected, resting and exercise heart rate and systolic blood pressure were depressed as a result of sympathetic inhibition, and oxygen delivery to tissues was reduced by 13 percent as a consequence of the decrease in cardiac output. As in the previous study, the decrease in exercise capacity was attributed to the cardiac output-dependent delivery of oxygen to working muscles [4].

Beta-blockade Also Affects Lipolysis
A contrasting theory for the beta-blocker-induced decrease in their aerobic exercise capacity.

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in exercise capacity was explored in 2000 in Belgium. In an experiment of the second design, twelve healthy men performed an aerobic exercise test at 70 percent of their aerobic ability on a bicycle ergometer. After receiving a placebo or a commonly prescribed beta-blocker daily for three weeks, the subjects performed another endurance exercise test. The aerobic exercise duration of those subjects taking the beta-blockers was decreased by 20 to 30 percent. The two drugs significantly reduced heart rate as well as systolic blood pressure during both rest and exercise. However, this study also found a concomitant increase in stroke volume, the amount of blood pumped out of the heart in each beat [2]. If the heart rate is slowed and venous return is unchanged, the ventricles of the heart have a greater filling time and thus experience greater stretch. This stretch causes greater elastic recoil and a more forceful push of blood out of the heart. The loss of heart rate was made up for by the increase in stroke volume, and cardiac output was roughly maintained in the subjects after beta-blocker therapy.

The endurance exercise capability of the beta-blocker subjects was still diminished in this study, contrasting with the theory that exercise capacity was affected by decreased blood flow. Interestingly, blood analysis during the exercise tests revealed that free fatty acid concentrations in the blood during exercise were severely depressed during beta-blocker therapy. Normally, during extended exercise, metabolism shifts from aerobically burning liver and muscle glycogen to aerobic oxidation of fatty acids. One of the many physiologic effects of activation of the sympathetic nervous system is the breakdown of lipids in adipose tissue, which increases plasma free fatty acid concentration. The working cells can then take up the fatty acids from the blood and use them as metabolic fuel. Using lipids as fuel is advantageous because lipids store roughly twice the energy of carbohydrates per unit mass. However, due to the extended duration of lipid oxidation and the large oxygen requirement, the body shifts to fatty acid metabolism only during extended exercise of moderate intensity. This study found that one of the non-cardiac effects of beta-blockers is the inhibition of lipolysis of adipose tissue. As a result, metabolism never shifts to fatty acids [2].

With the fatty acid supply cut off, muscle cells must use carbohydrates instead. Excessive carbohydrate metabolism leads to a buildup of lactic acid, which is converted to carbon dioxide in the body. A large increase in exhaled carbon dioxide in the study confirmed an increased dependence on carbohydrates as the major fuel source. In a healthy body, carbohydrates are only used as the predominant fuel source at the beginning of exercise until the metabolic machinery can be activated to begin burning fatty acids. As such, the carbohydrate energy supply is severely limited. The use of a short-term fuel source for sustained aerobic exercise severely limits endurance exercise performance.

The metabolic side effect of beta receptor blockade is especially important in chronic cardiovascular diseases like hypertension. In acute pathologies in which exercise is not often a viable treatment, such as a heart attack, beta-blockers are prescribed to protect the heart. The benefits of this physiologic control far outweigh the exercise limitations. However, chronically hypertensive individuals should be aware of the detrimental effects beta blocking drugs have on exercise capacity and the burning of fats. Exercise is an effective and natural treatment of high blood pressure, and a drug that improves a cardiovascular pathology but inhibits exercise should only be taken with a clear understanding of the consequences.

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References:
Science Illiteracy: A Blight on Society and Security
Leslie Lipsick

Myriad surveys illustrate the dismal state of American science literacy. One-third of participants in a survey by the American Museum of Natural History believed that “humans and dinosaurs existed at the same time” [1]. Many people do not grasp fundamental science-related concepts, and the National Science Foundation reports that “60 percent of adults believe they have not eaten genetically modified food, although in fact processed foods commonly contain genetically modified ingredients” [2]. Even graduating Harvard seniors struggled, as fewer than 10 percent could explain why summers are hotter than winters [3]. While these surveys present startling data and may even motivate policymakers, they do not paint a complete picture of what exactly makes a person scientifically literate or illiterate.

Science literacy is difficult to define, since science contains so many sub-fields, each with its own basic theories, important facts, and notable discoveries. One approach breaks science literacy into mutually exclusive categories—like practical, civic, and cultural—while another requires a purely academic understanding of the facts [4]. Definitions have also changed over time, reflecting wider societal currents. For example, the 1950s focused on science education and its outcomes, measuring the number of students becoming defense and engineering experts, a reflection of the Cold War’s push for defense innovations. Recent decades embraced the larger picture, aiming for more widespread literacy, which entailed “understand[ing] how science, technology, and society influence one another and...us[ing] this knowledge in...everyday decision-making” [5]. This article will utilize a definition most similar to the latter. This broader definition still demands knowledge of some basic facts, like those tested in popular surveys, as well as a more general ability to apply scientific methods.

While scholars may not agree on the exact definition of science literacy and many adults may not have an in-depth understanding of science, most people believe that science is important. Remarkably, 87 percent of Americans both “acknowledge that they benefit daily from science” and “support...government funding of basic research” [1, 2]. “Supporting” science, however, does not equate to working to actually understand and utilize the concepts. A survey by the Museum of Science and Industry in Chicago found that only “26 percent claimed a solid understanding of science” [6].

Why Literacy Matters
Science literacy affects societies globally in politics and policy, the economy, and health. The health of a democracy depends upon the ability of its people to express their views, both through debate and elections, equally and effectively. Several key issues—like climate change, genetic testing, and global epidemics like malaria and AIDS—have basic science at their core. All voters need a mutual, baseline understanding of the issues in order to express their opinions in a democracy. As Leon Lederman, a physicist and Nobel laureate, said, “A public that has a sense of science makes democracy work. If you don’t
understand the language in which people are discussing global warming or all the other issues, you cannot have a democracy” [8]. It does not make sense that a population, of which “35 percent said they were ‘not clear at all’ about the difference between reproductive and therapeutic cloning,” should dictate science’s access to stem cells.

People also cannot hold elected officials accountable if they do not understand the decisions they make. In the United States, the 2008 presidential election proved that often those very officials do not understand the science behind the issues. For example, Sarah Palin mocked fruit fly research as one of the tax payer-funded “projects having little or nothing to do with the public good” [9]. Ultimately, uninformed policy and electoral decisions harm scientific progress and constrain democracy. Politics, one might argue, has been driven by ignorant or apathetic voters for many years, but other realms of society, namely the economy, may not survive in a scientifically illiterate public.

The world has already entered the age of the “knowledge economy,” which values flexibility, expertise, and life-long learning. Famed management guru Peter Drucker asserted that “knowledge workers, collectively, are the new capitalists. Knowledge has become the key resource, and the only scarce one” [13]. Knowledge will be crucial in all classes of labor, from retrained former factory workers to elite researchers at newly restructured pharmaceutical companies. A low-level worker might not need to understand the complex processes of a wind turbine, but he must be comfortable with terminology and understand the larger picture of energy and the environment.

A knowledge economy is a globalized one, and developed nations now outsource cheap, large-scale production. Innovation and agility have become the strengths of nations like America. Their ability to solve emerging crises, namely energy ones, will produce ideas and products of value for exchange on the global market. Modern crises inevitably use science and technology-related terminology, and require that employees understand the larger environmental or biomedical impact. The products of such innovations will also flood individuals’ lives, requiring them to make scientifically informed decisions.

Innovations generally aim to improve consumers’ lives, like new vaccines and fortified foods. However, capitalism has never been paternalistic, and the consumer remains responsible for her decisions in the market. Basic scientific concepts help in logical processes, like considering empirical data, making hypotheses, and assessing risk. They also help to fully inform decisions like which kind of contraception to use or whether to participate in a clinical trial. People are tempted to rely on the Internet, but the amount of information available can be overwhelming and its credibility questionable.

Scientific literacy also affects the health and welfare of people in poorer countries that cannot access such innovations. For example, astrophysicist Benjamin Shen notes that “the Green Revolution in grain productivity...alleviated the food problem in some regions of the world and saved many lives. But [its] success depends precariously not only on an increased availability of fertilizers... but also on increased levels of science literacy on the part of the farmer” [4]. He points out that even poor populations within developed countries suffer without science literacy. The remarkably high infant mortality rate in the United States can be partially attributed to a “lack of basic health information on the part of young parents in the poorer communities” [4].
Culture or the Classroom? Looking for Solutions

Many societies today fail to recognize the urgency of science literacy problems, especially compared to fifty years ago during the Cold War. Officials and teachers from that era believe a trigger event, one that parallels Sputnik’s launch, will be required to motivate our generation. One former official remarked, “What we need is another Sputnik. Maybe what we should do is get the Japanese to put a Toyota into orbit” [10]. The difficulty has been getting Americans and other Western citizens to see the tie between science and economy, and economy and national security. In the 1950s, the Soviet Union, nuclear energy, and the space race clearly tied science, defense, and national security together.

The primary answer to Sputnik was the sweeping 1958 National Defense Education Act that overhauled curricula and made education a federal issue [10]. Many officials today advocate education as the answer once again, but the No Child Left Behind education legislation has not succeeded. Its focus on standardized testing as a measure of student performance may have harmed science education by “too much emphasis on memorizing terminology and not enough on concepts” [11]. Rigid curricula combined with declining budgets often extinguish the sparks of excitement that students experience with hands-on projects. Such projects not only inspire the researchers of tomorrow, but they also equip every student with basic scientific methods, like reasoning and experimenting.

All students, regardless of the method they are taught, need resources outside of the classroom that encourage curiosity and make science accessible. Museums have become more hands-on and engaging, but most other forms of scientific entertainment have failed. Adults are eager to learn, but the material presented to them has lacked depth: sound-bytes have undermined hard news reporting. Popular media outlets occasionally cover breakthroughs, but they also publish false or exaggerated claims that confuse the public and can demonize scientists. For example, disproportionate coverage has been given to sensational animal clones and recreated viruses, rather than feats of creativity and value, like the recent discovery of RNAi. Society has also moralized science by focusing on heated debates over intelligent design and abortion, which often paint scientists as megalomaniacs trying to “play God.”

A final factor in science literacy’s decline has been the culture of disregard for science present in the administration of former President George W. Bush. The President failed to increase funding for the National Institutes of Health despite major inflation, and his own staff censored scientists’ work on global warming [12]. Science advocacy groups pushed for President Barack Obama to appoint a Science Adviser within his cabinet, in hopes of restoring science’s prestige and priority on the national stage.

Raising science literacy rates requires a multi-faceted approach and must be spurred by a sense of urgency that has not yet taken hold of the public. Regardless, it is the job of policymakers and educators to prepare the next generation now to make informed decisions in the future. Science will advance, economies will transform, and biomedical will innovate. A scientifically literate citizen will be informed, engaged, and inevitably global.

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References:
Teaching Happiness
Matthew Scult

Happiness is a topic that is often underrated both within the scientific community and in the field of education. It is generally seen as an individual exploration that cannot be formally taught, but more recently researchers in the growing field of positive psychology have begun to reverse this trend and are studying the things that make people happy. Implementing educational changes based on the knowledge gained from these studies has the potential to improve the psychological health of students and to make them more successful in academic and social domains.

The study of positive psychology has been around for some time, but the field has gained great momentum since Martin Seligman became head of the American Psychological Association in 1998 and decided that the theme for his presidency would be an exploration of the range of positive emotions. Seligman did not intend for the emerging field to replace the study of mental disorders, but rather to bring new insights to prevent psychopathology and to improve the psychological well being of healthy individuals. Now, numerous scientific studies have been conducted focusing on “the strengths and virtues that enable individuals and communities to thrive” [1]. These studies have given valuable insight into common misconceptions about what will make people happy and have developed useful interventions to keep people happier and healthier.

Seligman divides happiness into pleasure, engagement, and meaning. He believes that you need pleasure, engagement, and meaning for a completely happy life [2].

According to Seligman, finding pleasure in life involves partaking in activities that lead to and extend positive emotions. These are usually more basic sensations, such as the enjoyment of eating a delicious meal, and a person can extend these emotions by becoming more aware of the present moment. In the example of eating, the awareness could involve chewing more slowly and savoring every bite [2].

Seligman suggests that finding engagement in life can be achieved by using one’s character strengths to become completely engrossed in an activity or activities. When this is achieved a person is so focused on the activity that he or she often loses all sense of time. Prominent researcher Mihaly Csikszentmihalyi has done a significant amount of research into this type of engagement, which he calls a state of “Flow” [2]. A person may enter this state while involved in a variety of activities ranging from teaching to rock-climbing, but the key aspect is the enjoyment derived from doing the activity for its own sake [2].

Finally, the meaningful life, according to Seligman, can be achieved when people use their strengths to help others [2].

Using Findings from Positive Psychology Research in Scholastic Settings
According to a study by Lyubomirsky, Sheldon, and Schkade, the overall happiness level of an individual is thought to be attributed to a combination of genetic factors (about 50 percent), circumstance (about 10 percent) and factors under voluntary control (about 40 percent) [3]. In order to test whether the part that is under voluntary control can be changed in a lasting fashion, researchers have conducted placebo-controlled studies to see the effects of various interventions.

One method consists of helping subjects find and develop their character strengths, which are a list of positive characteristics developed by Seligman and others that are shared across cultures. They compiled these characteristics into a parallel of the Diagnostic and Statistical Manual of Mental Disorders, which they called the Character Strengths and Virtues Handbook [4].

There are twenty-four strengths on the list, and questionnaires can be used to help people determine the ones that best characterize them. These strengths fall within six categories: wisdom and knowledge, courage, humanity, justice, temperance, and transcendence. Examples of strengths include curiosity, bravery, kindness, fairness, modesty and humor. Teaching people about character strengths has been shown to have lasting effects on psychological health. In one study, participants were asked to determine their signature strengths, the character strengths they identified with the most. Participants filled out an online questionnaire and then were asked to use one of their signature strengths in a new way each day for a week [4]. Their happiness levels were recorded before and after the intervention and then were compared to those of individuals who did a control exercise, which was not expected to significantly alter happiness levels and involved writing about early memories each day for a week. Participants who used their newfound character strengths had significantly higher happiness levels than those who did the control exercise [4].
strengths showed increased levels of happiness and fewer symptoms of depression for up to six months after the program. These results indicate that happiness levels can be consciously altered, which could be useful in academic settings.

