MANIPULATING THE MIND: THE ETHICS OF COGNITIVE ENHANCEMENT

BY

KELLY R DAIGLE

A Thesis Submitted to the Graduate Faculty of

WAKE FOREST UNIVERSITY GRADUATE SCHOOL OF ARTS AND SCIENCES

in Partial Fulfillment of the Requirements

for the Degree of

MASTER OF ARTS

Bioethics

December 2010

Winston-Salem, North Carolina

Approved By:

Nancy M. P. King, J.D., Advisor

Dwayne W. Godwin, Ph.D., Chair

Ana S. Iltis, Ph.D.

TABLE OF CONTENTS

Page

ABSTRACT

Kelly R Daigle

MANIPULATING THE MIND: THE ETHICS OF COGNITIVE ENHANCEMENT

Thesis under the direction of Nancy King, J.D., Professor in the Bioethics Program, Department of Social Sciences and Health Policy Faculty Member.

Cognitive enhancement involves the use of any natural or artificial intervention to improve cognitive functions—memory, learning, attention, focus, wakefulness, and so on—in normal individuals. Although many interventions including education and the use of computers can be called cognitive enhancers, it is the more unconventional means of cognitive enhancement that tends to be the center of ethical debate. These more unconventional methods include pharmacological, mechanical and genetic interventions. There are numerous arguments for and against cognitive enhancements in general that fall into the four principles of bioethics—respect for autonomy, beneficence, nonmaleficence, and justice. In addition to the ethical considerations that overlap between the three methods of achieving cognitive enhancement, each method also poses unique ethical issues that fall into the same principles.

This thesis includes an analysis of both the broad ethical considerations surrounding cognitive enhancement in general and the method-specific ethical considerations. The purpose of this discussion is to integrate the current state of research with an analysis of the current ethical debate to determine the moral permissibility of cognitive enhancements. Ultimately, I conclude that the balance of the ethical debate is in favor of allowing the use of cognitive enhancements as a matter of personal choice.

CHAPTER I

AN INTRODUCTION TO ENHANCING HUMAN COGNITION

Introduction

"That the administration of drugs would have any great impact on bodybuilding competition or enhance America's international lifting prestige occurred to no one at first".[1] However, not only did the administration of drugs provide a competitive edge to bodybuilders, but also to athletes competing in almost every other sport. Performance enhancement in sports—also known as doping—has existed as far back as ancient times, with the use of special diets and various concoctions thought to give athletes an advantage. Today, the methods of enhancing athletic performance have evolved to include the use of such things as anabolic steroids, stimulants, growth hormones, blood doping, and gene doping. With this evolution, however, also came the development of international standards and regulation of such enhancement via the establishment of the World Anti-Doping Agency (WADA) in 1999. WADA seeks to preserve what is "intrinsically valuable" about sporting and, as such, is responsible for publishing both an anti-doping code and a prohibited list of substances and techniques.[2,3]

While athletic enhancement has been explored in-depth on many levels, it is not the only area in which humans seek to enhance themselves. Brain function, particularly cognitive brain function, is one such area. Similar to athletic performance enhancement, cognitive enhancement in itself is not a new phenomenon. In ancient Greece, for example, students would entwine rosemary sprigs in their hair in an attempt to improve concentration and memory during exams.[4] However, unlike athletic performance

enhancement, cognitive enhancement has not been as thoroughly explored in scientific, medical, social, ethical or public policy discourse—and much of the discussion that does exist is incomplete and wrought with problematic assumptions. Most of the current discussion is also poorly balanced; in particular, the primarily scientific literature is often short on ethical discussion and, likewise, the ethical literature is often short on scientific discussion.

Although still in its relative infancy when compared to the extensive methods available in athletic performance enhancement, cognitive enhancement is rapidly progressing as science, medicine, and technology improve. Whereas athletic enhancement is confined to a relatively limited arena—specifically that of sports—cognitive enhancement has a much farther reach, with potential effects in everything from academics to the workplace to even the smallest activities in everyday life. It is precisely the rapid growth and far-reaching implications that gives rise to ethical concerns surrounding cognitive enhancement, and hence, why cognitive enhancement deserves a more thorough discussion than has taken place.

In the coming pages of this thesis, I intend to add to this necessary discussion by first defining enhancement and then taking a critical look at the current state of the cognitive enhancement debate. Then, in the subsequent chapters, I will focus on the various methodologies of cognitive enhancement in an effort to both contribute to the ethical debate and open a much-needed dialogue about cognitive enhancement between the scientists and clinicians advancing the research and the ethicists and philosophers advancing the moral discussion.

Defining Cognitive Enhancement

The central component of the mammalian nervous system is the brain. The brain is ultimately responsible for monitoring, regulating, and controlling the body's actions, reactions, and overall functioning. Breathing, heart rate, hunger, movement, sleep, emotion, and cognitive processes, for example, are among the many biological aspects that fall under the control and regulation of the brain. It is the cognitive processes of the brain, however, that are relevant to this discussion of enhancement.

In the broadest sense, cognition refers to the activity of the brain that creates what we commonly consider to be the mind.[5] Cognition involves the conscious and unconscious complex functions of the human brain. Cognition, in the simplest terms, refers to what we generally recognize as thinking, reasoning, remembering, associating, learning, wakefulness, and attentiveness. However, cognition also includes what is known as executive function, which encompasses higher-order processes such as planning, abstract thinking and problem solving, initiating appropriate actions, inhibiting inappropriate actions, and selecting relevant sensory information.[6,7] Mental activities such as self-awareness, mental imagery, and language usage and comprehension are also included when referring to cognition.

Cognitive enhancement, then, refers to the use of any intervention directed at improving any of these aspects. The definition of "improvement" in this context is relative; it can refer to whatever a normal individual deems to be better than his or her current state—be it quicker recall, sustained focus, more efficient thinking, and the like. The means by which this improvement is achieved can be natural or artificial. Cognitive enhancements can range from "conventional" means, such as education, mental

techniques like mnemonic tricks, and external technological devices like smartphones, to less "conventional" means such as drugs, implants, and genetic manipulations.[8] Although a discussion of cognitive enhancement will encompass all of these means, it is the latter, less conventional methods that are more controversial and likely to provoke moral concerns.

Cognitive enhancement can be achieved via three main methods—genetic, mechanical and pharmacological. Genetic cognitive enhancement occurs when genes involved in any of the cognitive processes are manipulated. For example, Dr. Joe Tsien at Princeton University genetically modified mice to produce more N-methyl-D-aspartate (NMDA) receptors, which are critical for the formation and maintenance of memories; these mice were able to learn faster then their unmodified counterparts.[9,10] Mechanical cognitive enhancement involves the integration of technology and the brain. This technology includes neuroprostheses such as cochlear implants and hippocampal memory mediation chips, internal direct brain interfaces such as deep brain stimulation, and external direct brain interfaces such as electroencephalogram (EEG) electrode arrays.[11] Pharmacological cognitive enhancement involves the use of drugs and chemicals to improve cognitive function. Stimulants such as Adderall, Ritalin, and Provigil that are currently prescribed largely for the treatment of various mental disorders can also improve concentration, focus, and wakefulness. Ampakines, compounds that stabilize α-amino-3-hydroxyl-5-methyl-4-isoxazole-propionate (AMPA) glutamate receptors, are among the drugs currently being developed without a disease in mind, but rather for the improvement of long-term memory in otherwise healthy adults.[12,13]

It is these three methodologies—pharmacological, genetic, and mechanical—that will compose the bulk of discussion in the coming chapters of this thesis. However, it is first important to discuss a few distinctions that exist when talking about cognitive enhancement.

Distinctions in the Cognitive Enhancement Debate

Enhancement versus Therapy

One possible distinction that arises in enhancing cognition involves the line between therapy and enhancement. Traditionally, medicine (or therapy) has sought to prevent, diagnose, treat and cure disease or injury, to reduce suffering, to reassure the "worried well", and to educate patients.[14] Preventing, treating, and curing a variety of pathologies such as diabetes, cancer, and pneumonia are goals at the forefront of therapy. Enhancement, on the other hand, aims to make a person better than well. Improvement is the goal when dealing with enhancement. Essentially, therapy aims to fix what is wrong, whereas enhancement aims to improve upon the norm.