In a scholastic environment, students could be encouraged to utilize their signature strengths in different activities in order to become more engaged in the learning process. For example, if students are reading a book for class, everyone could be split up into smaller discussion groups and each member of the group could be assigned a different role. A student who determines one of her character strengths to be leadership might choose to run the discussion, while a student who self-identifies as being more curious may come up with questions and a more creative student might bring in artistic representations of passages. If students are permitted to explore different roles and choose those they most enjoy, then they will more willingly engage in the learning process, which would have both academic and psychological benefits.

Improving Performance through Relaxation and Emotional Well Being

Positive psychology research has also found that positive affect can be increased through being more mindful of the present moment [2]. By becoming aware of one’s own physical and psychological state, an individual is better able to deal with stress and when faced with a difficult situation is able to act based on executive functioning rather than on gut instinct. This type of training may be useful in dealing with stresses associated with test-taking or in difficult social situations, where an individual will be better able to control his or her emotions rather than lashing out in anger or frustration.

A program developed by Jon Kabat-Zinn at the University of Massachusetts Medical School teaches mindfulness as a means of stress reduction. The program, called Mindfulness Based Stress Reduction (MBSR), has gained popularity in the psychology community and more recently has been adapted for use with kids in scholastic settings. In an increasing number of schools, breathing awareness and other forms of mindfulness training are being incorporated into health education classes or other aspects of the curriculum. Preliminary research and anecdotal evidence suggest that teaching forms of mindfulness in schools leads to decreased anxiety and increased attention, even for students who have Attention Deficit Hyperactivity Disorder [5, 6]. Further studies are currently underway to determine the efficacy of implementing MBSR in a greater number of primary and secondary schools.

Effects of Positive Affect on Other Measures of Success

In addition to having beneficial psychological outcomes, happiness has been shown to have other benefits as well. A study by Lyubomirsky and Diener found that happier individuals “are more likely than their less happy peers to have fulfilling marriages and relationships, high incomes, superior work performance, community involvement, robust health and a long life” [7]. While it may appear that individuals are happy because they are healthy and successful, this study found that in many cases happiness precedes success. This effect was shown in longitudinal and experimental studies and indicates that positive affect is not only desirable in its own right, but it also has other positive consequences that are common goals of education. As such, teaching strategies to promote happiness can serve to further many of the goals of the educational system. By changing school curricula to incorporate these methods, educational systems can better help students to be happier, healthier, and more successful in life.

Matthew Scult is an undergraduate student at Brown University.

References:
Attention Deficit Hyperactivity Disorder (ADHD) is one of the most commonly diagnosed childhood psychological disorders in the United States. Studies suggest that 8 to 12 percent of children have some form of the disorder [1]. Nevertheless, widespread misconceptions of what causes ADHD and of the precise nature of the disorder persist despite significant evidence that its basis is primarily neurobiological and genetic. Because of its close relationship to executive functions of the brain—working memory, problem solving, attention, and inhibition—the study of ADHD might reveal information about the underlying mechanisms of these processes. Furthermore, ADHD has wide social implications in addition to a high childhood prevalence, so its study could have far-reaching impacts on a number of lives.

History
In 1902, Dr. George Still, an English pediatrician, described symptoms similar to those seen in the disorder currently called ADHD as an “abnormal defect in moral control” [2]. In his words, the children he examined were unable to control their actions “for the good of all” [2]. The disorder was first termed minimal brain dysfunction in 1966 by S. D. Clements, and in 1967 it was termed hyperkinetic reaction of childhood disorder by the American Psychological Association’s DSM-II (Diagnostic Statistical Manual, second edition) [3]. It was not until 1980 that the DSM-III first called it attention deficit disorder and set out clear diagnostic criteria for its diagnosis. The current criteria for ADHD diagnosis are shown in Table 1 [4].

Neurobiological Basis and Treatment
From a cognitive perspective, Dr. Russell Barkley, an internationally recognized authority on ADHD, describes all patients with ADHD as exhibiting the following symptoms: a deficiency in the ability to inhibit an initial response to an event, difficulty stopping an ongoing response to an event, and difficulty preventing disruptions from competing events [5]. ADHD is further divided into three subtypes: primarily inattentive type, primarily hyperactive/impulsive type, and combined type, each exhibiting symptoms as outlined in Table 1 [4,5]. Each of the words Barkley uses to describe symptoms of the disorder—inhibit, stopping, and preventing—are characteristics of disinhibition.

Inhibition is crucial in many of the brain’s circuits and feedback loops, and its disruption can have dramatic consequences. In the motor system, for example, initiation of a behavior like walking begins with the transmission of the desire to walk from its neural origin to the area where the

<table>
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<tr>
<th>Table 1. Diagnostic Criteria for ADHD</th>
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<tr>
<td>A. Either 1 or 2:</td>
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<td>1.Six (or more) of the following symptoms of inattention have persisted for at least 6 months to a degree that it is maladaptive and inconsistent with development level:</td>
</tr>
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<td>Inattention:</td>
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<tr>
<td>(a) Often fails to give close attention to details or makes careless mistakes in schoolwork, work, or other activities</td>
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<tr>
<td>(b) Often has difficulty sustaining attention in tasks or play activities</td>
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<tr>
<td>(c) Often does not seem to listen when spoken to directly</td>
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<td>(d) Often does not follow through on instructions and fails to finish schoolwork, chores, or duties in the workplace (not due to oppositional behavior or failure to understand instructions)</td>
</tr>
<tr>
<td>(e) Often has difficulty organizing tasks and activities</td>
</tr>
<tr>
<td>(f) Often avoids tasks or activities (e.g., toys, school assignments, pencil, books, or tools)</td>
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<tr>
<td>(g) Often easily distracted by extraneous stimuli</td>
</tr>
<tr>
<td>(h) Often forgetful in daily activities</td>
</tr>
<tr>
<td>2. Six (or more) of the following symptoms of hyperactivity/impulsivity have persisted for at least 6 months to a degree that is maladaptive and inconsistent with development level:</td>
</tr>
<tr>
<td>Hyperactivity:</td>
</tr>
<tr>
<td>(a) Often fidgets with hands or feet or squirms in seat</td>
</tr>
<tr>
<td>(b) Often leaves seat in classroom or in other situations in which remaining seated is expected</td>
</tr>
<tr>
<td>(c) Often runs about or climbs excessively in situations in which it is inappropriate (in adolescents or adults, may be limited to subjective feelings of restlessness)</td>
</tr>
<tr>
<td>(d) Often has difficulty playing or engaging in leisure activities quickly</td>
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<tr>
<td>(e) Is often “on the go” or often acts as if “driven by a motor”</td>
</tr>
<tr>
<td>(f) Often talks excessively</td>
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<td>Impulsivity:</td>
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<tr>
<td>(g) Often blurts out answers before questions have been completed</td>
</tr>
<tr>
<td>(h) Often has difficulty awaiting turn</td>
</tr>
<tr>
<td>(i) Often interrupts or intrudes on others (e.g., butts into conversations or games)</td>
</tr>
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desire can be executed, such as the motor cortex. The signal does not simply pass from one part of the brain to another unhindered; the signal passes through various checkpoints that can inhibit it. Through this inhibition, unnecessary behaviors and excessive movements can be eliminated. If, for some reason, the inhibitory process is altered, the filters will not work as effectively, and unnecessary behaviors will be enacted. This disinhibition may manifest as impulsivity or hyperactivity.

The same process occurs in the inattentive subtype of ADHD. As information is received from various sense organs, it passes through inhibition filters before it is interpreted by executive function regions of the brain. If these inhibitory checkpoints are malfunctioning, unimportant stimuli may divert attention from a single point of focus.

A Synaptic Model
At the cellular level, the basic unit of neural interaction is the synapse, a microscopic space between two neurons. In signal transmission, a presynaptic neuron is stimulated to release neurotransmitters that bind to receptors on the postsynaptic neuron and stimulate it to release its own neurotransmitters to the next neuron.

The neurotransmitter dopamine is released in certain regions of the brain that are involved in motor function and motivation. Certain dopamine pathways are involved in the inhibitory loops between the frontal cortex (the location of executive functions) and subcortical areas (the filter). Evidence suggests that patients with ADHD tend to exhibit differences in dopamine pathways [6]. Specifically, malfunction of the D4 dopamine receptor (DRD4) has been implicated in ADHD [7]. This is one of many receptors that receives inhibitory signals and is an important player in the filtering of unimportant stimuli. Malfunction of the DRD4 could mean that signals are not properly passed on to an inhibitory neuron, causing disinhibition.

Other proteins, called transporters, are involved in synaptic transmission. Transporters remove neurotransmitters from the synapse after transmission so that the postsynaptic neuron is not continually stimulated. Dopamine transporters (DATs) remove dopamine from the synapse after a signal is transmitted. If inhibitory dopamine signals are already weak, as in the case of ADHD, then DATs work to weaken them further by lowering the level of dopamine at the synapse. Thus, targeting DATs has the potential to alter dopamine signaling and reduce the effects of ADHD.

In fact, DATs are the site of the action of the two most common drugs used to treat ADHD, methylphenidate (Ritalin) and amphetamine (Adderall). These drugs are DAT antagonists, meaning they block the action of transporters, increasing the concentration of dopamine in the synapse. As a result, dopamine signals become more effective and inhibition is more likely [8].

Beyond the Synapse
In addition to differences at the cognitive and cellular levels, there is also a large body of imaging evidence suggesting significant differences in the anatomy and physiology of the brain in people with ADHD. When discussing the results of image analysis, it is important to understand what is being evaluated during different types of imaging. Magnetic resonance imaging (MRI) is used to visualize the anatomy of brain structures. Comparisons of MRI studies in children with ADHD have shown reductions in the size of the frontal cortex, the location of most executive functions, including working memory, attention, problem solving, and control over one’s actions, or inhibition [9].

Functional magnetic resonance imaging (fMRI), measures activity of different parts of the brain, and is therefore a physiological evaluation tool. Investigators often have their patients perform certain tasks that involve executive functions. For example, in one experiment, a patient is instructed to press a button only when she sees a red light. During the test the investigators turn on lights of different colors and see which parts of the brain are activated while irrelevant stimuli (non-red lights) are filtered out. fMRI studies have shown significant differences in brain regions involved in processing conflicting information, attention, and detection of errors [10].
The Genetic Component

One of the most common misconceptions about ADHD is that it is due to bad parenting. There is, however, a substantial body of evidence suggesting a large genetic component for the disorder, indicating that nature, rather than nurture, is the primary root of ADHD. Twin studies, which compare the rate of disorders in identical twins to the rate in fraternal twins, are just one piece of the large body of evidence.

Twin studies of ADHD suggest that the disorder is 80 percent heritable [11]. Heritability measures how much a disorder is influenced by genetic factors. In addition to twin studies, parent-child correlations, which express how likely it is for a disorder to be passed on, showed that 60 to 68 percent of mothers of affected children had similar attention problems as their children [12]. Since mothers only share half of their DNA with their children, such a high parent-child correlation along with evidence from twin studies supports a very strong genetic basis for the disorder. It is important to remember, however, that finding a genetic component to ADHD is a far cry from rendering good parenting irrelevant. It simply provides another reason to shift the argument from a discussion about who is to blame to one about how we can begin to diagnose and treat the disorder.

Social Considerations

Children and adolescents with ADHD are more likely to have a broad range of difficulties during their development, from decreased academic achievement to difficulty socializing and disruptive conduct [11]. Additionally, they are more likely to take part in risky behaviors like drug and alcohol use and develop a substance abuse problem. In 30 to 50 percent of patients with ADHD as children, the disorder persists into adulthood [13]. Adults with ADHD are more likely to be unemployed, divorced, or separated and feel like they do not fit in well with their peers [14]. They have also expressed feelings of being disorganized and having trouble completing projects on time [11].

In 30 to 50 percent of patients with ADHD as children, the disorder persists into adulthood.

Despite a scientific consensus about the nature of the disorder and the imperative to make treatment options accessible, some of Still’s initial descriptions of the disorder can be found in common myths about the disorder. Access to treatment for psychological conditions depends on many factors, which are often out of any individual’s control, and the stigma associated with psychological disorders may discourage people from seeking treatment. Both the juvenile and adult forms of ADHD are widespread and widely misunderstood. More thorough scientific understanding and comprehensive public education about the disorder are only the first steps necessary to help those who need it.

Max Mathias is an undergraduate student at Brown University.

References:
[14] Faraone SV, Biederman J. Economic impact of adult ADHD. Annual APA Meeting; 2005 May 21-26; Atlanta, Georgia, USA.

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Menstruation puts an immense burden on women. Up to 80 percent of reproductive-aged women experience physical changes in association with menstruation, and 20 to 40 percent of women will experience negative cycle-related symptoms [1]. In addition, it is estimated that menstrual disorders such as dysmenorrhea, menorrhagia, anemia, and premenstrual syndrome (PMS) affect approximately 2.5 million women between the ages of eighteen and fifty in the United States alone, contributing to an inability to perform daily activities, a decrease in productivity, and increased medical costs [2]. In the US, the associated health costs are equal to 8 percent of women's wages [3]. Oral contraceptives may provide greater options to women suffering from these conditions, though the full range of side effects has not been determined.

Debilitating Disorders
A wide range of symptoms and conditions are associated with or exacerbated by menstruation. These conditions include dysmenorrhea, menorrhagia, anemia, and premenstrual syndrome (PMS).

Symptoms of dysmenorrhea include cramping and pelvic pain beginning shortly with the onset of menses and last between one and three days. Dysmenorrhea can occur either as a primary problem, so that the problem is present singularly, or it can be secondary to endometriosis or fibroids, meaning that these diseases include dysmenorrhea [4]. Dysmenorrhea is believed to be caused by vasoconstriction in the vasculature of the uterine wall, resulting in rhythmic uterine contractions [4]. These painful contractions can be accompanied by headache, backache, pain radiating down the thigh, nausea, vomiting, diarrhea, and lightheadedness. The prevalence of dysmenorrhea is quite high; it has been found that between 40 to 90 percent of women are affected, and the age group most commonly affected is adolescent women [4].