This distinction is not an easy one, necessarily, to make. Many interventions sit at the borderline between therapy and enhancement and could arguably fall on either side of the distinction. What about vaccinations, for example? A vaccine is technically an immune enhancement since there is no pathology present; however, a vaccine does prevent a possible pathology from occurring.[15] What about prosthetic limbs? On one hand, these limbs serve to compensate for loss due to an injury. On the other hand, there are cases where such prosthetics may not only serve to replace a limb, but may also give the person using the prosthetic an advantage such as the ability to run faster or, at the

very least, a limb that does not fatigue. Yet another example is the administration of growth hormone. Take, for example, two boys, both of whom are predicted to grow into "abnormally" short adults; one boy is short due to a brain tumor suppressing the production of growth hormone and the other is short merely because both his parents are.[16] While both suffer from the same problem—short stature—only one is likely to be considered sick. Giving growth hormone to the boy with the tumor would probably be considered therapy well within the realm of traditional medicine. However, giving growth hormone to the boy who is short because of the luck of the genetic lottery would in all likelihood be considered enhancement.

The line between therapy and enhancement is blurry, creating a large gray area where the distinction between what can reasonably be called therapy and what can reasonably be called enhancement is almost non-existent. It is because of this vast gray area that I contend that this distinction is not a necessary one for the purposes of this discussion. Based on the definition I previously provided of cognitive enhancement, these interventions will likely range from therapy to enhancement. So, while the therapy versus enhancement distinction may be relevant in later stages of the debate when considering the appropriate place and ensuing policies for the use of various cognitive enhancements, the distinction between therapy and enhancement serves to neither promote nor deter cognitive enhancements in general.

Instrumental Value versus Intrinsic Value

Another possible distinction that exists within the cognitive enhancement debate lies in the type of value these enhancements possess. Cognitive enhancements, in theory,

could either be instrumentally valuable or intrinsically valuable to those who make use of such enhancements. Something is said to have instrumental value when it confers an advantage or provides a means of achieving or obtaining something more valuable. For example, a million dollars has instrumental value, since money serves mostly as a means of obtaining something else of value to the possessor. Intrinsic value, on the other hand, refers to something being valuable in and of itself, not merely as means of acquiring something more valuable. Happiness can be said to have intrinsic value, since being happy is thought to be good on its own.

However cognitive enhancement is achieved, cognitive enhancements do have an intrinsic value. This is because cognitive functions themselves are not purely instrumental; these are intrinsically valuable to the individual irrespective of whether or not such functions lead to something more valuable. Cognitive functions are good in and of themselves. For example, having a creative mind or the ability to sustain focus is valuable in itself, whether or not others possess similar capabilities.[17] Therefore, any enhancement or improvement to these cognitive functions should have similar intrinsic value to the possessor. Despite this intrinsic value, some individuals or groups may use cognitive enhancements solely for the instrumental value these enhancements possess. For example, students may learn better and retain more information through the use of cognitive enhancements. While this alone is intrinsically valuable, some students may endeavor to use such enhancements solely to get better grades in their courses.

Admittedly, then, cognitive enhancements possess both an intrinsic value and an instrumental value. It is the latter value that has the potential to be problematic. However, the mere fact that cognitive enhancements possess an instrumental value does

not alone preclude moral permissibility. Many things have instrumental value. Money, as previously mentioned, is one example. However, even education—a regularly accepted form of cognitive enhancement—can be considered to have instrumental value, as it is regularly used as a means of obtaining something more valuable, usually a higher paying job; furthermore, highly educated individuals often have an advantage over others with less education. Simply having instrumental value says nothing about whether something should be considered acceptable.

There are two potential problems that arise with instrumental value. One problem arises when the instrumental value of cognitive enhancements comes from these enhancements being positional goods—that is, goods that are only valuable if no one else has them. The second problem arises if cognitive enhancements possess an instrumental value and not everyone can get access to them. Such unequal access can lead to unfair advantages for some individuals over others. While the distinction in value is an important one to recognize, the problems that arise with such a distinction—that cognitive enhancements may confer unfair advantages to individuals choosing to use such enhancements—is one of justice, which I will come back to at several points in later discussion.

Decisions for Others versus Decisions for Oneself

One final, yet crucial, distinction is between making decisions for oneself and deciding for another individual. While the typical adult may be capable of autonomously choosing to undergo a particular intervention, others may lack the autonomy to make an informed decision. These individuals lacking the decision-making capacity may include

children, future generations, the cognitively disabled, and the incarcerated. A young child, for example, is generally thought to lack the ability to decide what is best for him or her in many contexts, including medical situations. Generally, a parent or guardian is endowed with the responsibility to make such decisions on the child's behalf. Likewise, a person can be appointed to make decisions for a cognitively disabled person or the government can take responsibility for deciding on behalf of a prisoner. Parents are also able to make decisions about future generations—prospective offspring and so on—in mate selection or via available interventions such as in vitro fertilization, pre-implantation genetic diagnosis, sperm sorting, birth control, or even abortion.

While deciding for oneself can create ethical dilemmas in itself, proxy decision-making can become even more ethically problematic, particularly when dealing with controversial interventions or practices. The decision to enhance cognition is not immune from the many ethical issues that arise in either case, whether deciding for oneself or deciding for others. In general, much of the coming discussion is applicable to both situations; however, I will attempt to address this distinction where notable departures in commonality arise in the discussion.

The Current State of Debate

It is important to note that, despite methodological differences in achieving cognitive enhancement, many of the ethical and policy arguments made are intended to be applicable regardless of how cognitive enhancement is accomplished—whether pharmacologically, genetically, or mechanically. Instead, the pro and con arguments are

typically blanketing arguments aimed at encouraging or discouraging all forms of cognitive enhancement.

In 1977, Tom Beauchamp and James Childress published the first edition of their classic text, *Principles of Biomedical Ethics*, setting forth their principle-based approach to biomedical ethics.[18] Today the text is in its sixth edition and the principle-based approach is now widely used to examine ethical problems. Respect for autonomy, beneficence, nonmaleficence, and justice are the four principles they describe and apply.[18] It is these four principles that underlie the majority of the current arguments both for and against cognitive enhancement. Here, I will lay out many of these arguments using the four principles, and will show why none of these arguments are alone sufficient to dictate the moral status of cognitive enhancement.

Arguments Based in Autonomy

Autonomy refers to an individual's ability to self-govern. To respect this autonomy is to acknowledge and facilitate an individual's right to hold views, to make choices, and to take actions based on that individual's personal values and beliefs.[18(pg 103)] Essentially, a person should be free to make his or her own decisions. Autonomy, therefore, rests upon the individual's both possessing the capacity for intentional action and being free from controlling interferences—such as influence from others and limitations such as inadequate information.[18(pg 99-100)] It is this principle of autonomy that underlies at least part of the debate surrounding cognitive enhancement.

One salient argument in favor of enhancing cognition lies in the freedom of individual choice. In general, people have a right to pursue happiness and, as such, they

have a right to control their own means of doing so.[19] Many individuals believe that if people are given adequate information about beneficial effects and possible unwanted side effects, they should be free to weigh those and make their own decisions.[20] If a person is well-informed as to the potential risks and benefits, then the decision to enhance cognition or not enhance cognition rests solely with him or her.

While this argument is particularly powerful within the highly individualistic society in which we currently live, it is not enough by itself to justify the use of cognitive enhancements. While individual freedoms are important, any civil liberty must be appropriately balanced against safeguarding the public good.[20] Personal choice does not alone make something ethically, socially, or legally permissible. A person can decide to murder another individual, but the fact that it was a free, well-informed choice does not make a murder ethically, socially, or legally permissible. We institute policies and laws and we punish individuals for breaking these policies and laws, all in an effort to restrict, or at least dissuade, individuals from exercising their personal freedom in such a way that may harm others.

Arguments against cognitive enhancement express fear that coercion will become common practice and that individual autonomy will be threatened. The fear is that "explicit coercion might be seen with classes of individuals who might be expected to take certain medications or use other cognitive enhancers for the greater good," such as would be the case in the military setting.[12] One could also imagine that the standards of the workplace might be raised to reflect new abilities that workers acquire through the use of cognitive enhancement.[19] Could an employer require an individual to enhance? Explicit coercion is not the only fear. Widespread use of cognitive enhancers may

unduly influence others into taking them just to keep up with peers.[21] Even if employers, for example, didn't require enhancement, competing against enhanced colleagues might in itself act as an incentive to enhance oneself.[20] The pressures of undue influence are more complicated than explicit coercion, and in many cases can be more forceful. As already noted in the world of athletics, for example, the pressure to take advantage of even slight improvements—for example via the use of steroids—is enough for athletes to risk side effects, disqualification, and public sanctions. In a winner take all environment, slight incremental advantages can have disproportionate consequences.[12] The difference, for example, between a 38 and a 32 on the MCAT can be the difference between going and not going to medical school.