Menorrhagia is characterized by excessive blood flow, a total blood loss exceeding 80 mL of blood per cycle, or a menstrual cycle that lasts longer than seven days [5]. In the US, about 30 percent of women believe their menstrual blood flow is excessive. The clinical diagnosis of menorrhagia is, however, hampered by the lack of methods to accurately measure blood flow. Consequently, the diagnosis is based on a comprehensive menstrual history. But the subjective nature of diagnosis, which is regularly done through the woman's own estimations, does not correlate well with the actual level of blood loss. Women with menorrhagia should be treated because the disorder is associated with an increased risk for iron-deficiency anemia. Indeed, the reason that the 80 mL blood loss is the benchmark used to diagnose menorrhagia is because women with greater menstrual blood loss have significantly depleted total iron-binding capacity, reduced total iron stores, and an increased likelihood for developing iron-deficiency anemia [6]. Although treatments are available, most fail to achieve long-term alleviation of symptoms, which lead some women to finally undergo a hysterectomy. To further illustrate the extent of this problem, two-thirds of the 90,000 hysterectomies performed in the US are performed on women with menorrhagia [5].

Premenstrual syndrome (PMS) is defined as “the cyclic occurrence of symptoms that are of sufficient severity to interfere with some aspects of life and that appear with consistent and predictable relationship to the menses” [1]. PMS can manifest with physical symptoms—such as headache, cramps, breast tenderness, swelling, poor coordination, aches, and food cravings—as well as emotional changes including fatigue, irritability, anxiety, confusion and depression [1,7]. In their most severe form, the symptoms associated with PMS may meet the Diagnostic and Statistical Manual of Mental Disorders criteria for premenstrual dysphoric disorder (PMDD) [7,8].

Considerable advances have been made in understanding...
PMS. Although levels of progesterone, estrogen, and testosterone are normal in women with PMS, some women may have an increased sensitivity to the effects of these hormones as a result of interactions between central nervous system mediators and sex hormones that lead to mood instability [1].

Currently, there are no specific treatments for PMS, so women use various methods to treat their symptoms, such as painkillers and herbal remedies. Although many women seek medical assistance for their symptoms, they report that only one in four physicians provides them with helpful treatment [9]. Drugs approved to treat PMDD are available, including selective serotonin reuptake inhibitors Sertraline and Fluoxetine [9]. However, women suffering from the condition are still under-treated.

Relief from Symptoms
Many women derive health benefits from reducing the frequency of menstruation or suppressing the menstrual cycle because there is a reduction in the occurrence of these menstrual-related disorders and other conditions, including menstrual migraines and anemia.

Newly introduced oral contraceptives (OCs), which are either extended or continuous use, seek to provide an alternative to these debilitating conditions. Extended oral contraceptives, such as Seasonique, promise women only four periods a year. Continuous oral contraceptives, such as Lybrel, completely eliminate menstrual periods. Both continuous and extended oral contraceptives, therefore, offer treatment options for these menstrual disorders.

In addition to relief of these serious conditions, the use of continuous or extended oral contraceptives is associated with a reduced incidence of ovarian and endometrial cancers. Long-term risk of ovarian cancer is reduced by 40 percent after four years of use, 54 percent after eight years and 60 percent after twelve years [10]. The risk of endometrial cancer is reduced by 56 percent after four years of use, 67 percent after eight years and 72 percent after twelve years [10]. Protection against these two forms of cancer continues for many years after discontinuation of OC use. It has also been found that use of OCs is related to a reduced incidence of benign breast disease, pelvic inflammatory disease (PID), ectopic pregnancy, and iron-deficiency anemia [10]. The link between OC use and increased bone mineral density is currently being investigated, as are the lowered incidences of uterine fibroid tumors, toxic shock syndrome, and colorectal cancer.

Opposition
While there are clear benefits for the abolition or reduction in menstrual period frequency, there are many medical and legal arguments against the use of continuous or extended oral contraceptives. Many feminists are opposed to the cycle-suppressing contraception; they argue that it is being marketed to young girls as a way to avoid the angst of teenage transition [11]. Some feminists believe that period suppression is being sold as a cosmetic fix, a way for women to avoid bloating, “feel bikini-ready, and be able to slip into skinny jeans,” and that these new pills are “medicalizing a normal female bodily function” [11]. On the medical front, these pills also continue to face skeptics. Most doctors say that these various drugs are very safe and similar to the type of period suppression women have experienced for the past forty years on standard oral contraceptives. However, many doctors argue long-term studies are still needed. One of the chief concerns is that constant use of hormonal birth control cuts testosterone levels, which influence a woman’s bone and cardiovascular health, mood, and sex drive. There may also be other side effects that are currently unknown [11].

Conclusion
While there are opponents to continuous or extended cycle oral contraceptives, there are still many benefits to using these types of contraception. The various non-contraceptive benefits of using continuous or extended oral contraceptives are extremely important in improving the quality of life for millions of women. Not only will women who suffer from menstrual cycle-related disorders suffer less from symptoms, they will also be able to protect themselves from life-threatening diseases such as endometrial and ovarian cancers. While various arguments against using extended or continuous oral contraceptives exist, the majority of findings point to the fact that they are a helpful medical advance for many women and have the possibility to improve their quality of life.

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References:
[12] http://www.fda.gov/Cder/about/history/GRAPHICS/ThePill.JPG
Nose Job: A Work in Perfection
Jack Cossman & Quynh-Giao Nguyen

“Behold the nose that mars the harmony
Of its master’s phiz! blushing its treachery!”

So Cyrano de Bergerac says of his infamous nose [1]. In response to his dull critics, Cyrano rattles off a list of intelligent insults for his big nose, a demonstration of pride for possessing a nose of such size. In reality, Cyrano’s pride is hard to come by; many Westerners are dissatisfied with their appearance and rely on cosmetic procedures for permanent change. This is not a recent phenomenon, though. Indeed, the attempts to reconstruct, correct, and perfect the organ through rhinoplasty—a common subdivision of plastic surgery—are ancient, passing through Indian, European, and American civilizations. Rhinoplasty today hardly resembles its earliest stages of evolution, but the desires and principles underlying the procedure today are a modern translation of those surrounding a procedure integral to human history.

The Nose in Ancient Indian Society
Nasal surgery dates back over 3000 years to ancient Indian society. In its earliest forms, nasal surgery existed as deliberate mutilation of the nose, most notably rhinectomy—complete or partial excision of the nose. Hindus regarded the nose as a symbol of honor and respect, an organ that is readily apparent and not easily concealed [2]. It was in fact common in ancient Indian society for children born with facial defects to be killed at birth or left to die, an act to spare the disfigured child from “diminished social acceptability” [3]. Thus, those with congenital nasal defects rarely reached an acceptable age to undergo surgery to correct the nose.

As the nose was symbol of self-pride, it is not surprising, then, that the nose was the target of punishment, through rhinectomy, for the convicted. The Hindus created a specific term, nacta, to describe this procedure [2]. As early as 1500 B.C.E., cultures in areas such as the state of Gujarat cut off the noses of women condemned of witchcraft. The common procedures of nose amputation in India eventually led to nasal reconstruction, a procedure more similar to our modern definition of rhinoplasty [2]. The techniques learned from nacta allowed surgeons to more proficiently operate on the nose, and, in conjunction with a rise in need for nasal repair, led to the invention of techniques to repair the mutilated or congenitally deformed nose. Since the nose was regarded with esteem, the advent of nasal correction quickly gained popularity.

Notable during this period was surgical pioneer Sushruta (600 B.C.E.), who discovered and recorded techniques of nasal reconstruction in his book Sushruta Samhita [3]. After 600 B.C.E., Hindu medicine transformed from being a superstitious art to a more practical craft. Sushruta fathered one of the earliest forms of rhinoplasty, using a method of removing flaps from the cheek to reconstruct a nose. His Indian successors then created a variation of Sushruta’s method using skin flaps from the adjoining forehead instead of the cheek, what is now known as the “Indian Method” [2]. The Indian Method finally allowed people with nasal defects to achieve a semblance of societal acceptance and personal satisfaction.

Evolution of Rhinoplasty in Europe
Conservatism, or the belief of plastic surgery as bodily desecration, buried most worldwide practices of plastic surgery, including rhinoplasty, after Sushruta’s time until the Renaissance. In Renaissance Europe, anatomical discoveries and medical innovations blossomed in combination with artistic, scientific, and societal advancements. The advancements effectively moved rhinoplasty into the realm of reconstructive surgery, owing to the increasing numbers of syphilis-sufferers, punished thieves, and duel-losers whose noses had been chopped off in brawl [4]. Additionally, as human anatomy was explored and glorified, it became increasingly taboo for society to accept somebody with a visible deformity, especially if it involved the nose [4]. Driven by inquiry and demand, plastic surgery grew into a field increasingly more scientific and aesthetic.

Beginning in the fifteenth century, more or less contemporaneous with Leonardo da Vinci—whose anatomical drawings and medical treatises spurred further medical inquiry—were the Brancas, a Sicilian family of surgeons known for developing new plastic techniques. In regards to their new rhinoplasty technique, Italian poet Elisio Calenzio wrote in a 1442 letter: “Branca of Sicily… has found out how to give a person a new nose, which he either builds from the arm or borrows from a slave…. Now if you come, you shall return home with as much nose as you please. Fly!” [3] Their practice is not only credited with introducing the Indian rhinoplasty to Europe but also of apprenticing Gaspare Tagliacozzi (1545-1599), who perfected the Branca technique and formalized a consistent procedure of rhinoplastic surgery [3]. Although this procedure became highly praised, surgery in Europe languished again for several hundred years after Tagliacozzi when conservatism again prevailed [5].

Despite this conservatism, plastic surgery and rhinoplasty as medical practices did not fall into oblivion. The practices continued, but broader medical concerns, arising specifically from the lack of anesthesia, prevented rhinoplasty from becoming a commonly performed procedure. Throughout the nineteenth and early twentieth centuries, surgeons continued to publish...
new techniques, shaping rhinoplasty into a standardized procedure [6]. The World Wars then accelerated the development of reconstructive surgery in response to increasingly severe facial injuries. Improved reconstructive techniques inspired surgeons to expand the market for aesthetic surgery, including rhinoplasty [7]. While rhinoplasty had always served to recreate an appropriate nose, the capabilities to aesthetically enhance the nose began to improve.

**Rhinoplasty in the Modern World**

Thereafter rhinoplasty entered mainstream Western medicine, its ancient cultural roles transforming into a modern practice. Just as it was removed to decrease social status in ancient India as well as glorified in Renaissance art and medicine, the nose today is aesthetically perfected to promote a sense of self-worth and societal acceptance. Even corrective and reconstructive rhinoplasties consider the natural aesthetics of the nose. According to Rhode Island Hospital cosmetic and reconstructive surgeon Lee Edstrom, M.D., “One end [of rhinoplasty] is the purely cosmetic and the other end is the purely reconstructive or corrective. But most of the things [surgeons] do are in the middle, a combination of the two” [8]. Although modern techniques have advanced from the earliest forms of rhinoplasty, the goal is still to render the nose both functional and aesthetic.

Despite that aestheticism is always the goal of a rhinoplasty, the ancient connection between aesthetics and status, social and personal, has been lost. Whereas older societies consciously perceived the nose, independent from other features, as a symbol of status, modern Westerners tend to focus on the nose’s relationship to its surrounding features [7]. According to Edstrom, any aesthetic enhancement is considered an “economic luxury” and, thus, not ordinarily reimbursed by insurance companies [5]. Insurance companies today have, therefore, categorized cosmetic rhinoplasty as inessential and distinct from medical procedures. This distinction is further noted in malpractice regulations: The law will protect a patient when an improper rhinoplasty jeopardizes health, but offers little protection when a patient is only unhappy with the outcome [8]. By categorizing aesthetic rhinoplasty as a non-reimbursable and superfluous procedure, the modern medical system connotes that ailing self-esteem and pride have little value in the conception of human health and wellbeing.

Whether modern rhinoplasty is an economic luxury or a necessity, concerns for nasal aesthetics are consistent with the focus placed on the nose throughout human history. The nose was denigrated as punishment and also glorified as beauty; as the centremost feature of the face, civilizations have given it a status equivalent to the entire human identity. However, most modern perceptions of rhinoplasty regard it as an economic luxury or necessity, concerns for nasal aesthetics are consistent with the focus placed on the nose throughout human history. The nose was denigrated as punishment and also glorified as beauty; as the centremost feature of the face, civilizations have given it a status equivalent to the entire human identity. However, most modern perceptions of rhinoplasty regard it as

**References:**


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Vaccinating Against Illegal Drugs to Prevent Use or Treat Abuse?
Economic and Ethical Considerations
Rebecca Kaufman

The vaccine is one of the most trusted, commonplace medical tools in the western world, as ubiquitous as the medical checkup from birth. We trust vaccines to reliably prevent diseases ranging from meningitis to the human papillomavirus from childhood to adulthood. What if we trusted another battle to the power of the vaccine, a medical battle more nuanced and impassioned than the fight against disease—what if the vaccine became a weapon in the fight against illicit drug abuse? Ethical pressures limit the use of the vaccine as a preventative measure against drug use, but the ethicality and economic feasibility are in place for the vaccine to become a major component of drug addiction treatments.

What is a Vaccine Against Illicit Drugs?

An addict’s brain has created a connection between drug use and euphoria; the high experienced each time a person is under the influence reinforces this neural connection. Drug vaccines, an addiction treatment currently being developed, prevent drugs from entering the brain at the speed required to produce these reinforcing effects. They operate by binding to or metabolizing specific drug molecules, decreasing the speed at which drugs cross the blood-brain barrier and in turn decreasing the reinforcing effects of drug abuse. These are currently being developed for nicotine, phencyclidine (PCP), methamphetamine, and cocaine. These vaccines have been observed to bind up anywhere from 25 to 80 percent of drugs present in the body [1]. Such immunization to drugs is done either actively, by generating antibodies through vaccine administration, or passively, by administering antibodies produced by a cell of a vaccinated animal. The drug vaccines on the horizon are the active nicotine and cocaine vaccinations, both of which are in clinical trials. As these vaccines move closer towards approval by the Federal Drug Administration, the question of where and how these vaccines will be used must be addressed.

A Drug Abuse Prevention Strategy

Use of drug vaccines to prevent drug abuse would necessitate vaccination before the first encounter with drugs. Could a drug vaccine become universally mandated to prevent drug use? There will most likely be constitutional issues with a mandatory universal vaccine [2]. Additionally, practical issues may emerge; adverse side effects to the vaccine will manifest as the vaccine sees widespread use, and this risk, in addition to the monetary cost of universal vaccination, may ultimately outweigh the benefits [3].

Although a universal vaccination may not be on the horizon, many populations have been identified as at risk for drug abuse: children of substance abusers, delinquents, foster children, and runaways, for example [4]. Could these populations be singled out for preventative use of this vaccine? Constitutional issues with this employment of the vaccine should prevent use of the vaccine in this manner [2].

Ultimately, individuals could elect to be vaccinated against illicit drugs. A consenting, paying adult could opt to be vaccinated, but electing to vaccinate a child is more complicated [2,3,5]. Could a parent elect to have their child vaccinated? Could schools or camps, which mandate certain vaccinations as a prerequisite for attendance, add drug vaccines to the list? Medically, children do not necessarily react in the same way to drugs as adults, necessitating clinical trials in children before any such questions can be addressed [3]. Even so, a parent could not elect for a child to undergo the vaccination under the assumption that minors should have “a substantial, although not exclusive, role in medical decisions” [2]. In terms of school and camp mandates, that question begs to be addressed, although ethical problems are likely to emerge.

These issues remain unsettled, and will remain contested areas as these vaccines progress towards FDA approval. Dr. Thomas Kosten, a researcher involved in the development of a cocaine vaccine in clinical trials, supports “immunizing children from addiction” to prevent drug use [5]. Despite many apparent ethical issues, personal attitudes and experiences with drug use may further complicate the ethical imperatives outlined above.

A Treatment for Addiction

Although employment of drug vaccines to prevent drug use in the general population is questionable, use of the vaccines to prevent drug use in those who have already exhibited a need for treatment is promising. Drug vaccines would provide the greatest benefit within treatment of recovering addicts.

Although there is a wide variety of treatment options...
available for addicts, many of which are extremely expensive.

The most successful addiction treatments are those focused on intensive care, which involve many doctors, nurses, and therapists, and often residential stays in treatment facilities—all of which are associated with high monetary costs [7, 8]. Additionally, addicts often relapse, necessitating a second spell in a treatment program.

Pharmaceuticals play a unique role within addiction treatment, providing a less intensive and potentially less costly tool to facilitate recovery. Despite their utility, there are potential problems to consider. Methadone, like drug vaccines, provides a relief from the brain’s dependence on drugs, in this case heroin. Methadone effectively prevents heroin use when it is taken regularly, and is associated with a lower weekly cost than other addiction treatments [9]. Nonetheless, treatment often extends for two years as compared to thirteen to seventeen weeks in intensive treatment programs, accumulating a higher overall cost than intensive treatments [8]. This problem would not be encountered with use of a vaccine, which has a fixed number of treatments while maintaining a lower cost. Despite the potential of a drug vaccine, the complexity of addiction must not be underestimated; heroin addicts undergoing methadone treatment were often found to abuse cocaine as an alternative [10]. One could expect to observe the same behavior in vaccinated addicts. Although vaccination can serve as a helpful tool, it is not a cure for addiction. Other treatment methods must supplement the vaccines to ensure successful rehabilitation of an addict.

The high cost, complexity, and uncertainty of treating a recovering addict has created a demand for a reliable, inexpensive, and accessible treatment options such as the drug vaccine. Within the market for addiction treatments, the drug vaccine will presumably see success; nonetheless, it is important to remain critical of these vaccines and to avoid overdependence on pharmacological therapies.

The Pharmaceutical Market for Addiction Treatments

Drug vaccines are favorably situated in the pharmaceutical market, increasing their potential as an addiction treatment. The current market for addiction treatments substantial, though primarily focused on nicotine addiction therapies. Therapies to treat nicotine addiction are widely researched and advertised by pharmaceutical companies in order to tap into the large number of smokers, all of whom are bombarded with information on the negative effects of smoking [11, 12]. One of the few drugs available to treat addiction to an illegal drug is methadone, a daily treatment for heroin addiction. Vaccines against illicit drugs would open up the possibilities for pharmaceutical companies operating within this market.

A large amount of public money is used to treat drug addiction despite the number of addicts who remain untreated. In 2006 the American government spent $181 billion to alleviate illicit drug abuse, yet in the same year almost 90 percent of Americans who needed treatment for illicit drug or alcohol abuse did not receive it, in comparison to 80 percent of addicts receiving treatment in the European Union in 1999 [1, 6]. Potentially, drug vaccines could allow more addicts to be treated and alleviate the large burden of addiction—attractive attributes to both patients and the government.

The demand for an effective addiction treatment is echoed by pharmaceutical companies’ desires to acquire drug vaccines. According to Visiongain, an independent business serving the pharmaceutical industry, “the global addiction market is significantly undervalued” [13]. A second report by BioPortfolio titled “Anti-addiction Therapies, 2006-2011 — The Pharmaceutical Industry’s Next Viagra?” expresses hope that addiction therapies are the source of “the next blockbuster drug” [14]. Economically, drug companies see addiction therapies as a new frontier and will undoubtedly pursue drug vaccines with great interest in all potential markets, including both prevention and treatment of drug abuse.

Conclusions

Drug vaccines, instead of vaccinating against a pernicious disease, vaccinate against a potentially dangerous behavior: drug abuse. Although the benefits of vaccinating a recovering addict are apparent, the ethical and monetary issues entangled in preventative vaccination may outweigh the potential benefits of its implementation. Nonetheless, the financial cost of drug abuse and addiction are substantial and will underlie the development and application of this vaccine in the future.

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References:

Overreaching for the International Mainstream?:
China’s Science Community
Soobin Kim

In announcing the National Science and Technology Development Program (2006-2020), President Hu Jintao of China declared that by 2020 the nation will qualify to “join the ranks of the world’s most innovative countries” [1]. But why does China, already the world’s second largest publisher of science articles and the second highest investor in research and development, want to “join the ranks” of the international science mainstream? Proving itself in the international community is important for any nation, but an overemphasis on entering the category of scientifically advanced nations means that other aspects of the science community may be overlooked. As of now, China does not seem free from that overemphasis, which hinders rather than helps the growth of the Chinese science community [1].

Too much Focus on the International Scientific Standards?
The Chinese science community’s overemphasis on publishing in international journals, especially those listed in the Science Citation Index (SCI), is a classic example of the community’s insistence on joining the category of scientifically advanced nations. The SCI, published by Thomson Reuters, is an internationally recognized database of scientific bibliographic references. China’s citation impact score, which tracks the number of times the research papers conducted by Chinese scientists are cited, has doubled in a decade [2]. Tenure and pay at national universities in China are decided on the basis of the number of articles published in SCI journals, Chinese scientists report [2]. This practice reflects the Chinese government’s goal of becoming one of the top five countries worldwide in number of scientific citations [1].

However, this fixation on publishing in international journals has some important consequences. First, because most SCI journals publish in English, information on new technology or research results are not sufficiently available to the businesses in China [2]. This makes it difficult for domestic businesses to use the research outcomes of the Chinese science community. In fact, only 0.03 percent of the Chinese firms own the intellectual property rights of their core product technologies, which seriously affects profitability because of the high cost of using patented technologies owned by foreign firms [1]. Even as high-tech product exports from China grow 22 percent each year, technology accounts for only 4 percent of China’s exports a year [1].

The overemphasis on publishing in international journals also makes difficult the Chinese scientists’ access to most of China’s best research results. To many, the international journals are not regularly accessible due to language or price barriers [2]. This reduces the possible synergies from new research results. Finally, the need to publish in international journals shapes Chinese scientists’ research priorities. High-technology topics pursued in developed nations are easier to publish in science journals based in those nations, and are subsequently more often taken up by the Chinese scientists [2]. Yet these topics are likely to have less relevance or immediate urgency a developing nation such as China, which faces unique problems such as health epidemics and environment crises.

The Chinese government needs to step in. Unfortunately, many Chinese journals are caught in a vicious cycle: as most high quality submissions are sent abroad, the impact level of the domestic journals drops, and with it the number of high quality submissions in the future [2]. The government so far has done nothing in this regard, and the National Science and Technology Development Program (2006-2020), which set the national policy on scientific research development, does not mention this issue.

Balancing the FDIs and the Local Research Community
China should balance its attraction of foreign direct investments in research with appropriate support to help the local institutions cope. Thanks to the active efforts on the part of the Chinese Ministry of Science and Technology, China has successfully attractive many such foreign direct investments and hosts about 750 such multinational research and devel-
development centers, compared to 150 in India [1]. Multinational research and development centers such as Microsoft China Research and Development Group and Beijing Proctor & Gamble Technology Co., Ltd., are valuable for providing high skill job positions and employment opportunities. However, the influx of foreign direct investments came without adequate support to balance the competitiveness of the local science institutions.

This has resulted first of all in diminishing the competitiveness of the public research positions for high-caliber research personnel. The influx of attractive jobs in multinational research and development centers has not been balanced by making public research positions equally attractive. The starting position salary at Microsoft China R&D Group is comparable to that of a public research institute’s senior researcher [3]. By regulations, only a small percentage of the government research funding can currently be spent on personnel [3]. The outflow of talent to multinational research and development centers hampers China’s basic research community, which consists mostly of public research institutes [4]. Basic research focuses on areas such as pure mathematics and physics, whose research outcomes cannot immediately be put into commercial use, and thus mostly performed with the governmental funding [4]. The undermining of the basic research community is problematic, as basic research serves as the source of new ideas and methods and is an important arena for long-term training high-caliber human resources [4]. In recognition of the deficient basic research, the Chinese government has decided to increase funding for basic research projects [5]. However, without competitive compensation to correct the imbalance in the jobs between multinational centers and the public institutes, any increase in funding is likely to be ineffective.

The influx of the foreign direct investments has also diminished the effectiveness of China’s Science and Technology Industrial Parks. The parks were started under China’s Torch program to encourage collaboration on the local level between the research community and the technology-related businesses [6]. The parks usually host venture technology research institutes and firms, which enjoy tax break incentives from the government [6]. However, the current tax break system has encouraged the firms to manufacture for other firms rather than carry out innovations on their own [6]. This, combined with the influx of foreign direct investments, has led many parks to make a series of collaboration agreements with foreign governments and business entities. The result has been a consistent deviation away from the parks’ original mission to serve as the incubators for technological innovations and the collaborations with local businesses, which are often less attractive to manufacture for due to their sizes and name values. The parks, therefore, often end up becoming mere high-technology export manufacturing parks for multinational companies [6].

In addition, there are also signs that the overemphasis on reaching out to the international community has made the Chinese policymakers overlook potential opportunities within the Chinese science community, in particular in regards to the Science and Technology Industrial Parks. The Organization for Economic Co-operation and Development report on China’s research community described the parks as an “archipelago” of innovative islands with no efforts for collaboration between them, although the parks often specialize in certain technology areas [6]. China’s lack of efforts in creating synergies among the parks is striking, especially when contrasted to China’s vigorous attempt at creating international synergies through over a hundred inter-governmental Scientific and Technological Cooperation agreements.

References

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Despite major advances in the ability of medicine to treat and prevent a variety of human diseases, an uphill battle continues to be fought against many conditions, such as sepsis, a situation in which the body's own mechanisms are responsible for the pathology. Sepsis is the third leading cause of death in the developing world and the tenth leading cause of death in the United States with an estimated 28 to 50 percent mortality rate even when treated [2, 1]. Common definitions of sepsis include blood poisoning or severe infection; such definitions are correct but misleading by oversimplification. Sepsis is a massive, unchecked inflammatory response to bodily trauma. An infection may be the root cause, but the life-threatening nature of this state is due to the actions of the body itself. The internal as opposed to external nature of sepsis pathology limits the existing treatment options available, and the medical community clearly needs a new and more effective avenue to manage this condition.

What is Sepsis?
When untreated, sepsis severity proceeds along a continuum from Systemic Inflammatory Response Syndrome (SIRS) to sepsis, severe sepsis, and finally septic shock. A diagnosis of SIRS is made when a patient exhibits two or more of the following: body temperature above 100.4 or below 96.8 degrees Fahrenheit heart rate above 90 beats per minute; respiration above 20 breaths per minute; and a white blood cell count above 12,000/cubic milliliter or below 4,000/cubic milliliter [1]. When the patient is positively determined to have an infection in addition to the symptoms of SIRS, the diagnosis of sepsis is made. Severe sepsis exists when the criteria for SIRS are met in addition to one or more organ dysfunctions including acute lung injury, coagulation abnormalities, thrombocytopenia, altered mental state, hypoperfusion with lactic acidosis, and renal, liver, or cardiac difficulties or failure. Septic shock is defined as clinical sepsis with the presence of refractory hypotension, which occurs when mean arterial pressure falls below 65 mm Hg [1]. Unfortunately, all of the aforementioned symptoms can also result from a number of other illnesses, greatly complicating the doctor’s task of diagnosis and treatment, and time is usually of the essence in such determination.

The sequence of events comprising a bacterial infection can illustrate the biology of sepsis. After a patient has received, for example, a laceration to the leg, Staphylococcus aureus bacteria can enter the surrounding tissue and proliferate. Cells damaged by the laceration release chemicals that activate the proteins of the complement system, causing the blood vessels closest to the site of injury to become more permeable [2]. As a result, fluid begins to seep into the affected tissues, carrying with it white blood cells to contain and eliminate any pathogens that may have entered the body. Meanwhile, the area around the patient's wound has begun to swell and turn red from the extra blood flow. The presence of S. aureus and the toxins it secretes activates macrophages—white blood cells involved in the innate immune response—and causes them to secrete a variety of cytokines [2]. Cytokines increase the inflammatory response and make it easier for more fluid and white blood cells to enter the damaged tissues. During this response, the clotting system is also activated and begins sealing the wound to help block the spread of the bacteria [1]. Normally, these reactions occur quickly to minimize the threat of the pathogen. Additionally, the body produces a counter response to contain the inflammation to the infected areas of the body and prevent any inflammatory-related tissue damage.

Inflammation in Excess
Sometimes the body loses its ability to control this inflammation—for instance, in those who are chronically ill or immuno-suppressed. Consequently, the infection may spread rapidly and cause a dramatic amplification of pro-inflammatory mediators, or the anti-inflammatory mediators that are part of the bodies counter response may be degraded to the point that they can no longer function effectively. It is at this point—when the balance tips towards pro-inflammation—that the symptoms of sepsis manifest. The body’s inflammatory mechanisms continue to act as previously described but are now disproportionately widespread. Large portions of blood vessel endothelium become too permeable, and fluid begins to drain into other tissues and even into organs. The activated clotting system begins to block much-needed microcirculation [3]. These combined factors lead to a drop in blood pressure and prevent oxygen from reaching the bodily tissues, causing the body to enter a state of lactic acidosis. In turn, these events lead to organ dysfunction and organ failure, which can be fatal [4]. Even those who survive the actual course of sepsis have a poor prognosis short term survival, since extensive lymphocyte apoptosis occurs as a final effort to stop the secretion by these cells of cytokines and inflammatory mediators [5].