Issues with coercion and infringements upon autonomy are valid concerns, but do not in and of themselves preclude the use of cognitive enhancement. The pressure to enhance will probably be no greater than similar societal pressures that already exist. As one commentator notes, "it's not as though we don't all face competitive pressures anyway—to get into and graduate from good universities, to constantly upgrade skills, to buy better computers and more productive software, whatever."[9] We wouldn't ban any of these pressures merely to prevent individuals from feeling coercion. In fact, "placing constraints on people's actions so as to protect others from feelings of coercion is arguably no less an attack on personal freedom."[21]

Furthermore, by definition, cognitive enhancers affect brain chemistry. Unlike enhancement technologies that alter physical appearance or abilities, cognitive enhancement can directly alter personality and an individual's character traits.[22] Similarly, any intervention aimed at affecting the brain has the potential to alter an

individual's moral agency—his or her ability to make moral judgments and take actions based on those moral judgments. This has the potential to directly manipulate a person's autonomy, potentially causing that person to make decisions in a manner that he or she otherwise would not. "Neuroenhancement drugs may alter cognition, emotion, and personality, and could potentially alter the decision-making capacity of autonomous individuals who must decide whether the benefits outweigh the risks of continuing to take the drug."[14] For example, many drugs of abuse alter the motivational hierarchy causing an individual to behave in ways he or she otherwise would not; drug-seeking behaviors can develop and can seem quite rational to the person exhibiting the behaviors. Cognitive enhancements may result in similar behavioral changes.

While cognitive enhancement does directly affect brain chemistry, it does not follow that every form of cognitive enhancement will affect autonomy nor does it follow that cognitive enhancements that do affect autonomy are inherently bad or wrong. Individuals using cognitive enhancements may very well make different choices in general and possess an altered moral agency than they would otherwise without such enhancements. While negative changes are a distinct possibility, positive changes in autonomous decision-making and moral agency may be equally as likely. It is quite possible that cognitive enhancements may enhance one's decision-making ability, causing one to make better decisions. Likewise, a person's moral agency may also be enhanced, leading to clearer moral perceptions and better moral judgments and actions. Furthermore, it is unlikely that cognitive enhancement will render an individual completely incapable of making competent decisions; even if this does occur, as is the case with drugs of abuse, a proper physician-patient relationship can help mitigate this

concern. Altering brain chemistry is the desired effect of cognitive enhancement and the individual should be able to make his or her own judgment call as to whether the benefits and risks are appropriate.

Arguments Based in Nonmaleficence

The principle of nonmaleficence imposes the obligation not to inflict harm on others.[18(pg 149)] Like the principle of respect for autonomy, the principle of nonmaleficence plays a role in a portion of the cognitive enhancement debate.

The most obvious concern falling under the purview of the principle of nonmaleficence is that of safety. Unlike interventions that exist to cure and treat disease, cognitive enhancements are meant to improve upon the "normal" human condition. The question becomes whether any risks are tolerable when the alternative is normality.[12] "The pendulum swings…when considering the administration of drugs to healthy individuals; greater benefits and/or diminishing risks are required to ensure that any intervention, even in the informed individual, remains justified."[20] Particularly salient is the fact that using any drug brings with it the risk of physical bodily harm; common sense dictates that any drug powerful enough to alter behavior is powerful enough to do serious damage.[23] No intervention is without potential side effects, even when used or applied as directed. Aside from its abuse potential, Ritalin may aggravate mental illness, produce sleep disturbances, and is associated with cerebrovascular complications.[21] Among Adderall's side effects are elevated blood pressure, restlessness, dizziness, insomnia, euphoria, dryness of mouth, diarrhea, constipation, and impotence.[24] Other forms of cognitive enhancement are not without safety concern. The genetically altered mice that

express more NMDA receptors—while they show improved memory and learning—also possess a greater ability to recall aversive events.[21] In fact, the greatest potential negative effect may not be physical discomfort, but rather subtle and undesirable mental changes.[22] While being able to instantly recall all sorts of information might be considered as a truly rewarding benefit, enhancing memory may also lead to the recalling of memories better left unremembered—a traumatic event, for example. A better memory could also be debilitating if it keeps one from focusing on the important issues in life.[19] This could prove harmful to the human mental state; perhaps some things are meant to be forgotten as a way of protecting ourselves.

With respect to safety, the concerns are very much valid. The safety of people using cognitive enhancement is paramount, especially when dealing with methods powerful enough to modify brain chemistry and alter behaviors. However, many of the cognitive enhancing drugs have few or no side-effects. Furthermore, long-term effects of any intervention are rarely known in advance. To that extent, even education is a risky enhancement. While education can enhance cognitive abilities, education can "create fanatics, dogmatics, sophistic arguers, skilled rationalizers, cynical manipulators, and indoctrinated, prejudiced, confused, or selfishly calculating minds."[17] One can't predict what effect education will have upon one's personality or identity any more so than one can predict what effect other cognitive enhancers will have. Furthermore, many people already pursue risky and often invasive interventions that have no therapeutic value; cosmetic surgery, for example, is a relatively common enhancement practice with numerous safety concerns. In any case, further research is clearly needed to determine the long-term effects of cognitive enhancement in humans; this could readily be achieved

via clinical trials using healthy volunteers. We will never know our limits until we test them out. Therefore, the issue of questionable safety alone does not serve to discourage cognitive enhancement, but instead only gives reason to continue slowly and cautiously forward in its current and expanded application.

Beyond the basic concerns of safety, there are concerns about doing harm to human character. This argument holds that, essentially, struggling is a necessary part of being human and, more importantly, it builds character. Humans are defined by both their limitations and their attributes; by reducing or eliminating shortcomings, cognitive enhancements fundamentally alter the essence of what it means to be an individual.[22] The concern is that "unnatural interventions that ease the acquisition and retention of skill and knowledge undermine good character. Improving without working is cheating, and cheating cheapens us all."[20] Cognitive enhancement is thought to be somehow cheating—popping a pill, for example, is too easy; forgoing the hard work to reach an end forces a person to miss out on building character. The idea is that "struggling in some situations and experiencing distress and failure are quintessential aspects of the human experience … [and] these experiences give rise to desirable personal attributes."[12] Traits, such as the dignity that comes with hard work, may be undermined by enhancements that reduce the need for effort.[22]

This argument, like the ones before it, is not very strong by itself. If struggling is vital to humanity, then the struggling that comes with disease should not be problematic. However, we regularly endeavor to eliminate such struggling when we attempt to treat illness. It can be argued that popping a pill to overcome a disease undermines the potential for building character that struggling with the disease could offer. However, we

allow struggling to be circumvented in this case. It is highly problematic to claim that one form of struggling is superior to another. It can also be argued that cognitive enhancement doesn't undermine good character, no more than does making use of any other tool humans have invented: "Cars, computers, and washing machines have tremendously enhanced our ability to deal with formerly formidable tasks. That doesn't mean life's struggles have disappeared—just that we can now tackle new ones."[9] Despite the numerous tools developed in an effort to simplify life, there will always be plenty of hurdles and hardships for humans to overcome. Cognitive enhancement is not a solution for all of life's problems; rather, it is a tool to improve how we handle those problems.

Arguments from Beneficence

"Morality requires not only that we treat persons autonomously and refrain from harming them, but also that we contribute to their welfare."[18(pg 197)] This contribution to other's welfare is the principle of beneficence. Beneficence, broadly defined, includes all forms of action intended to benefit others.[18(pg 197)] Despite the threat of potential harms, there is also the obvious effect of cognitive enhancements benefiting both individuals and society; therefore the principle of beneficence, just like the previously discussed principles, also underlies a part of the cognitive enhancement debate.

With the use of cognitive enhancements, society has the potential to benefit from more (and more profound) individual contributions that can add to overall productivity.[9] Cognitive enhancements can help individuals excel where they otherwise may not have. For example, maybe there will be an individual who makes use of cognitive enhancement to improve his or her learning in science who then goes on to discover a cure for cancer.

This is probably an extreme example, and it is much more likely that the gains achieved via cognitive enhancement will be marginal at best, at least with the current technologies available. However, as Nick Bostrom notes, "there are approximately 10 million scientists in the world; if you could improve their cognition by 1%, the gain would hardly be noticeable in a single individual, but it could be equivalent to instantly creating 100,000 new scientists."[25] Cognitive enhancements have the potential to improve life for those who take advantage of them, as well as for society in general.