Since sepsis is caused by inflammation, why aren’t anti-inflammatory drugs an easy solution? While attempts have been made to target specific pro-inflammatory mediators, such attempts have been met with disappointing results due to the narrow window of therapeutic intervention [6]. The current standard treatment is called Early Goal-Directed Therapy (EGDT). EGDT was initially developed to take into account...
the fact that the symptoms of sepsis can mimic other conditions. In EGDT, any patient displaying symptoms similar to those found in SIRS, systolic blood pressure below 90 mm Hg, and lactic acid above 4 mmol/liter (the criteria for severe sepsis) is considered septic and undergoes aggressive treatment [7]. Such treatment may consist of catheterization with a central venous line capable of measuring oxygen saturation that can also be used to administer the following: fluids to keep venous pressure between 8 and 12 mm Hg and vasopressors, norepinephrine in particular, to maintain mean arterial pressure above 65 mm Hg or vasodilators to keep it below 90 mm Hg [7].

With the implementation of EGDT, mean sepsis mortality at thirteen major medical centers decreased from 44.8 to 24.5 percent. While additional therapies have been developed, few have been as successful as EGDT, as most have a narrower time range of application and can have some significant side effects [8]. While the reduction of sepsis mortality to approximately 25 percent is good news, there is clearly still much ground to be covered. To lower the mortality rate even more, it is necessary to find a method of recognizing the symptoms of sepsis in its early stages so that early treatment might prevent the progression of excessive inflammation.

**Inter-Alpha-Trypsin Inhibitor may be the key to defeating sepsis**

A single molecule known as inter-alpha-trypsin inhibitor (ITI) may hold the key to both quicker diagnosis and improved survival. This “wonder molecule” is a protease inhibitor that is synthesized in the liver. Structurally, it consists of a light chain protease inhibitor, frequently bikunin, and two heavy chains [9]. In the presence of an inflammatory state, the half-life of ITI spikes from 5.6 to 11.8 hours, enabling the molecule to remain active and control inflammation for a longer period of time [10]. However, despite the increase in half-life, numerous studies have found that ITI levels significantly decrease during sepsis, with lower levels corresponding to more severe cases and higher likelihood of death [9]. This correlation between ITI levels and sepsis severity forms the basis for its potential to be used as a test to determine if a patient is septic. The decrease in ITI levels has several causes.

Neutrophils, white blood cells that become highly active during sepsis, can secrete pro-inflammatory cytokines—all of which are major sources of the induction and continuation of inflammation [9]. The fact that it cannot eliminate some of these products as effectively as other inhibitors is a benefit as well because the over-suppression of these factors could cause under-responsiveness of the immune system, leaving the patient susceptible to further infections. This reduces the chances of negative side effects.

Finally, ITI works in vivo in animal models of sepsis. In a process known as cecal ligation and puncture, a lab mouse had a portion of its intestine perforated multiple times, inducing sepsis in the animal. Depending on the elapsed time since commencement of sepsis and amount administered, ITI increases survival rates from 40 to 89 percent [12]. All animals exhibit significantly improved chances of survival with ITI administration, and the earlier the better. If similar results could be replicated in humans, the treatment of sepsis would be revolutionized and thousands of lives could be saved.

The discovery of this use for ITI and the conquest of sepsis would represent another major step forward in the improvement of the quality and longevity of life, especially for individuals suffering from sepsis. While ITI currently shows a lot of potential, research is still in the early stages of fully unlocking all the capabilities of this molecule. It will be some time before ITI appears alongside EGDT as a standard of treatment. In the meantime, decreases in sepsis mortality will rely on the skill of emergency room and intensive care unit doctors in their ability to recognize and address this condition early and effectively.

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References


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Is the United States Losing Its Dominance in Science?

Jason Chan

Over the past several decades, the United States' advances in technology and science have been unmatched by other countries. Not surprisingly, in 2008, the United States raked in four of the eleven Nobel Prizes in science, continuing a fifty-year trend of claiming about half of the total number of science Nobel prizes, a feat unrivaled by any other nation. Nonetheless, there has perhaps not been another time in recent history where the progress of American science has come under greater scrutiny. As the world's largest particle accelerator emerges from the Franco-Swiss border, India launches its first unmanned mission to the moon, and China moves forward from its first spacewalk, it seems that the United States may be losing its edge in science and technology [1]. Over the past decade, changes in job prospects, fluctuations in federal funding, and inadequate early science education have been three contributing factors to America's declining dominance in science.

Ahead for the last half century
For much of the twentieth century, the United States has been the undisputed leader in science, technology, and medicine. The ability to harness nuclear energy was perhaps the watershed of America's dominance. During the 1940s, nuclear fission was accomplished on American soil when prominent European physicists like Hans Bethe and Albert Einstein fled to the United States. This marked the beginning of the Atomic Age, where nuclear energy was applied in the development of military weapons, power, and medicine. Tentative advancements in space exploration were made, and the Space Age was born. The advancement of atomic theory as well as space exploration were collectively the start of the era of “Big Science,” when the American government began to heavily sponsor scientific research for its political agenda [2]. Through unprecedented investments in technology, industrialization, and medicine, the United States emerged from World War II as the standard-bearer in virtually all fields of scientific research. However, since the turn of the twenty-first century, there have been strong indications that America is losing this leadership in several fields while countries in Asia and Europe are quickly emerging, or re-emerging, at the forefront of science.

Less Incoming Talent
The United States' shrinking patronage for technological products is one reason for its eroding leadership in science: America does not appeal as it once did. The United States in recent years has produced fewer and fewer high-technology products relative to the rest of the world. From a $54 billion trade surplus in 1990, the nation plunged to a $50 billion trade deficit in high-tech goods in just eleven years [3]. By the end of 2008, this deficit is expected to reach a record high of $60 billion. Furthermore, in 2004, China overtook the United States as the leading exporter of information-technology products. Also, beginning in 2008, the world's most powerful high-energy particle accelerator, now the Large Hadron Collider (LHC), will for the first time in history be located outside of the United States [4]. The LHC represents a triumph for Europe over the United States and arguably re-establishes Europe's pre-World War II superiority in physics.

In addition to losing sophisticated material goods and facilities, the United States should also be concerned with both losing and being unable to attract skilled scientists from overseas. Decades ago, Americans benefited at the cost of many Asian countries due to a phenomenon affectionately known as the “brain drain,” where talented individuals immigrated to the United States in hope for a more promising career in science. Today, one often sees the reverse “brain gain” phenomenon,
where countries like China and India are retaining more and more of their high-potential scientists [5]. Not only has the United States been less successful in attracting talent from other countries, but domestic job prospects have declined in several scientific fields.

**Changing Job Prospects**

While the United States remains dominant and competitive in interdisciplinary sciences such as biological chemistry, materials chemistry, and nanotechnology, traditional fields such as chemistry have become unpopular career choices in recent years [5]. In 2003, only 8 percent of all published papers in the US were in the field of chemistry. In comparison, 25 percent and 27 percent of all scientific papers from China and India, respectively, were in chemistry.

The lack of interest in chemistry exists in industry as well as in academia: the last new refinery in the United States was built in 1976 [6]. Furthermore, in 2004, seventy chemical facilities were closed in the United States, and forty were tagged for shutdown. Since then, of the 120 chemical plants in the world each costing over $1 billion, only one is in the United States, while fifty are in China [6]. Clearly, job opportunities in chemistry seem to be waning in the United States as compared to other nations.

Relative to China and India, the US also shows a lack of research interest in the fields of physics and engineering. Only about 9 percent and 7 percent of all scientific papers published in the US are in physics and engineering, respectively. The United States’ global share of published papers fell by 8 percent from 1988 to 2003 [5]. The smaller global proportion of published papers in the US suggests that being a scientist, especially in certain fields, does not appeal to talented American individuals as much as it used to.

**Decrease in Federal Funding**

A potential reason for this decrease in interest in scientific research is inadequate federal funding; in fact, changes in federal funding in recent years seem to be inextricably linked to the waning leadership of American science. Junior faculty and young investigators are currently struggling to compete for grants. “The statistics are scary,” says Keith Yamamoto of the University of California, San Francisco, adding, “In 1980, 86 percent of new faculty members won a grant the first time they applied for one; now only 18 percent do. At the same time, they’re getting older: the average Ph.D. gets his or her first real job at age 38 and first R01-type grant at 42” [7]. In addition, the past two years saw no increase in federal funding for general science and engineering. The NSF reports that such a scenario has never been witnessed in thirty-six years.

However, despite the discouraging job prospects in science fields due to inadequate federal funding, some may argue that the problem is much more fundamental—that it resides in children in secondary school or younger. Young students from the US consistently fall short of international standards for mathematics. Of the forty countries that participated in an examination administered by the Program for International Student Assessment, the international standardized test of scholastic performance, US fifteen-year-olds ranked twenty-fourth [6]. In the same report, US twelfth graders performed below the international average for twenty-one countries on a test of general knowledge in mathematics and science. Perhaps this lack of proper early training in basic science and mathematics results in the deficiency of scientists and engineers.

**No Longer the Standard**

All things considered, it seems undeniable that the United States may soon find itself no longer the benchmark for science. In the last half century, America’s unmatched government support for science and technology was one contributing factor to its success in research as well as industry. Yet over the past decade, the American government has demonstrated a relatively decreased commitment to science, which leads to dwindling talent arriving from overseas as well as worsening job prospects in the fields of science and technology. Even from early childhood, young potential scientists do not seem to be receiving the scientific and mathematical training required to succeed.

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**References:**


For many, science is regarded as an esoteric field, and because of scientific jargon and the nature of basic research, there has traditionally been a lack of communication between scientists and the general public. To solve this problem, Tamar Schlick, a professor of chemistry, mathematics, and computer science at New York University, has proposed a collaboration between science and art. Schlick argues that “we can make well-informed and open-minded decisions if artists and scientists collaborate on scientific themes in a supportive manner” [1].

However, artists and scientists have not yet found an effective approach to collaboration. Such partnerships are crucial because of the underlying close relationship between art and science; not only is there often an artistic aspect in science, scientific ideas are often involved in artwork. Art and science, though they may not appear related, can benefit by working together.

What Art Can Tell Us about the Brain
Pablo Picasso said that “art is the lie that helps us tell the truth” [1]. In other words, art is a tool that can explain scientific facts. Over the last century, prominent scientists such as Stephen Jay Gould, Carl Sagan, and James Watson used writing to convey abstract scientific concepts. The City University of New York recently developed a program that “presents dance, theater, music, and art with science as the theme” [1]. Moreover, recently there have been several attempts by scientists to find a connection between neuroscience and art.

Margaret Livingstone, a professor of neurobiology at Harvard Medical School, visited Brown University on April 22, 2008 to give a lecture titled “What Art Can Tell Us about the Brain.” Artists, she said, realized the principles of neural systems before there were neuroscientists and had applied such ideas in their art long before the first neurons were stained.

For example, because highest visual acuity lies in the small region of the retina called the fovea, viewers must shift their eyes to be able to see a large piece of art. Since viewers can examine the same objects from multiple points of view, a kind of “alternate physics” is applicable to artwork [2]. Some artists who knew that single-point perspective is not always necessary for recognizing image “make images that flagrantly violate the idea of one-point perspective rules” [2]. They have created images of single objects that integrate different perspectives; one example is the Mona Lisa, a famous painting by Leonardo da Vinci.

Mona Lisa’s smile has intrigued many viewers. Dr. Livingstone explained the elusive nature of the smile by filtering the original image of Mona Lisa to different spatial frequencies. Her smile is almost entirely in low spatial frequencies, as you can see in the leftmost picture in Figure 1, and therefore the smile is best seen by peripheral vision. When you look at the background or the eyes, you see a smile like the one on the left of Figure 1. But when you look directly at her mouth, you perceive the image as more like the rightmost picture in Figure 1 and think she is not smiling. That the degree of her smile varies makes her expression dynamic, and that her smile vanishes when one looks directly at her mouth makes the smile elusive [3].

Another relevant neurological perception is “peak shift effect,” defined by Dr. Vilayanur S. Ramachandran in University of California at San Diego [4]. When people see the most salient part of an image, neuronal activity in the brain increases. People remember pictures by exaggerating and ignoring different aspects of an image to capture its essence. Picasso was indirectly aware of this fact through his experiences and applied it when he drew pictures of his acquaintances, as shown in Figure 2. These works are significant in that Picasso “combines both exaggeration and the use of multiple perspectives” [2].

Artists, indeed, were aware of neurobiological principles without directly analyzing the human brain; they didn’t know physiology or anatomy, but they relied on artistic experiences to figure out how to attract viewers with multiple-point perspective and exaggeration. Artists showed and proved to us that science is not always the only useful tool in analyzing scientific problems.

Johannes Borgstein, author of The Poetry of Genetics, argues that poetry can be a useful tool in explaining...
genome sequencing. Just as literary works may be read at multiple levels, there are multiple levels of “reading” the human genome. The levels that can be applied to both poetry and genomics are the following: 1. distinguishing individual letters in Latin script (or the genetic sequence), 2. understanding the “language,” 3) identification of whole “words” out of continuous sequences of letters, 4) determining “phrases” that belong together, and 5) selecting separate “poems” (or protein structures) [5]. A genetic code is a language with almost infinite possibilities within the framework of a fixed alphabet. To help the general public better understand the analysis of the human genome, Dr. Borgstein uses poetry as an approachable alternative:

I keep to see a world six honest serving men (they taught me all I knew) in a grain of sand their names are what and a Heaven in a wild flower why and hold infinity when in the palm of your hand and how and where and who eternity in an hour. [5]

After levels 1, 2, and 3 suggested by Dr. Borgstein, the sequence can be arranged as understandable English sentences.

I keep to see a world six honest serving men (they taught me all I knew) in a grain of sand their names are what and a Heaven in a wild flower why and hold infinity when in the palm of your hand and how and where and who eternity in an hour. [5]

Then one needs literary knowledge to be able to “separate the phrases, which belong together and are to be read sequentially. Completing level 4 can achieve this goal.

I keep to see a world six honest serving men (they taught me all I knew) in a grain of sand their names are what and a Heaven in a wild flower why and hold infinity when in the palm of your hand and how and where and who eternity in an hour. [5]

Through properly putting together the italicized phrases, the original alphabet sequence can be transformed into two finished poems:

To see a world in a grain of sand
and a Heaven in a wild flower
hold infinity in the palm of your hand
and eternity in an hour. (William Blake)

I keep six honest serving men
(they taught me all I knew)
Their names are What and Why and When
And How and Where and Who. (Rudyard Kipling) [5]
Instead of presenting an explanation of the human genome riddled with intimidating scientific jargon, describing it in terms of poetry enables the public to realize that the genome project is not as abstract as it seems. Sequencing the human genome is similar to analyzing poetry, except scientists solve the sequence through their knowledge of biology, mathematics, and computer science.

How Can We Combine Art and Science?
One of the most important steps in integrating art and science is to reform the education system to enable students to apply scientific knowledge in art and artistic experience in science, instead of teaching mere rote memorization of scientific principles.

Brown University, for example, has taken an initiative in merging science and art in college education. The following is a description of a physics course called “Images from Science, Artist. But images, objects, and animations can also help in the understanding of deep and subtle scientific ideas. In this course we present some basic ideas of physics and cosmology. These suggest images that can inspire works of art as well as those that can aid in explaining science. [6]

Throughout the course, students analyzed scientific pictures artistically and applied scientific theories while looking at the images [7]. This course directly demonstrates that combining art and science in education is not just an idealistic approach, but a realistic one.

Conclusion
While learning scientific principles is important, scientists can also acquire a different type of insight by integrating artistic knowledge. Science is a highly analytical branch of study striving to reveal valuable aspects in our lives. Through science, people find treatments for fatal diseases, send astronauts to the moon, and talk to others who are on the opposite side of the earth. Yet, an analytic perspective alone cannot meet all human needs. Artists create music, draw beautiful pictures, and bring interesting stories to life through writing.

Neither art nor science is more important than the other. Through merging art and science, we can help fix the problem in current science education by bringing a different type of interest to the table. Moreover, we can increase communication between scientists and non-scientists through finding artistic aspects in science and scientific aspects in artwork. Though the gap between artists and scientists is hard to overcome, we can make the gap smaller by educating the future generation with an innovative education system that combines art and science.

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Images for Science”:
Images and objects that come from nature and science—from Elm trees to galaxies—can be a source of inspiration for the artist. But images, objects, and animations can also help in the understanding of deep and subtle scientific ideas. In this course we present some basic ideas of physics and cosmology. These suggest images that can inspire works of art as well as those that can aid in explaining science. [6]

Figure 3. Reproduced from [5].

References:
A modern movement employing a collaborative perspective from both the empirical sciences and Buddhism is beginning to address the study of consciousness as never before: from the inside out. This mode of inquiry has often been dismissed as subjective; however, this first-person analysis can be valuable, as noted by the Dalai Lama in 2005:

Buddhism has a long history of investigation into the nature of the mind and its various aspects... Unlike that of modern science... the contemplative method, as developed by Buddhism, is an empirical use of introspection, sustained by rigorous training in technique and robust testing of the reliability of experience. All meditatively valid subjective experiences must be verifiable both through repetition by the same practitioner and through other individuals being able to attain the same state by the same practice. [1]

The first-person method of investigating consciousness is an alternative way to obtain identifiable results about the state of consciousness. Using this method, Buddhism has created a complex theory of consciousness through 2,500 years of investigation. Although this time-tested tradition has resulted in extensive literature on the processes of the mind, the Dalai Lama told the Society for Neuroscience in 2005 that Buddhism could accommodate modern scientific practice:

I have often remarked to my Buddhist colleagues that the empirically verified insights of modern cosmology and astronomy must compel us now to modify, or in some cases reject, many aspects of traditional cosmology as found in ancient Buddhist texts. [2]

Buddhism’s flexibility regarding empirically verified research and its rigorous method of investigation allows for cooperation with modern science in the study of consciousness. In 1987, the Dalai Lama met with neuroscientists, philosophers and Buddhist practitioners in Dharamsala, India, for the first conference of the Mind & Life Institute, an organization whose goal is to understand the nature of reality through utilizing both modern scientific and Buddhist methodologies. Since 1987, hundreds of participants from many nations have attended Mind & Life conferences, which include both scientific dialogue and intensive meditation.
Buddhism-inspired research has addressed both basic science and clinical applications.

**Meditation and Basic Science**

Dr. Richard Davidson, the director of the Waisman Center for Affective Neuroscience at the University of Wisconsin-Madison, has conducted pioneering research addressing the effects of Buddhist meditation. In a 2004 study, Davidson sought to answer the question of whether meditation can lead to long-lasting changes in cognition and emotion [3]. The study utilized electroencephalography (EEG) to analyze the brains of eight long-term Buddhist meditation practitioners against a control of ten college students. The meditators had between 10,000 and 50,000 hours of meditation experience during the course of their lives. The non-meditators were given a week of meditation instruction before the testing. The subjects were to meditate on “unconditional loving kindness and compassion,” which is described as an “unrestricted readiness and availability to help living beings” [3]. EEGs were recorded using a 128-channel geodesic sensor net. At baseline, the meditators were found to have much more gamma activity. During the meditation period they had extremely high degrees of synchronized gamma activity, this high activity was correlated with meditation experience; a larger amount of meditation hours logged correlated with higher gamma synchrony. In one subject, synchronization between the hemispheres increased by over 30 percent during the meditation period [3].

Gamma synchrony occurs when regions of the brain exhibit in-phase, high-frequency brainwave activity. The gamma synchrony recorded by Davidson’s study were the highest ever recorded in a non-pathological state [3, 4]. Dr. James Austin theorizes that this synchrony is intimately related to alertness/readiness:

Various lines of evidence converge to suggest that much of our binding of sensory features hinges not just on gamma activity per se but on the way the stimulus goes on to induce gamma activity which becomes synchronized and in phase. Recent evidence suggests that our implicit intentional focus involves a similarly induced gamma activity, as well as gamma oscillations that then evolve further during the whole sequential process. [5]

Another important question related to meditation and science is whether meditation can alter brain structure. In 2005, Dr. Sara Lazar of Harvard Medical School addressed this issue. The study utilized magnetic resonance imaging (MRI) technology to assess cortical thickness in twenty subjects who had extensive Buddhist meditation experience [6]. The participants averaged 9.1 years of meditation practice at 6.2 hours per week. The subjects in this study were found to have thicker prefrontal cortex and right anterior insula, which are areas associated with attention, interoception, and sensory processing. The study also found that older meditators had the most pronounced cortical thickness difference when compared to controls in their age group. This suggests that meditation may have effects on age-related cortical thinning. The subjects’ cortical thickness was also associated with how much meditation experience that particular person had, indicating possible experience-dependence cortical plasticity associated with meditation practice [6].

Stress physiology may also be affected by meditation. This could have far reaching consequences. According to the American Psychological Association, 79 percent of Americans consider stress to be a “fact of life [7].” In 2008, Dr. Thaddeus Pace of Emory University’s School of Medicine addressed the impact the mediation may have on physiological pathways...
that are modulated by stress and relevant to disease. In the study, sixty-one adults participated in a six-week compassion meditation training followed by the Trier social stress test (TSST), and twenty-eight control subjects also completed the TSST but did not participate in the meditation training. In the TSST, participants are negatively critiqued by trained interviewers. Cortisol and interleukin—chemicals associated with stress reactivity—levels were recorded post-TSST, and the subjects also completed the Profile of Mood States (POMS). Increased meditation practice was correlated with lower TSST-induced interleukin and POMS distress scores. The data suggests that compassion meditation may reduce stress-induced immune and behavioral responses [8].

The research of Davidson, Lazar, and Pace do not definitively prove whether or not meditation can induce cognitive, structural, or physiological changes, but they do shed light on the process and complexity of meditation and consciousness from a neuroscientific and Buddhist perspective.

Meditation and Clinical Research
The purpose of practicing meditation is to train attention and other cognitive and emotional processes, and for this reason, it can have benefits for people with various mental illnesses such as depression and anxiety. Meditation is inexpensive and has seemingly limited negative side effects. In effect, meditation can alter the current psychological paradigm, with respect to perception and treatment of mental disorders.

Research has shown that 18 percent of Americans may be affected by anxiety disorders [9]. Generalized anxiety disorder (GAD) affects over 6.8 million American adults [10]. In 2008, Professor Susan Evans and colleagues of the Weill Cornell Medical College studied subjects diagnosed with GAD. The effects of mindfulness-based stress reduction (MBSR), an adapted meditation program for clinical psychological patients, were assessed on this GAD experimental group. In MBSR, patients meditate in an attempt to increase mindfulness, which is present-moment awareness. Increased mindfulness allows one to react to experience in a more skillful manner, reducing negative consequences. Eleven subjects completed the program and showed significant reductions in anxiety and depressive symptoms from baseline to the end of treatment. Although there were methodological flaws, including lacking a control group, the study gives future direction in possible meditation therapies for GAD populations [11].

A 2008 study conducted by Dr. Marijke Hansdete of Tilburg University in the Netherlands also addressed mental illness, in this case obsessive compulsive disorder (OCD). OCD is characterized by excessive intrusive thoughts and related compulsive behaviors. The participants in Tilburg’s study included eight subjects to participate in the meditation group, and nine in the wait-list control group [12]. The meditation training was a specific program modified for OCD patients, including emphasis on meditative breathing, body-scan and mindful daily living. The meditation group had a significant and large effect on mindfulness, OCD symptoms, letting go, and thought-action fusion. The author believes that this may be the first study indicating mindfulness intervention and decrease in OCD symptoms and that a study done with a larger clinical sample could help indicate that mindfulness training may be an alternative therapy for OCD.

Contemplative Science
The potential of meditation in clinical and basic scientific settings has just begun to be appreciated, and meditation research continues to grow. Using “meditation” as a query on the PubMed database results in the recovery of over 1,500 articles [13]. Meditation research labs are emerging at universities such as UC Davis, UC San Francisco, Harvard, Princeton, and Brown [14]. Contemplative science has potential not only in basic science, but also in clinical applications. In the words of the Dalai Lama,

Such collaborative study [between Buddhism and modern science] will contribute not only to greater human understanding of consciousness but also to a better understanding of the dynamics of the human mind and its relation to suffering. [12]

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References:

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The Rise of Cognitive Steroids: A Discussion on Fairness and the Need for Regulation

Theresa Lii

If you were offered a pill that would improve memory and concentration, would you take it? If the drug had no adverse side effects, then the discussion becomes an argument of fairness: would using the drug in order to outperform others be considered cheating? When Major League Baseball outfielder Barry Bonds broke the home run record, many critics suggested that an asterisk be placed next to the new record indicating that Bonds had taken performance-enhancing drugs. Would people suggest placing asterisks next to Nobel Prize winners’ names to indicate the use of drugs that enhance cognitive abilities? Although the fairness of using of cognition-enhancing drugs for nonmedical purposes is suspect, there is no doubt that use of these drugs is rising. To ensure that these drugs are safe for consumption, regulation must be implemented.

Off-Label Usage
Nootropics are drugs that enhance cognition, meaning the brain processes that underlie mental activity such as attention, perception, learning, memory, language, planning and decision-making [1]. For people who suffer from neurological and psychiatric disorders, nootropics can improve quality of life. However, according to a report by the Academy of Medical Sciences, non-prescription use of nootropics by healthy people is becoming increasingly widespread [1]. Off-label usage is particularly rampant in academic circles, where selective pressure for high performance is causing some to seek a competitive edge [2]. According to an informal survey conducted by Nature on its readers, one in five scientists and other professionals—out of 1,400 surveyed—admit to using drugs such as methylphenidates (Ritalin or Concerta), Modafinil (Provigil), and beta-blockers to improve their performance at work [3].

According to the Nature survey, the two most commonly used nootropics in academia are methylphenidates and Modafinil. These drugs were developed by pharmaceutical companies and certified by the FDA to treat symptoms of attention-deficit hyperactivity disorder and sleep disorders, respectively. Methylphenidates such as Ritalin are amphetamine-like drugs that improve attentiveness and focus; Modafinil is a popular drug reputed to offer similar benefits without the undesirable side effects, such as needing to make up for lost sleep in “sleep rebound” or developing tolerance for the drug [4]. According to several studies, Modafinil was shown to reduce fatigue while improving motivation, reaction time, and vigilance [5, 6]. These observed benefits translate to increased productivity and more time that can be spent in the laboratory or cramming for exams. While Modafinil is approved to treat narcolepsy and other sleep disorders, Cephalon—the pharmaceutical company that markets Modafinil—reports that as much as 90 percent of its sales come from people who are using it “off-label” to stay awake for long stretches of time [7].

But Is This Abuse?
Many people use Modafinil to enhance cognition and wakefulness, but is this a potentially harmful misuse of an otherwise beneficial drug? What remains unclear is the definition of “abuse” in this context. For example, caffeine has been shown to provide temporary improvements in vigilance, learning,
memory, and mood [8]. Caffeine is used worldwide to increase productivity because it staves off sleep. Despite the benefits that caffeine confers, most people would not equate caffeine with other performance enhancing drugs such as steroids.

As brain-boosting drugs become more sophisticated, however, when do we declare that a substance has entered the domain of cognitive steroids? Not surprisingly, there are already people in the sports industry who disapprove of wakefulness- and concentration-boosting drugs. In 2004, the World Anti-Doping Agency added Modafinil to its list of prohibited drugs [9]. If a sports watchdog organization deems Modafinil unethical in athletic settings, should it also be unethical in academic settings? Increased use of nootropics in general could raise the standard for “normal” academic performance and, as a result, lead to an “achievement gap” between those who can obtain these medications and those who cannot. Because so many cannot afford or access the drugs, using nootropics to gain a competitive advantage is an inherently unfair practice.

With increased use lies the possibility of developing a severe psychological dependence on these drugs. For example, students may begin to believe that the only way they can maximize their academic performance is by taking daily doses of a nootropic. They may become reluctant to stop taking the drug for fear of losing their perceived gain in intellectual function. Here, the use of cognitive enhancers poses not only an ethical problem but also a practical one. Using drugs to boost one’s productivity may prove useful in the short run, but if one becomes dependent on the drug, then both the financial burden of continual self-medication as well as the psychological dependence may not be worth the short-term gain.

Potential Effects on Society
Psychological dependence at the individual level can also lead to dependence at the societal level. In a pharmaceutical race to become the best and brightest, everyone may become pressured into consuming nootropics. Workers who see their colleagues taking nootropic pills may feel compelled to take these drugs so they do not lag behind in productivity. Parents may also feel that their children will be at a disadvantage if they are not taking cognition-enhancing drugs. Although the long-term effects of methylphenidates on children are not well-documented, many researchers agree that methylphenidates do have long-term consequences on normal-functioning brains [10, 11, 12]. Due to the possibility that nootropics can harm young and developing brains, protective measures should be taken to prevent the unnecessary medicating of children. According to an article by Mark Henderson, science editor of The Times, “more formal laws may be required to prevent coercive use of such drugs... by parents or teachers who want their children to perform better at school” [13]. But how the government should enforce such laws remains unclear.