This argument, while appealing, is still insufficient. While cognitive enhancement can provide benefit on both an individual and a societal level, this does not, in and of itself, make the use of cognitive enhancers ethically acceptable. The use of steroids in athletics, for example, benefits the players by giving them a competitive edge in the sport; there is also a benefit to fans, giving more of a spectacle for their viewing pleasure. However, the use of performance enhancers, such as steroids, in sports is still looked down upon and fairly heavily regulated. Not only do people tend to disagree about what constitutes benefit, but also any perceived benefit must be weighed against potential harms, such as the negative health effects of steroids on the individual. While there may be a benefit to both those that are cognitively enhanced and to the society in which they reside, just as in the area of performance enhancement, it does not follow that cognitive enhancements should be allowed. Other factors must still be considered and balanced with these benefits prior to accepting cognitive enhancements as morally and socially permissible.

Arguments from Justice

The fourth and final principle upon which much of the cognitive enhancement debate rests is the principle of justice. Justice is the fair, equitable, and appropriate treatment given what is due or owed to a person or persons.[18(pg 241)] One particular type of justice, distributive justice, is of particular relevance in the cognitive enhancement debate. Distributive justice refers to the distribution of benefits and burdens, rights and responsibilities, among members within society.

One fear of cognitive enhancement is that it will further the inequality that is already prevalent in our society. Essentially, there exists the threat that cognitive enhancements will increase the gap between haves and have-nots. The fear is that if cognitive enhancers are not fairly distributed—that is, made available to all who want them—only the rich will gain the advantage.[20] The wealthy will be able to avail themselves of designer drugs, for example, and the poor will be confined to coffee and cigarettes.[12] The idea of cognitive enhancements furthering inequalities also comes back to the idea that cognitive enhancements have an instrumental value such that those who enhance cognition will gain a more valuable end—better grades, better job prospects, and so on. There may arise a time where the gap between the enhanced and the un-enhanced may become too wide to bridge, "making the latter into dinosaurs in a hypercompetitive world."[15] The availability of cognitive enhancers will accentuate disparities that exist in society.

This argument, however, is more sensibly located within the entire economic system, rather than within the cognitive enhancement debate.[26] In general, certain inequalities—social, economic, genetic—already exist in our society and are generally

well-tolerated and even accepted. Biologically, there are already disparities insomuch as there already are groups of people who are genetically rich, comparable to others. This disparity occurred through the genetic lottery, not medical intervention. It should be noted that "a sizeable proportion of one's academic successes [may be] due to the genes with which one has been naturally endowed. Moreover, resources that influence academic performance are also unevenly distributed across social classes."[21] Computer access, private tutors, and even proper nutrition vary greatly across social class. It is arguably a lot easier for people to take pills than to pay for tutors and tennis lessons.[9] Just because a service is not available to all does not automatically mean that it is unfairly distributed, nor does it mean that cognitive enhancements should be prohibited. The society in which we live "is full of inequality already and it may be no more grounds for prohibiting access to enhancement then it is for other forms of cognitive assistance, such as continuing education."[20] Every high school student cannot afford to attend Stanford University and yet Stanford still exists.

Another somewhat similar concern involves the infliction of social conformity and the subsequent loss of diversity that follows from unequal access. The idea is that cognitive enhancement threatens to harm individuality. While focusing on children, the President's Council on Bioethics (PCBE) argue that a behavior-modifying agent gives teachers, parents, and doctors the ability to intervene directly with a child's brain chemistry and that doing so raises questions about the measure of liberty afforded to children.[23] The utilization of these drugs limits many of the characteristics of the child that may set him or her apart from other children; that is, adults are coercing children into social conformity. These drugs have the ability to stifle the diversity among children,

crafting conformity by promoting a limited range of appropriate behavior. According to the PCBE, making children conform "diminishes our openness to the diversity of human temperament."[23] Michael Sandel, a prominent critic of enhancement, fears that altering children represents "a kind of hyperagency—a Promethean aspiration to remake nature, including human nature, to serve our purposes and satisfy our desires."[27] Like Sandel, the PCBE argues that altering children via stimulant drugs remakes the very nature of childhood to serve social purposes—improving behavior and promoting compliance at home and in the classroom. Beyond childhood and into adulthood, dissenters argue that cognitive enhancers would promote "more of the same."[28] Essentially, widespread use would create population homogeneity and loss of diversity.

The weakness in this argument is that there are non-pharmacological practices already in use to try to enforce conformity. Using cognitive enhancement serves as a direct way to do what is already indirectly being done. For example, getting a tutor and taking Ritalin can both be used to increase attentiveness in class. While there are differences in the methods, both means can achieve a similar desired result. Both means can also have unwanted side effects. For example, a person could become dependent upon Ritalin for doing well on exams; a person could just as easily become dependent upon the tutor's assistance in getting homework done. It is admittedly true that side effects between the two methods are quite different. Using a tutor has no likelihood of causing the physical harms that Ritalin might. Using Ritalin will likely not cause the embarrassment or social awkwardness of relying upon someone else for help. In either case, the set of side effects an individual is willing to accept becomes a personal choice, not necessarily a reason to permit or prohibit either method.

With regard to loss of diversity, people of all ages regularly conform to social norms. People want to be popular and "fit in" and this is generally not looked down upon. In spite of this desire to fit in, there is still great diversity. Each person is still unique, having his or her own personality independent of behavioral modification. To say that cognitive enhancement will lead to population homogeneity makes the faulty assumption that everyone seeks the exact same thing. There is no universal idea of what is good. What one person sees as ideal does not necessarily fit with another person's ideal. One person may want to score a 40 on his or her MCAT, while another may just want to remember where he or she put the car keys. "More likely, society will consist of a continuum of differently modified people, ranging from the unenhanced, through those who have undergone a small amount of enhancement, to those who have undergone major enhancement."[29] Improvement can be a common goal without resulting in loss of diversity.

Summary

While there are many principle-based arguments put forth both for and against all forms of cognitive enhancement, none of these arguments are strong enough to provide a solid case for either side of the debate. Each argument is insufficient alone and cannot independently serve to deter or justify the use of cognitive enhancement. In the coming chapters, I will attempt to provide both an overview of the current research into each method of cognitive enhancement, as well as a critical analysis of method-specific ethical issues. Each of these methodology-specific chapters is intended for publication as perspective articles in scientific journals, such as Nature Reviews Neuroscience. I

ultimately contend that it is the balance of the arguments and issues taken together that leads to the conclusion that all forms of cognitive enhancement—pharmacological, genetic, and mechanical—are morally permissible. Essentially, there is no good reason at present to disallow the use of cognitive enhancements as a matter of personal choice.

CHAPTER II

ENHANCING COGNITION VIA GENETICS

Introduction

In a simple one page journal article published in 1953, Watson and Crick hypothesized a novel, and as we now know accurate, structure for DNA.[30] Exactly fifty years later, in 2003, the full sequence of human DNA was unveiled with the completion of the human genome project. It is now known that the human genome contains between 20000-25000 genes, with over 50% of these genes having unknown functionality.[31] Much research has been done already and much more is currently underway to refine our knowledge of human genetics. This refinement includes determining both the function of each individual gene and also the extent of their interaction with each other and the environment to create human phenotypes.

The vast majority of the research into genetics has been in an attempt to understand the roles of genes both in the normal condition such as in development and also in pathological states of disease and disorder. Genetic abnormalities, including single gene mutations and chromosomal anomalies, have already been shown to cause or play a major role in many cognitive disorders and deficits. Fragile X Syndrome, the most common form of inherited mental impairment, is known to be caused by a mutation in the FMR1 gene located on the X chromosome.[32] Alzheimer's disease, the most common form of dementia, has been found to be associated with abnormalities in any of several genes, including the APP gene on chromosome 21, the Presenilin1 on chromosome 14 and Presenilin2 on chromosome 1. [33] It has been predicted that cognitive impairments

afflict at least one in 20 people worldwide.[34] It is no surprise then that genetics research has largely focused on alleviating specific disorders such as Fragile X Syndrome, Alzheimer's disease, and many others.

However, some research has, perhaps incidentally, also focused on enhancing various aspects of human cognition. Research into the mechanisms of learning and memory, for example, has resulted in numerous recent publications indicating some potential for enhancement of these areas. In a recent review article, Lee and Silva compiled a list of over 30 genes in mice that if manipulated result in observable increases in learning and memory performance.[34] With research rapidly advancing, the question is no longer if cognitive enhancement via genetic manipulation is possible, but rather when it will become possible in humans.