Need for Regulation
While no student, physician, or scientist should require an exogenous substance for his or her mental creativity and performance on the job, there will undoubtedly be people who do use nootropics regularly to boost their cognitive function. Therefore, nootropics should be regulated like any other medicinal drug in order to lessen the likelihood of abuse and harm.

Currently, drugs are developed and labeled for a specific disorder, and non-prescription usage goes largely unchecked [14]. The current “wink and nod” acceptance of off-label usage...
by the general public is unwise, as it provides little opportunity to assess risks. Right now, “we simply do not know what the long-term effect of the use of such drugs in healthy populations will be,” a British Medical Association report concludes [15].

The risks are not limited to chemical toxicity; there may be secondary hazards associated with nootropics’ intended purpose. For example, drugs that increase wakefulness sap necessary hours of sleep from their users, leading to disorientation, impaired judgment, and increased risk-taking that result from prolonged insomnia [16]. Such drugs make users believe that they need less sleep, but in reality people still need seven to nine hours of sleep every day, as recommended by the National Sleep Foundation [17]. Despite the urgent need for testing and risk assessment, it is possible that regulation of nootropics may not be implemented until a sleep-deprivation-induced accident, whether behind the wheel or on the operating table, occurs. A much healthier approach would be to accept the fact that cognitive enhancers might one day be widely used, determine which age groups can safely use these drugs, carry out appropriate studies to thoroughly assess effects and side-effects, and then use these results to label drugs that are offered for public consumption. In short, nootropics should be explicitly labeled as cognition-enhancers and subject to rigorous testing like any other FDA-regulated drug.

Role of Pharmaceutical Companies

Of course, pharmaceutical companies have already picked up on the demand for nootropics. There are certainly potential profits in repackaging certain drugs so that they are marketed as cognition enhancers. However, before doing so, these companies must again go through testing to earn the FDA seal of approval. Many pharmaceutical companies are currently conducting research on the cognition-enhancing properties of drugs that are approved for other purposes.

Cephalon recently sponsored a study that assesses the memory-enhancing properties of its product Modafinil. Amy DiCamillo, who heads the Cephalon-sponsored study, presented a poster on this topic at the 2008 Society for Neuroscience annual meeting [18]. Her study specifically evaluated whether Modafinil improves short-term and working memory in rats.

In addition to recycling old drugs, pharmaceutical companies are also beginning to investigate and develop novel compounds that will enhance cognition. Abbott Laboratories sponsored an animal-based study on the effects of a novel H3 receptor agonist on learning and memory, and it will not be long before testing moves from animal studies to human-based clinical trials [19]. Eventually, drugs whose primary purpose is cognitive enhancement may be manufactured for public consumption.

From an ethical standpoint, the use of nootropics for gaining an academic advantage is inherently unfair. However, there will always be people who have no qualms about taking nootropics to get ahead. Because a market for these drugs exists, the same kind of FDA regulation that is applied to all other medications should be applied to nootropics as well. Regulation places responsibility on drug companies so that their products are rigorously tested to protect the public’s health. This way, nootropic usage can become mainstream in a safe and regulated manner. The development of cognition-enhancing pharmaceuticals is moving forward at an incredible pace—yet ethics still has to catch up and define the boundaries between “fair” and “unfair.” Despite the opposition to tampering with the brain in a way that confers unnecessary advantages, nootropics are here to stay.

References:

[21] https://cams.lfnl.gov/graphics/Fotolia_2948261_sm.jpg

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In August of 1982, a bold proposal was put forth by Dr. Leon M. Lederman, director of the Fermi National Accelerator Laboratory (Fermilab) in Chicago, Illinois. After fifteen years of operation, the particle accelerator at Fermilab had become worn down and was in need of expensive upgrades. A project to make another particle accelerator, ISABELLE, at the Brookhaven National Laboratory in New York, was dropped after three years of poor planning and designing. Dr. Lederman proposed to set aside both machines in favor of a larger and more powerful particle accelerator [1]. It would be a behemoth – a massive monster of a particle accelerator roaring underneath the Texan desert—and would have 20 times more energy than the existing accelerator at Fermilab.

A Dream Deferred
The purpose of the particle accelerator was simple: take two particles, smash them together with as much energy as possible, and observe the result. The energy of the particles’ collision would break them apart into smaller, constituent particles which are not seen under normal conditions. One such particle is the Higgs boson, or what Dr. Lederman famously called the “God Particle,” in the title of his 1993 book. This infinitesimal particle, hypothesized for decades under the Standard Model of quantum theory, is important because it gives all other particles their mass. The discovery and analysis of the Higgs Boson would teach physicists much about how and why objects have mass—a fundamental property of all matter in the universe. [3]. Because of its small size, only a strong-enough accelerator can generate the powerful collision needed to prove Higgs Boson’s existence.

To meet this goal, the Superconducting Super Collider (SSC) was approved for construction in 1987, after years of extensive review [1]. Nearing the end of a military nuclear arms race, the United States did not intend to lose the analogous academic race in experimental nuclear physics, in which it had long dominated. Once completed, the SSC would be the most crucial machine of modern physics, Texas would be home to the most groundbreaking...
experiments of the coming century, and America would stand at the pinnacle of the scientific world forever – or so it seemed.

The SSC project soon ran into difficulties. Congress had originally been told that the project would cost $4.4 billion; after six years and multiple design issues, the price tag had leapt to over $12 billion. Worse yet, international financial investment in the project dwindled as investors in Japan and Taiwan realized that they would be paying large sums of money and receiving little credit or practical use for the research. Europe, meanwhile, was preparing to rally behind its own project at the European Organization for Nuclear Research (CERN) and was not inclined to lend money to its rival across the Atlantic. Left with little support, the citizens of Texas were left to bear the burden of the SSC, which, at this point, was little more than an 87-kilometer-long hole in the ground. Public opinion turned against the scientists, funding dried up, and Congress finally voted to halt the project in 1993 [1].

The failure of the SSC taught the scientific community several lessons. First, research funding was limited, and businessmen and taxpayers alike preferred to fund projects that would lead to tangible and applicable results. Second, and more importantly, the experiment had grown too large and too sophisticated for even a country as large as the United States to conduct by itself. For further advances to be made in research – especially in particle physics – science would have to rise to the world stage. The SSC project was a solemn warning that, in the future, cooperation among the international community would be a necessity. The Higgs boson would have to wait for another day.

The Large Hadron Collider
In 1994, after a decade of scientific planning and prototype experiments, CERN approved the construction of the Large Hadron Collider (LHC), a massive, circular particle accelerator under the Franco-Swiss border, one of the largest scientific experiments in history. The global community looked, hopeful but also doubtful, upon the birth of the future of high-energy physics. Fresh from the collapse of the SSC, some American citizens, including a number of physicists, wondered whether the Higgs boson was really worth the effort. The Cold War had ended, and the immediate applicability of nuclear physics had diminished significantly in the public mindset. Princeton physicist William Happer lamented the prevailing attitude, saying that thousands of Americans were “doing nothing” in weapons factories, and that “high-energy physics labs suffered from a less severe form of the same disease” [4]. Calling the LHC “the last frontier of physics,” Happer argued for American financial and scientific involvement in the quest to verify the existence of the Higgs boson. “As a nation that has prided itself on attacking every frontier, I can’t believe we would back out of this,” Happer stated in 1994 [4]. Many physicists had similar opinions; drawn to the field of high-energy physics by the prospect of a fundamental breakthrough, they did not want to miss this exciting new opportunity, regardless of which side of the Atlantic it ultimately occurred.

But even if high-energy physics was worth the intellectual effort, would it be worth the huge financial sacrifices as well? Faced with limited finances, the Department of Energy would have to cut funding at American physics laboratories in order to contribute to the LHC, which, like its doomed predecessor, was looking more and more expensive as the project evolved [5]. As Harvard theorist Mitch Goldin said, the dilemma came down to “people's livelihood versus science. Something has to give somewhere” [4]. Money spent across the Atlantic instead of in American laboratories would result in the loss of domestic jobs, and many Americans couldn’t afford to be generous. Congressman Joe Barton, representing the would-have-been home of the SSC, swore to oppose the Department of Energy’s cooperation with CERN, complaining that CERN “didn’t help us, and they went out of their way to stop the SSC. I’ll be beep-beep-beeped if we send a dollar to Europe” [6].

However, CERN understood the dynamics of this debate in the United States, and it took steps to ensure a sense of open, international involvement in the LHC. Knowing that American physicists wanted to be a part of the project but were financially handicapped, CERN promised to accommodate as many as 400 U.S. physicists in return for financial help. “We can’t make it on our own resources,” admitted CERN’s director-general, Christopher Llewellyn Smith. However, he noted that the United States should receive a stake in the direction of the project in return for its resources, acknowledging that Americans “don’t want taxation without representation” [4].

With this openness, CERN shattered the national boundaries of scientific involvement that had so badly crippled the SSC. The United States, along with many other countries, soon announced its financial and scientific commitment to the LHC, and construction was slated to begin in 1998. The machine was completed ten years later in September, 2008. Equipped with the most sophisticated sensors ever built, supported by the most powerful supercomputer in the world, and spanning more than 26 kilometers in circumference underneath the Franco-Swiss border, the Large Hadron Collider was ready for its debut [7].

The Last Frontier… Or Is It?
At the time of this writing, the LHC had only just witnessed its inauguration ceremony on October 21, 2008. However, the machine sits dormant; a faulty electrical connection led to a helium leak on September 19 – only 9 days after a proton first accelerated to 99.9999991% the speed of light in the LHC tunnel. The influx of helium gas created pressure in the normally vacuum-like tunnel, damaging several magnets in one section. Because the machine...
is now undergoing extensive investigation, repairs, and precautionary maintenance, it will not resume operations until spring of 2009. For the next few months, and perhaps for the next few years, the world will have to continue holding its breath as it awaits the results of one of the greatest scientific collaborations in history [2].

With regards to the existence of the Higgs Boson, there are only two possible outcomes. If the Higgs boson does not exist, the Standard Model of quantum physics will be missing its final, fundamental piece. For many physicists, this would mean an anticlimactic return to the drawing board, perhaps to look more closely at alternative theories of how the universe works. Professor Stephen Hawking, a world-renowned theoretical physicist and best-selling author, believes that the “God Particle” will not be discovered. Hawking believes that “it will be much more exciting if we don’t find the Higgs. That will show something is wrong, and we need to think again” [8]. Even if the Higgs boson is never found, many experts agree that a machine as powerful as the LHC will reveal other surprises, offering us some direction regarding what to do next.

And what if the Higgs boson does exist and the LHC’s sensors detect it? What if the Standard Model is fully supported, and scientists gain crucial insight into the properties of fundamental particles? What happens next? Already, scientists are proposing plans for the even more powerful particle accelerator, the International Linear Collider, which may provide even more detailed results than the LHC [9]. Will countries spend billions of taxpayers’ money on it, too?

The answers to these questions are neither simple nor immediate. The struggles of modern physics are grand in scale and scope, and physicists strive to explain subjects as lofty and abstract as faraway astronomical anomalies, the fundamental properties of nature, and the beginning and end of the universe [10]. Some of these struggles are about to cross over into our observable world, inside the chamber of a gigantic particle accelerator, but it is not easy to see why they are relevant to our everyday lives. Indeed, some leading scientific figures have criticized the international focus on the LHC, arguing that the most immediate issues that are affecting our world – such as poverty, genie, and climate change – require urgent scientific attention. Days before the LHC’s first test run, Sir David King, former chief scientist of the United Kingdom, commented, “It’s all very well to demonstrate that we can land a craft on Mars; it’s all very well to discover whether or not there is a Higgs boson…but I would just suggest that we need to pull people towards, perhaps, the bigger challenges, where the outcome for our civilization is really crucial” [11]. In his opinion, the quest to validate the Higgs Boson is just that – a quest for glory.

But those who label the Large Hadron Collider as “science for science’s sake” have failed to see its greatest significance. This machine isn’t just a tool for physicists to test impractical or pointless theories. It isn’t just a thumbs-up or thumbs-down to a miniscule particle that most of us will never know existed. It is a tribute to the ingenuity of the human race—a symbol of what we can achieve with our intelligence, our curiosity, and our passion. Furthermore, the Large Hadron Collider represents what the world can accomplish through international cooperation, mutual investment, and shared responsibility. As Nobel laureate Frank Wilczek put it, the LHC is “modern civilization’s answer to the pyramids of Egypt, but better: a monument to curiosity, not superstition, whose scale reflects function, not vainglory” [12]. If we, as an international community, can visualize the infinitely small Higgs boson, is there a feat we cannot accomplish? If we can answer the fundamental questions of the universe, is there a problem that we cannot solve?

These questions are the most pivotal ones facing us as we step forward into the 21st century. Through the catalyst of the LHC, science has emerged on the international stage as an endeavor that is grander in scale and larger in importance than ever before. Like the physicists from around the world who have prepared history’s greatest physics experiment, we must face forward, join forces, and ready ourselves to tackle the problems confronting our world. Next spring, when the Large Hadron Collider comes to life once more, the last frontier in particle physics may very well be broken – but a new age of science will have only just arrived. Will we, as a world, be there to answer its call?

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References:

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Avastin: Questionable Hope During Desperate Times

Jane Yang

When a patient with advanced cancer faces a bleak prognosis, the “wonder drug” Avastin appears as a tantalizing promise for a longer life. Manufactured by Genentech, Avastin is a monoclonal antibody that combats cancer cells by disabling vascular endothelial growth factor, which, in turn, severs nutrient supplies to cancer cells. Praised for this combative mechanism, Avastin is one of the most popular cancer drugs worldwide [1]. But even during desperate times, is this drug a worthwhile investment?

Recently, Avastin has been criticized for its inability to extend patients’ lives, which is especially troublesome considering the costliness of the drug. Avastin failed its first trial against breast cancer and only slowed the growth of colorectal cancer when compared with current chemotherapy. Despite such drawbacks, patients desperate for the slim chance of survival are willing to give Avastin a chance. And so the dilemma presents itself: on the one hand, this cancer drug is a beacon of hope for patients who have no other options; however, these patients may also be pouring money into a treatment that can theoretically prolong life for a few months, if at all. Furthermore, the price of this drug is so high that some patients do not have the luxury of receiving treatment. In the case of Avastin, the controversial approval by the Food and Drug Administration, compounded with its costly charges and debatable advantages, creates a multitude of problems for the patients [1].

Avastin: Mechanism, Treatment, and Side Effects

Avastin, also known as bevacizumab, is a monoclonal antibody that is specifically designed to attack one target — vascular endothelial growth factor. By binding to vascular endothelial growth factors, Avastin inhibits the growth factors’ interaction with tyrosine kinase receptors found on the cell surface. This growth factor plays a key role in regulating angiogenesis, the physiological process of blood vessel growth. Research has shown that inhibiting angiogenesis may be an effective method to combat cancer, because it would separate nutrient and oxygen sources from cancer cells. In doing so, Avastin halts the growth of tumors and delays the worsening of cancer [2]. This mechanism would possibly extend the life span of patients.

Avastin first arrived on the market in 2004, fifteen years after its initial development. The FDA approved the drug for treatment of metastatic colorectal cancer when it was found to extend patient life by four months. In 2006, the drug was approved for lung cancer treatment, and was recently approved in February 2008 for treatment of breast cancer. Patients using this drug reported an improvement in the quality of life, such as alleviation of pain and exhaustion [1]. Avastin is able to enhance the beneficial effects of chemotherapy, but is not effective when used alone [1]. It also displays certain side effects that are particularly detrimental, such as blood clots, perforation of the colon, heart failure, and kidney damage. In rare instances, Avastin was shown to cause inflammation of the eye [3,4].

Testing for Efficacy

One research study demonstrated that there was little difference between patients who took the drug and those who only had chemotherapy and a placebo [1]. Furthermore, many studies proposed the use of Avastin with standard chemotherapy drugs, such as Taxol. In these dual drug prescription cases, the patient inevitably experiences the side effects of chemotherapy, an adverse reaction Avastin originally meant to avoid [1,5].

In its first clinical trial, Avastin failed to meet its goal of delaying the worsening of cancer [1]. Out of 363 female patients who received Avastin for treatment of breast cancer in another trial, five or six patients died from the drug itself [6]. In a phase III trial, 722 patients were treated with either paclitaxel, a chemotherapy drug, or Avastin with paclitaxel. The results from the trial showed that Avastin doubled median progression-free survival, the time during which the disease did not worsen, from 5.9 months to 11.8 months [7]. Dr. Ian Haines of Monash University in Melbourne, Australia, however, claims that progression free-survival was “an unreliable measure of benefit in metastatic cancer” [8]. Additionally, the overall survival time among patients who received Avastin with paclitaxel was similar compared to those who received paclitaxel alone. Results exhibited a statistically insignificant improvement of 1.5 months. In the same study, incidences of hypertension, proteinuria (excess of proteins in urine), and headaches were higher in patients who received Avastin with paclitaxel [7].

Expensive Promises

On top of its questionable efficacy, Avastin also wields a high price tag. As one of the most popular drugs in the world, Avastin accumulated $3.5 billion in sales worldwide in 2007. The extension of the drug’s use to breast cancer was predicted to help Genentech’s sales by $1 billion or more per year [6].

Using this drug can cost from $4000 to more than $9000 a month. Therefore, one patient spends roughly $100,000 a year — a high price tag considering only about five percent of patients benefit significantly from the drug [1]. The rising costs of cancer drugs in general have prompted some insurance companies to begin restructuring their tiered copayment policies, which assign a fixed amount for the patient to pay according
to the type of drug. Avastin, now considered a tier 4 drug for its high cost, will require “coinsurance.” Unlike copayments, coinsurance charges a percentage, usually 20 to 33% of the cost [10]. Therefore, a patient can pay up to $20,000 a year in order to sustain treatment. Genentech justified these costs as years of costly research, testing, and approval processes—all amounting to the “high side of the industry average” [1].

Compared to other cancer drugs that attack a tumor’s blood supply, Avastin is second highest in cost behind Bristol-Meyers’ Erbitux, which costs $9,600 per month. Unlike most other cancer drugs that target one cancer type, Avastin is approved for three types of cancer, which broadens its influence in the drug market [9].

**FDA’s Role Leads to Bigger Question**

In 2008, the U.S. Food and Drug Administration approved Avastin for advanced breast cancer against the advise of its panel experts [1]. Some factors the FDA considers for efficacy of cancer drugs are survival, quality of life, tumor response, and time until treatment failure, with survival and quality of life as the primary parameters. Even though the requirement of survival is inconsistent among different classes of drugs, survival is the main concern of metastatic cancer patients [11]. The vote against approval of the drug by the FDA’s advisors was a slim 5-4 margin in December 2007. Based on data from clinical trials, the panel of experts, comprised of oncologists and patient representatives, was not convinced of Avastin’s ability to improve the patient’s quality of life or prolong their lifespan. Trials also demonstrated the toxic effects of the drug [6].

The FDA ultimately overruled their advisors’ decision, because Avastin reduced tumor volume and increased progression free-survival [6]. From their standpoint, the drug’s ability to hamper disease progression overshadowed its toxicity. These two opposing opinions raise issues that plague guidelines for approving cancer drugs: what should determine the efficacy of a cancer drug—its ability to prolong life, or its ability to delay the worsening of cancer? In a clash between a federal agency and its advisory committee, whose opinions should dominate? [1]. While some experts like Dr. Haine believe progression free-survival is an unreliable indicator, supporters of the drug believe that the goal of the drug is to “maximize disease control and quality of life, thereby, sparing patients for as long as possible from symptoms of progressive breast cancer … and the psychological burden and uncertainty that come with progression” [8].

The case of Avastin epitomizes the ambiguities surrounding the cancer drug approval process. Although increased survival is the main criterion for approval of a drug, the FDA based its decision on a drug’s ability to control disease. This form of measurement for efficacy is still debatable among experts. For the past four years, Avastin demonstrated its staying power in the cancer drug market. Currently, Avastin is studied as a potential treatment for eye diseases and even brain cancer, one of the most formidable cancers [12,13]. However, if an expensive drug delays disease progression but does not extend life, it may not be as cost-effective as manufacturers, regulators, or patients have hoped. 

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Mirror Neurons: Potential Answers or Empty Promises?

Laura Felley

It was a discovery that stunned neurologists and psychologists alike, one so rich with exciting implications that it quickly made its way into popular media. In the early 1990s, researchers at the University of Parma discovered a new type of neuron in several regions of the Macaque monkey brain. These cells fired when the monkey used its hands in a goal-oriented manner: grasping for food, peeling a banana, or cracking open a peanut. Such neuronal behavior was fascinating, but not unexpected. These neurons, however, were not solely activated in response to this self-initiated motion—they produced the same firing pattern when the monkey observed another monkey conducting the same goal-oriented action. Furthermore, these neurons were highly specific. In many cases, only observation of an action identical to the one performed by the monkey caused the neuron to fire [1]. The study was well-supported by empirical evidence, as the researchers were able to locate individual neurons in a region of the premotor cortex (F5) and part of the inferior parietal lobule (PF).

The possibilities for the function of such cells seemed limitless; they became a sort of miracle neuron, capable of anything. Many scientists, abandoning the reservations that typically accompany such startlingly new discoveries, have come to ascribe a huge number of higher-order functions to mirror neurons, from physical imitation to language learning to the development of theory of mind, the knowledge that enables us to recognize the differences in mental perspectives between ourselves and others. As one journalist notes, the discovery of the mirror neuron “shifted the way psychologists discuss the brain.” [2] Perhaps as a result of this momentum, seemingly few paused and asked the fundamental question: Does the evidence suffice? This question, though basic, is essential, as mirror neurons have never been found in humans, and concrete mechanisms for their hypothesized role in higher-order functions have not yet been established. A more sober review of the relevant research, in conjunction with a consideration of the pitfalls inherent to neurological research in humans, will shed light on the current position of the mirror neuron, hopefully clarifying the true significance of their discovery.

When first discovered, researchers postulated two roles for mirror neurons in monkeys: they might serve as the basis of both imitation and action comprehension [1]. Imitation may seem like a simple cognitive skill, but in reality it is quite complex. With the exception of birds’ ability to imitate songs, a distinct phenomenon, only primates have been found to exhibit imitation [3]. Studies in Macaque monkeys have shown that mirror neurons may give them the ability to determine intentionality in actions, as well as the ability to code the likely future actions of others, enabling the prediction of behavior. In a review of the components of imitation and imitative learning, Iacoboni hypothesizes that these two skills may form the basis of imitation [4]. The second proposed function of mirror neurons, action comprehension, may explain a puzzling symptom seen a small number of stroke patients. Individuals who suffer a stroke in the right hemisphere and experience paralysis of the left side of the body are aware of their condition, and are able to talk about it appropriately. However, 5% of those who suffer a stroke will vehemently deny any paralysis, even though they are completely coherent and lucid in all other areas. This condition, known as anosognia, is not limited to a misrepresentation when seeing other stroke sufferers of anosognia will vehemently deny that anything is wrong with them! It has been hypothesized that this interesting problem may be a result of damaged mirror neurons in humans. If mirror neurons form the basis of action comprehension, it is possible that they serve as a sort of “virtual reality” system; every time an individual wishes to analyze the action (or lack of action) of another, he must run a “virtual reality simulation” in order to study the information in terms his own repertoire of actions. Without functional mirror neurons, a stroke patient might be rendered unable to interpret the meaning of both his own actions and the actions of another [5].

Mirror neurons in monkeys are easy to study due to the more invasive techniques permitted in animal research. The existence of mirror neurons in uniquely human abilities is more difficult to verify. Some studies have indicated that regions of the human brain that correspond to the F5 and PF
regions of the Macaque brain show consistent patterns of activation when subjects are asked both to observe and to perform a particular action [6]. As a result, scientists have set forth a huge number of hypotheses regarding the role of mirror neurons in human-specific skills. Some believe mirror neurons to be essential in the production of language, claiming that mirror neurons are the missing link needed to close the gap between “doing” and “communicating” [7]. Others believe mirror neurons to be essential in the development of empathy, sympathy, or a theory of mind [8]. Given these theoretical functions of mirror neurons, some researchers have begun to consider the possibility that autism, a disorder typified by impaired language skills, reduced empathy, and problems in theory of mind, is perhaps affected or even caused by a failure of mirror neuron systems. One study examined activity in the human analog of F5, an area of the Macaque prefrontal motor cortex found to contain mirror neurons. Autistic and normally-developing children were shown pictures of facial expressions, and were either told to imitate the expression or merely observe it. Although regions in the brain dedicated to face attention were equally active in both groups, indicating that all subjects were paying equal attention to the stimulus, autistic children showed significantly less activity in this purported mirror region than normal children. Furthermore, more robust activity in this region in autistic children was inversely coordinated with the severity of symptoms [6]. Thus, some researchers have taken this preliminary evidence as an indication of the existence of mirror neuron regions in humans, as well as the suggestion of the function of mirror-neurons in critical social functions.

However, methodological problems abound in these studies. While investigation of animal neural systems is extremely regulated and finely localized, the less-invasive nature of techniques designed to investigate human neurobiology necessarily makes them more difficult to control. Although the researchers in the autism facial expression study did control as best they could for attention to the stimulus, a reader is left with unanswered questions. For example, how did they ensure that the autistic subjects, many of whom have behavioral problems, behaved appropriately and as expected in the MRI machine [6]? Undergoing an MRI is a difficult experience for normal subjects—hundreds of trials must be completed and averaged in order to produce usable results. The pragmatic challenges of this study must have been huge, and may have affected the results. More generally, Dr. Jean Decety, a psychologist studying the neurology of empathy and empathic disorders, cautions against hasty experimental designs, pointing out that “many functional neuroimaging studies that pretend to report “mirror-neuron” activation do not have the appropriate conditions to say that” [8]. Many of these studies lack a motor performance condition, a characteristic necessary in order to study purported mirror neurons. Such design flaws result in “much speculation grounded on little evidence”, and facilitate inappropriate leaps in logic. Thus, some researchers have come to consider activation of Broca’s area, a region of the brain necessary for speech production, to be evidence of mirror neurons, simply because the region is thought to be homologous to one of the areas in the monkey brain containing mirror neurons [8].

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In fact, such conclusions may be erroneous not only as a function of their logical flaws; new evidence has indicated that one of the “mirror regions” in the human brain does not actually show the pattern of activation expected of a mirror neuron region. The aIPS region of the human brain is roughly analogous to one of the Macaque brain regions proven to contain mirror neurons. Human subjects were placed in an MRI machine and asked to play a game of rock-paper-scissors, a task that involves the observation and the execution of the same physical motion. The aIPS was activated during both the execution and observation trials, but it was found that there were distinct patterns of activation in the aIPS that differed based on whether the subject was observing or executing an action. The researchers offer two possible explanations for these results: the aIPS may contain subpopulations of both motor and visual neurons, or it may contain a new class of “promiscuous” visuomotor neurons that respond to one observed movement and one executed movement [9].

One must also consider the fact that, of the evidence available so far, the functions of mirror neurons may be far less impressive than predicted. In the study of patients with anosognosia, which Ramachandran regards as potentially caused by mirror neuron deficits, no deficits in empathy or theory of mind are reported [5]. Furthermore, monkeys, which do possess mirror neurons, are not skilled imitators, and there is insufficient evidence to indicate that mirror neurons play a role in imitative learning [4]. Such problems may eventually be clarified by further research, but the existence of these doubts serves as a reminder of the danger of over-enthusiastic speculation. However, to suggest that mirror neurons may be involved in language learning may be a step too far, even in terms of speculation. Even if mirror neurons provide an acceptable representation for both sounds and meanings, they do not seem to be able to form a basis for the “central, essential structural relation in human language”—the arbitrary relationship between the signified concept and the signified sound. There is nothing in their function that indicates that they would play a role in sign-learning [7]. Some researchers have even expressed doubt that mirror neurons truly reflect an innate neuronal capacity for dual representation; mirror neurons can be activated by something as trivial as the sound of a peanut cracking, indicating perhaps that the mirror neuron response is learned [7]. A simple experiment might clarify this point. Strong headphones and auditory limitation might be used to teach a monkey to associate another sound with the opening of a peanut; neurologists could then check to determine whether the mirror neuron response changes accordingly [7].

Mirror neurons hold much promise for neurologists and psychologists alike, but excitement inspired by the potential of these cells should never eclipse the need to design and interpret experiments with meticulousness and caution. Many researchers take the existence of mirror neurons for granted, assuming they exist in humans simply because they exist in other primates, but such a tendency is misleading and supremely unhelpful. Careful studies on both primates and humans must be conducted in the future in order to establish the function and limitations of mirror neurons.

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References:
[5] Ramachandran, VS. 2000 “Mirror neurons and imitation learning as the driving force behind “the great leap forward” in human evolution.”
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