It is at this point—during the early research and prior to any form of application—that the ethics of such discoveries and such progress should be considered. Genetic manipulation, with potential applications ranging from cloning to engineering to therapies for many disorders, has had its fair share of ethical debate. In 1996, the birth of Dolly the sheep, the first mammal to be cloned from an adult cell, fueled the ethical controversy surrounding cloning.[35] In 1999, the ethical debate surrounding gene therapy exploded when a clinical trial ended with the death of a participant named Jesse Gelsinger, a teenager suffering from a rare metabolic disorder called orinthine transcarbamylase deficiency.[36] The idea of genetic cognitive enhancement, like these other areas of genetic manipulation, is also spawning its own ethical debate and the issues brought up in this debate merit consideration early on in the research and development process.

The purpose of the coming discussion is to both briefly summarize the current state of research into genetic cognitive enhancement and to shed an important light on the ethical issues that can arise if such research evolves into practical application in humans. It is imperative that scientists carefully consider not only these ethical concerns, but also any new ones yet to arise, when continuing the research into the genetics of cognition, particularly when such discoveries can be used for enhancement purposes. Despite the need to keep the ethical issues in mind, I ultimately contend that genetic cognitive enhancement is morally permissible.

The Current State of Research

Transgenic and knock-out (KO) studies in animals have revealed a surprisingly large number of mutations that seem to enhance cognitive function.[34] These mutations target a wide range of signaling pathways and, hence, also affect a wide range of cognitive functions. Genes involved in neurotrophism, histaminergic signaling, adenosine receptor signaling, reactive oxygen species formation, calcium homeostasis, kinase and phosphatase activity, and NMDA receptor signaling, among a plethora of others, all have significant potential for use in enhancing cognition.

Glial cell line-derived neurotrophic factor (GDNF) is known to be important in the development and maintenance of neural tissues and has been implicated specifically in the survival of dopaminergic neurons of the midbrain.[37] These midbrain dopaminergic neurons are separated into functionally distinct subgroups called the substantia nigra compacta, which regulate motor function, and the ventral tegmental area, which are known to be involved in emotional behavior and mechanisms of natural motivation and

reward.[38] Dr. Kordower and colleagues at Rush University has found that injecting lentivirus containing GDNF in nonhuman primates prevented degeneration and induced regeneration of neurons in the substantia nigra, leading to reversed functional deficits in monkeys with Parkinson's disease.[39] The Nestler lab has shown that infusion of GDNF into the ventral tegmental area blocks certain biochemical adaptations to chronic cocaine or morphine as well as the rewarding effects of cocaine.[40] While research such as this is directed solely at treating or curing a specific illness—in this case Parkinson's disease and drug addiction—discoveries involving neuronal regeneration do have practical implications for cognitive enhancement in the normal aging brain where at least some degeneration occurs naturally. In addition, learning, memory and drug addiction share certain intracellular signaling cascades.[41] Hence, studies involving GDNF in the ventral tegmental area also have similar implications for improving cognition.

Other research has more direct implications. Brain-derived neurotrophic factor (BDNF) is a neurotrophin similar to GDNF that has been implicated in the differentiation and survival of neurons and, more recently, has also emerged as an important regulator of synaptogenesis, the making of new synapses, and synaptic plasticity, the modification of existing synapses, as mechanisms underlying learning and memory in the adult central nervous system.[42] By selectively deleting BDNF from the forebrain of mice using the Cre site-specific DNA recombinase, researchers at the University of Colorado at Boulder were able to study the requirements for BDNF in behaviors such as learning and anxiety and they found that an absence of forebrain BDNF does not disrupt acoustic sensory processing or alter baseline anxiety, but does severely impair some specific forms of learning.[43] Furthermore, the Yanamoto lab at Osaka University found that increased

levels of BDNF in the brain enhanced spatial learning and memory function in genetically engineered transgenic BDNF over-expressing mice.[44] These results strongly suggest not only a role for BDNF in normal learning, but also a potential mechanism of cognitive enhancement.

The N-methyl-D-aspartate (NMDA) receptor is a particular type of glutamate receptor that is unique in that these receptors require the binding of two separate ligands, glycine and glutamate, and are normally blocked by extracellular magnesium ions making their activation voltage-dependent. Once activated via ligand binding and neuronal depolarization, the magnesium block is relieved and NMDA receptors conduct positive ions, most notably of which are calcium ions. Calcium is an important cellular messenger. Thus, calcium influx into the neuron establishes the distinctive nature of the NMDA receptor as being an important molecular switch for synaptic plasticity and, in turn, learning and memory.[45] Dr. Joe Tsien at Princeton University genetically modified mice to produce more of these NMDA receptors; these mice were able to learn faster then their unmodified counterparts.[9] According to Tsien, these results suggest that genetic enhancement of mental and cognitive attributes such as intelligence and memory in mammals is feasible.[10]

Ethical Concerns Surrounding Genetic Cognitive Enhancement

Manipulating our genetic material, first and foremost, implies permanency. The idea of altering the very basic material that makes us who we are is a frightening one. There is a fear that in undertaking such alterations, we will become something that is no longer distinguishable as human. In attempting such enhancement, humans want nothing

less than to liberate the human race from its biological constraints; humans aspire to steal their "biological destiny from evolution's blind process of random variation and adaptation and move to the next stage as a species."[46] People from various perspectives believe that any interference with the randomness of nature is inherently wrong and question our right to toy with the product of years of natural selection.[47]

Perhaps the evolution of humans has occurred in such a way—with particular cognitive limitations—for a reason. While the mice engineered to contain more NMDA receptors show improvements in learning and memory, as previously mentioned, a debate has ensued as to whether these mice also feel more pain. While Tsien and colleagues contend that these mice are just better at remembering whether an experience is pleasant or not, results from the Zhuo lab suggest that genetic manipulation of forebrain NMDA receptors could enhance persistent behavioral responses to tissue injury, as demonstrated by an enhanced response to injections of two inflammatory stimuli.[48] Therefore, a genetic manipulation conferring enhanced cognitive abilities may also lead to unintended consequences, such as increased susceptibility to persistent pain. Although results at this stage are debatable, a valid point still exists—limitations on cognitive abilities may, in fact, be a protective measure.

Toying with nature and our limitations is not the only concern. From the perspective of religion, there is the belief that to intervene in such fundamental biological processes is "playing God" or attempting to place humans above God.[47] Considering our talents and powers to be wholly our own doing is to misunderstand our place in creation and to confuse our role with that of God.[27] Manipulating our genetic material is not for us to do, as it is not our place to go above our maker to craft such integral changes to

humanity. Not only are we overstepping religiously imposed boundaries between the mortal and the divine, but we are also critically shifting responsibility for our destiny from God to science. According to Michael Sandel, one of the blessings of seeing ourselves as creatures of nature, God, or fortune is that we are not wholly responsible for the way we are.[27] In taking over the genetic reigns, we are asserting that we are responsible for who we are and what we will become, a responsibility only a deity should possess. While important to consider, the concept of "playing God" relies upon one particular view about the existence and will of God; concerns grounded in religion cannot work in a secular, religiously pluralistic society.

A final, yet crucial, area of concern involves germ line manipulations and genetic changes in children. A central concern for adult genetic cognitive enhancements is whether the benefit of extraneous enhancement outweighs potential risks of the intervention. This concern runs deeper when dealing with children and future generations. It is almost always presumed that parents have the best interest of their children in mind; this is an assumption that is heavily relied upon in many areas, especially the medical setting where decisions about the treatment of a child are usually made by the parents. But can this same consent by proxy for children and future children be enough, or even be allowed, for genetic cognitive enhancements where there is no pathology and the alternative is relative normalcy? Germ line manipulations can extend indefinitely into the future and there in lies a major ethical problem: an endeavor into germ line manipulation would be tantamount to a clinical experiment on unconsenting subjects, which are the affected members of future generations.[49]

It is not uncommon today for parents to impose their dreams and desires upon their children—private tutors to get children into great schools, music lessons to shape children into award-winning musicians, sports practices to develop the next Olympic superstar, and so on. Whether one considers this practice problematic in itself, the issue does heighten when discussing changes that are both irreversible and affect countless future individuals. Since germ line alterations are meant to impose permanent changes upon the genetic material, any qualitative alterations to the phenotype that result from germ line changes may prove to be highly desirable or undesirable to future persons depending on the adaptive value of the resulting traits in unknown future environments.[50]

The Moral Permissibility of Genetic Cognitive Enhancement

Humans have a long history of using our knowledge and tools to overcome problems and ultimately simplify our lives. In the realm of therapeutic interventions, humans have spent countless resources on identifying causes of, and subsequent treatments or cures for, nearly every medical problem afflicting humans. The cumulative knowledge we have gained from genetics is a valuable tool in this regard. Genes involved in a number of disorders have been identified and some are already being targeted for potential intervention. Just as it has been, and will continue to be, a valuable tool in developing medical interventions, our genetic wisdom can also be a valuable means of enhancing cognitive abilities.

We already use our knowledge and technologies we have developed from our knowledge to enhance ourselves. From the small to the dramatic, humans can alter pretty much any trait deemed undesirable. We can dye our hair practically any color we

choose. We can change our eye color with contact lenses. We can alter nearly every aspect of our bodies with restrictive diets, liposuction, and cosmetic surgeries. We can run marathons or lift cars with proper physical training. We can enter into psychotherapy, or pop a pill, to alter personality traits.

Genetic cognitive enhancement is a more direct means of achieving and furthering what we already do to enhance ourselves. For example, a gene encoding a particular dopamine receptor could be inserted into the brain directly to enhance attentiveness, yielding effects similar to those seen with Ritalin use. This genetic manipulation would simply provide a more deliberate and permanent means of altering brain chemistry. Genetic cognitive enhancement is just another tool that that we can employ—one that serves to further what it means to be human.

Even in applying genetic cognitive enhancement as just another tool in our toolbox, it is important also to remember that the genetic machinery is not without flaws. Even with genetic cognitive enhancement, mutations will still occur, which makes our own changes no more significant than the current genetic lottery. If new alleles were introduced by gene transfer, the impact on the species would be negligible; in any case, there is no certainty that genetically enhanced individuals would have greater biological fitness, as measured by reproductive success.[47] Even in the case of germline manipulations, it is unlikely that any such changes will affect the gene pool, or eventually, the human species as a whole.

While we may exert more control over particular traits, there will still be those traits that will be beyond our control. The shear complexity of the interactions that occur between and among numerous genes puts some manipulations well out of our reach.

Beyond what goes on in the genome, we must not overlook the role of the environment. Even genetic manipulations to cognitive traits that we are able to undertake have the potential to be ineffectual given environmental conditions. Environmental enrichment has been shown to lead to smarter children; hence, the presence or absence of such a factor could very well have an impact on any genetic change that is made. Even if it does not, we must still consider individual variation. An individual, for example, can undergo a genetic manipulation conferring the ability to learn faster, but that doesn't necessitate that the individual will have the motivation to learn.

Summary and Conclusions

Enhancing human cognition via genetic manipulation is rapidly becoming a very real possibility. A number of genes have already been identified as having a role in cognitive processes, such as learning and memory. However, just as is the case with other types of genetic manipulation—cloning, gene therapies, and so on—employing genetic manipulation to enhance cognition leads to many ethical concerns. The inherent wrongness of toying with evolution, playing God, and decisions about manipulating the genetics of others are among the many concerns. Despite these concerns, genetic cognitive enhancement is a logical progression in our use of tools, and is morally permissible.

CHAPTER III

ENHANCING COGNITION VIA MECHANICAL MEANS

Introduction

The use of implants dates back at least to the ancient Egyptian practice of hammering sea shells into the jaw to replace missing teeth; however, it was only in the twentieth century that a wide selection of implanted devices were introduced in surgical treatment, from pacemakers to intraocular lenses, from artificial hip joints to cochlear implants.[51] Today the technology has expanded so that there are at least three million people worldwide living with artificial implants.[52] These implants span almost the entire human body. One of the most interesting areas of artificial implantation, however, involves the brain. Correspondingly so, research into brain technologies has received a lot of attention.

Various forms of technology have already played an enormous role in nearly aspect of human life. Calculators allow us to do complex math problems with ease. Computers have made handwritten documents nearly obsolete. These technologies have also had an impact on human cognition—changing how we approach tasks and solve problems. Likewise, research into mechanical interventions, such as neuroprosthetics and direct brain-computer interfaces, has the potential to do the same—to have a significant impact on human cognition. While the current research is largely focused on therapeutic interventions, various mechanical brain interventions also hold great promise for enhancing cognitive abilities, not only in states of impairment but also in healthy individuals.

In light of such promise, many ethical concerns arise, each of which merit consideration by researchers. In the coming discussion, I will briefly summarize the current research into mechanical interventions such as neuroprosthetics, internal direct brain interfaces, and external direct brain interfaces. In addition, I will layout a few potential cognitive enhancement applications of this research. I will also consider some of the specific ethical issues that arise with such research and potential application. However, I ultimately will contend that, despite ethical concerns, mechanical cognitive enhancement is morally permissible.

The Current State of Research

Neuroprostheses are devices that contain sensors and/or actuators, implanted in or communicating with the brain, to replace neural and sensory function.[11] The most common examples include cochlear implants, intended to correct hearing impairments, and retinal implants, intended to correct vision impairments.

Internal direct brain interfaces, like neuroprostheses, are implanted in the brain and connect directly with biological neural structures, but do not replace neural function.[11] Deep brain stimulation (DBS) is one form that is already widely accepted as a therapeutic intervention. Tens of thousands of patients already have DBS implants, mostly for the treatment of involuntary movement disorders.[53] In addition to movement disorders, DBS has also been tested for other applications, including a range of psychiatric disorders. Studies have shown that DBS, in five different target regions including the nucleus accumbens and the subcallosal cingulated gyrus, is a promising treatment for major depressive disorder.[54] DBS in the nucleus accumbens has also been

shown to be an effective treatment for obsessive-compulsive disorder.[55] In addition, DBS has been suggested for use in a number of other disorders including epilepsy, Tourette's syndrome and obesity.[56,57]

Although the exact mechanism of DBS is not well understood, the safety and side effects have been relatively well studied. In a study of 522 surgical procedures for DBS implant in the subthalamic nucleus, the incidence of adverse effects was observed, including surgical complications in 5.6% of patients, medical delayed adverse events in 1.4% of patients, infections in 5.6% of patients resulting in the removal of the hardware 3.6% of the time, and hardware-adverse events in 7% of patients.[58] A separate study conducted by Burdick and colleagues found that subthalamic nucleus and globus pallidus internus DBS for Parkinson's disease were associated with significantly higher anger scores following DBS as compared to ventralis intermedius thalamic nucleus DBS for essential tremor.[59] Yet another study looked at a cohort of patients eight years post-DBS implant and found that DBS of the subthalamic nucleus is a safe procedure with regard to cognitive and behavioral morbidity, with no significant increase in side effects over the long term.[60]

External direct brain interfaces rely on sensing electrical activity associated with nerve impulses through the skin.[11] Electroencephalogram (EEG) and electrocorticograph (ECOG) are examples of two of the forms currently being studied. EEG relies on electrode arrays mounted on the scalp to sense brain activity. ECOG, on the other hand, is a more invasive technique, where the electrodes are instead placed directly on the surface of the brain rather than on the scalp. A study by McFarland and colleagues showed that humans can learn over a series of training sessions to use EEG for three-

dimensional control.[61] Equally promising results have been shown in ECOG studies. While previous invasive brain-computer interface research in humans has used signals exclusively from the motor cortex to control a computer cursor or prosthetic device, one recent study has shown that ECOG signals from electrodes both overlying and outside the language cortex, in patients with epilepsy, can reliably control a visual keyboard to generate language output without voice or limb movements.[62] Using both technologies, subjects can be trained to modify normal brain activity to provide a signal that can be captured and turned into a computer command.[11]

Potential Research Applications

At present, the vast majority of research into mechanical interventions has focused on treating pathologies. However, as previously mentioned, these mechanical interventions possess potential beyond illness. While neuroprosthetics are aimed at replacing lost function, they may also have the potential to replace even normal function. Vision could be "corrected" beyond the standard twenty-twenty norm with retinal implants. Honey bees are spectrally sensitive to ultraviolet light. Perhaps human eyesight could be supplemented in such a way to have the same ability. Similarly, normal human hearing ranges could be expanded using cochlear implants. It may even become possible to implant a computer chip to restore the memory of a person with amnesia or Alzheimer's disease. If that is the case, it may likewise be possible to supplement one's memory using the same technology. Just as we store seemingly endless information on our computer harddrives, we may also be able to have an endless memory with computer chip implants.

Direct brain interfaces, both internal and external, offer the same potential. External interfaces, for example, could allow humans to interact via robots. In fact, Sergey Brin, the co-founder of Google, recently became part man and part machine; while the real Mr. Brin sat miles away at a computer capable of remotely steering a robot—one consisting of a printer-size base with wheels attached to a boxy, head-height screen glowing with an image of Mr. Brin's face—the robot version of Mr. Brin rolled around talking with various individuals.[63] Internal interfaces could also allow humans to interact in new ways. At the University of Reading in England, Dr. Kevin Warwick instigated a series of pioneering experiments involving the surgical implantation of a device into the nerves of his left arm in order to link his nervous system directly to a computer; Dr. Warwick was also successful with the first extra-sensory input for a human and with the first purely electronic communication experiment between the nervous systems of two humans.[64] Such technology has incredible potential, including the obvious possibility that individuals could communicate with one another using only thoughts.

As previously mentioned, DBS, another internal direct brain interface, is already being studied for an ever-growing range of both motor and psychiatric disorders. However, DBS has also been shown to work in stimulating the reward pathways of the brain.[65] This technology could also serve as a cognitive enhancement if used to enforce particular behaviors, such as increased focus or improved attention.

Ethical Concerns in Mechanical Cognitive Enhancement

Modifying the brain and its powers has the potential to alter both the self-concept of the user and our understanding of what it means to be human.[52] It is the latter alteration that seems to immediately generate a negative gut reaction. The concept of the cyborg indicates that something is the matter, that boundaries are transgressed, familiar categorizations challenged, creating unease and uncertainty.[66] The blending of man and machine is itself an unsettling concept for many; turning humans into cybernetic creations opens up a new realm of evolution. Rejection of wiring brains directly to a computer stems from a desire for bodily integrity, and intuitions about the sanctity of the body.[52] With such a vast array of potential applications, a single individual could feasibly replace his or her entire brain. The concern is truly that we will rapidly evolve into something no longer recognizable as humans.

Furthermore, with technology incorporated directly into our brains, there exists the possibility of not only having endless information coming in, but also of having endless information transmitted out. The implantation of a technical device opens up the possibility of data exchange.[67] Privacy, then, becomes a concern. GPS tracking of neural implants may allow an individual's every move to be followed. If the potential for "cyberthink"—invisible communication with others via neural implants—becomes a reality, private thoughts may become public knowledge.[52] Just as cellular phones, computers and wireless networks can be hacked, the technology implanted into our brains may have the same pitfall, but possibly even more dangerous. It is scary enough that with the current technology our social security numbers, bank account and credit card numbers, and so on can be accessed and stolen by complete strangers with a few

malignant keystrokes. It becomes even scarier when we consider that our brains could be hacked in much the same manner; our identities, all the way down to our most intimate thoughts, could potentially be stolen.

In addition to privacy concerns, there are also concerns about mind control. The idea of two-way data exchange opens up the possibility of monitoring and manipulation in both directions; not only should we be concerned with the privacy of information coming from our brains but also with the manipulation of signals to the brain.[67] Bolstered by mass media and sci-fi, is the fear that neural implants can lead to intrusive, and notably uninvited, manipulation of the human mind, including things such as altering actions, thoughts and even perceptions of reality. Arguably, the most frightening implication of this technology is the grave possibility that it would facilitate totalitarian control of humans.[52]

Issues in individual responsibility may also arise. Mechanical failure in the devices we develop and use is not unusual. If the wearer of a neural implant carries out a particular action, it might be possible that he or she is not responsible in the complete sense, perhaps in the case of an implant failing to function according to its specifications.[67] A nerve signal could be misinterpreted by an implant, leading to an action that causes harm to others. It is unrealistic to expect complete freedom from error and interpretations that have to be 100% correct.[68] The issue is who to hold responsible when harm results from a failure of technology within the brain. If a person commits murder, for example, as a result of a signal misinterpretation, is that person responsible? Or does it become an unfortunate side effect of new technology, just as fatal car accidents have become an acceptable side effect of increased car use?

Not only can responsibility be questioned in the case of technical failure, but it can also be questioned because the technology may unpredictably alter an individual's personality.[68] Such technology may alter a range of mental states critical to thought, personality and behavior and this can disrupt the integrity and continuity of the psychological properties that constitute the self and one's experience of persisting through time as the same person.[69] An otherwise nice person could become manic, depressed, or even violent, for example. Just as with the case of pure mechanical failure, if harm results from altered personality, who is to blame?

Some believe that a person can take responsibility for his future behavior by taking certain actions.[66] If a person chooses to undergo mechanical cognitive enhancement, he or she accepts the risk of possible mechanical failure or unpredictable personality change; therefore, the individual also accepts responsibility for outcomes of those risks. However, there are already precedents for dealing with liability when biology and technology fail to work; increasing knowledge of human genetics, for example, led to attempts to reject criminal responsibility that were based on the belief that genes predetermine actions.[70] There is the distinct possibility that in the midst of using cognitive enhancing technology, similar legal precedent may arise when someone exclaims: "my implant made me do it!"

The Moral Permissibility of Mechanical Cognitive Enhancement

Cognitive enhancement by mechanical means is a logical next step in our ever-growing use of tools. As one commentator noted, brain–machine interfaces represent a highly sophisticated case of tool use, but they are still just that.[70] We already thrive via

the use of the newest technological advances. Technology today has made it possible to put the entire wealth of human knowledge at our fingertips via computers, smart phones, and the internet. Need to know the capital of Botswana? In a couple clicks, the knowledge is yours. Students have traded tedious long division for the instantaneous results provided by calculators and massive encyclopedias for the simplicity of the internet. Handwriting letters has become an antiquated practice, rapidly falling behind advances in technology such as email, video conferencing and text messaging. It can easily be argued that such technology has greatly improved our lives.

Mechanically enhancing our cognition comes down to a matter of internal versus external implementation of such technology. Is there a difference between having the knowledge at your fingertips and having it conveniently in your head? We can store endless knowledge on our computers for easy access—why not store this on a chip implanted in the brain for easier access?

Some do argue that there is a distinction to be made between internal and external modifications—that there is a crucial difference between using a computer and having one integrated into oneself. Fritz Allhoff and others, for instance, claim that this distinction is significant in that utilizing internal methods has the potential to evolve our personal identity.[15] However, this distinction is difficult to defend. This is because everything that a person does affects the chemistry of the brain. For example, a teacher rewarding a child for good behavior with a treat activates the dopamine pathway of the brain, inducing feelings of pleasure in the child—feelings that the teacher hopes will lead to more of the good behavior. The reactions that occur with this external mode are no different from the reactions that can be induced directly with stimulant drugs such as

Ritalin or Adderall. Internal versus external is distinguishable only by method, not by either behavioral or chemical result; there can be no issue of personal identity with internal methods if there is not also an issue of personal identity with external methods.

Ultimately, employing mechanical cognitive enhancements is the next logical step in our technological progression. Our technological advances have come in many forms, but all of these advancements have served as tools to improve human life. Mechanical cognitive enhancement—microchips and electrodes for stimulating the brain—is merely an extension of the tools we already use. It is but another tool available for use to improve and simplify our lives. A claim that we are somehow no longer human based on our use of this technology is a difficult one to make. In fact, the extent to which we use technology goes straight to the core of what it means to be human; it is exactly what makes us different from other animals.

Like other tools, mechanical cognitive enhancement improves our lives by offering more efficient and convenient ways of accomplishing tasks. We already regularly use prosthetics in medicine—cochlear implants to recover hearing, artificial limbs for amputees and pacemakers to assist heart function. For the most part, these medical advances are lauded rather than frowned upon. Mechanical interventions such as these are seen as a means of reestablishing "normal" function in the recipient. Extending the use of mechanical devices to the realm of strictly enhancement is not a leap but an easy progression. Just as we do not frown upon the use of mechanical interventions as above, nor should we look down upon mechanical means of enhancement.

Summary and Conclusions

Implants in the human body are nothing new. Spanning almost every part of the body, mechanical interventions have done wonders for treating numerous disorders. Particularly interesting are those mechanical interventions occurring in the brain. Much research has been done to both advance these interventions and develop new ones. In addition to the strides being made for therapeutic purposes, mechanical brain interventions hold the potential to enhance cognition in healthy individuals, from DBS in the reward pathway to enforce desired behaviors to a merging of computers with neurons for a variety of enhancement purposes. With these possibilities, also comes a range of ethical considerations. Mechanical cognitive enhancement brings to light concerns ranging from mind control to privacy infringements to personal responsibility. All of these concerns merit careful examination. However, despite these concerns, mechanical cognitive enhancement is morally permissible, serving as the next step in our technological progression.

CHAPTER IV

ENHANCING COGNITION VIA PHARMACOLOGY

Introduction

The desire to improve our minds is not at all a new phenomenon. As Henry Greely claims, language may very well have been our first significant attempt at cognitive enhancement as a species.[71] There is no doubt that the integration of language, both verbal and written, into our lives has drastically changed how we think and remember. As a result, human cognitive abilities are irrevocably enhanced. The use of herbs and synthetic chemicals to enhance cognition is also not a new phenomenon.

Caffeine, a compound known to produce cognitive benefit, has been consumed in various forms for literally thousands of years. The earliest use of tea is thought to be before the tenth century BC in China and it was first imported to Europe in the 1600s.[72] Coffee use is much more recent, with the first record of its cultivation being in Arabia about 675 AD; coffee was first introduced to the UK as a medicine but became very fashionable to drink in the 1670s.[72] Over the years, caffeine has been joined by nicotine and glucose, herbal supplements such as gingko biloba, and a wide array of dual-use drugs—those developed with a disorder in mind, but that also have enhancement capabilities in normal individuals—including methylphenidate, Adderall and donepezil. As one journalist put it: "In the 1960s, the Rolling Stones dubbed tranquilizers and antidepressants 'mother's little helper.' Forty years later, Adderall is 'brother's little helper.' And sister's."[24]

While it is difficult to get exact statistics, the prevalence of drug use to improve academic performance is apparently increasing dramatically. College campuses have become laboratories for experimentation with cognitive enhancement.[73] Studies have estimated that up to 25% of college students use prescription medication, particularly stimulants such as Ritalin and Adderall, to improve class performance.[20,24] A study conducted in 1998 at Indiana University of 44,232 students found that 6.8 percent of ninth-graders reported using Ritalin illicitly at least once.[74] Furthermore, in some schools, up to a third of boys are on Ritalin, even though many of them do not have ADHD.[28] In fact, the proportion of boys taking Ritalin in United States classrooms has exceeded the highest estimated prevalence of ADHD.[20]

If anything, our use of pharmaceuticals to improve cognitive function has both expanded and evolved over time. With this rapid and widespread increase in the use of pharmaceuticals for cognitive enhancement, there comes an urgent need to examine the ethical implications of such use. We have already witnessed an explosion of the ethical debate surrounding performance enhancement in professional sports. The use of pharmaceuticals such as steroids and stimulants in sports has lead to rapid social and policy change, including the establishment of the World Anti-Doping Agency (WADA) and the implementation of strict testing policies and penalties for positive testing. It is not out of the realm of possibility that the rapidly growing use of pharmaceuticals for cognitive enhancement will induce similar ethical concerns and subsequent changes in policy.

The purpose of the coming discussion is to offer both a brief summary of the current research into pharmaceutical cognitive enhancement and a look at the ethical

concerns that need to be considered when continuing this research. Furthermore, I will contend that, while it is important to keep ethical concerns in mind when conducting such research, pharmaceutical cognitive enhancement is morally permissible.

The Current State of Research

Many herbal medications have long been used, and are being researched, for their positive effects on cognitive functions. Gingko biloba is the most common of these. Some studies have shown that Gingko biloba supplements—among the best-selling herbal medications in the United States—can improve memory in people with dementia.[75] However, results in healthy individuals are less clear. A randomized, double-blind study of over 3000 elderly participants found that 120 milligrams of Gingko biloba taken twice daily did not result in less cognitive decline in older adults with normal cognition or with mild cognitive impairment, as compared to a placebo.[76] Another study found that over a six week period, ginkgo did not facilitate performance on standard neuropsychological tests of learning, memory, attention, and concentration or naming and verbal fluency in elderly adults without cognitive impairment.[77] Other herbal medications, such as *Bacopa monnieri*, have had more promising results in healthy individuals. *Bacopa monnieri*, an aquatic plant used for many centuries in India, has been shown to significantly improve memory acquisition and retention in healthy individuals over age 55 as compared to a placebo.[78]

In addition to herbal medications, many chemicals that are well-established in society have also been shown to enhance cognition in those who use them. Glucose, caffeine and nicotine are all known to enhance cognition in healthy individuals. As

previously mentioned, caffeine—found in a wide variety of food and drinks including tea, coffee, and soft drinks—is the most widely consumed stimulant drug worldwide.[79] Caffeine affects a wide array of cognitive functions, including enhancing attention and vigilance, stabilizing mood, increasing energy, and improving memory particularly in the presence of stressful or noxious stimuli.[79,80] Both caffeine and glucose, when used together, have been shown to have beneficial effects on attention, learning, and consolidation of verbal memory.[81] Both caffeine and nicotine, administered independently, can protect neurons from degeneration against MPTP, a chemical used to mimic Parkinson's disease in model organisms.[82] In addition to therapeutic effects, studies have indicated that nicotine enhances cognitive performance by improving working memory in both smokers and non-smokers.[83]

Donepezil, commonly marketed as Aricept, is a cholinesterase inhibitor prescribed for the treatment of Alzheimer's disease.[20] However, donepezil is also known to have beneficial effects on cognition in healthy individuals. A study by Mumenthaler and colleagues tested the effects of nicotine, donepezil and alcohol in aircraft pilots and found that all three drugs had large effects on overall flight performance: nicotine and donepezil improved while alcohol impaired overall flight performance as compared to placebo.[84] Another study, also conducted on licensed pilots, yielded results further indicating that donepezil appears to have beneficial effects on retention of training on complex aviation tasks in non-demented older adults.[85]

Stimulants, currently prescribed largely for the treatment of various mental disorders, such as Ritalin, Adderall and Provigil have been shown to have cognition enhancing effects in healthy individuals. Methylphenidate, better known as Ritalin, is a

one of the most common stimulant drugs approved for the treatment of attention-deficit hyperactivity disorder (ADHD). First synthesized in 1944 and put into use in the 1950's, methylphenidate works by raising levels of dopamine—the neurotransmitter associated with feelings of pleasure that is naturally released as part of the reward pathway.[86] The drug improves attention and alertness in people with ADHD. However, methylphenidate also has similar beneficial effects in otherwise healthy people. Agay and colleagues found that working memory, as indicated by average digit-span test score, was improved in groups receiving methylphenidate as compared to groups receiving a placebo, independent of whether the subjects had been diagnosed with ADHD.[87]

The combination of dextroamphetamine and amphetamine, more commonly known as Adderall, is another of the psychostimulant drugs known to have both therapeutic and enhancement uses. While Adderall is prescribed largely for the treatment of ADHD, much like methylphenidate, it is used to treat narcolepsy, a disorder causing excessive daytime sleepiness as well.[88] As expected then, Adderall produces wakefulness, heightened focus, and improved attention in those who use it. One study looking at effects on creativity demonstrated that Adderall affected performance on tasks requiring convergent thought, in one case enhancing it, particularly for lower-performing individuals, and in the other case enhancing it for the lower-performing and impairing it for higher-performing individuals.[89]

Modafinil, often prescribed under the brand name Provigil, is primarily used in treating narcolepsy, although experimental applications range from treating Alzheimer's disease to depression.[90] Modafinil attenuated sleep deprivation effects in helicopter pilots on four of six flight maneuvers, reduced slow-wave EEG activity, and lessened self-

reported problems with mood and alertness in comparison to placebo.[91] These results suggest a possible enhancement use of modafinil in healthy individuals required to operate with limited sleep, such as is the case in pilots and emergency personnel. Executive function improvements have also been studied. For instance, humor appreciation for cartoon stimuli was enhanced by modafinil relative to both placebo and caffeine, but there was no enhancing effect on the appreciation of verbal humor during sleep loss.[92] However, multiple studies have shown that modafinil may only be useful in enhancing performance in sleep deprivation situations. There were no significant effects of modafinil compared with placebo for healthy young subjects in tests of long-term memory, executive function, visuospatial and constructional ability, or category fluency.[93] Similar results have also been shown in middle-aged healthy individuals.[94]

As already noted in studies of modafinil, particular attention has been paid to the potential for stimulant-based enhancement of cognition in healthy, but sleep-deprived individuals. A series of studies have shown that, relative to placebo, various stimulants—caffeine, dextroamphetamine and modafinil—were all equally effective in restoring simple psychomotor vigilance and objective alertness, although the duration of action was shortest for caffeine and longest for dextroamphetamine.[95,96] Furthermore, in a series of tests examining executive function, the same set of stimulants all conferred differential advantages which seemed to depend on the cognitive demands of each test.[97]

Ampakines are among the drugs being developed without a disease in mind, but rather for the improvement of long-term memory in otherwise healthy adults.[12] By binding to a site on the AMPA receptor, a receptor important for synaptic plasticity, ampakines stabilize these receptors in the channel-open state following the binding of

released transmitter; this prolongs current flow through the receptor and thus enhances synaptic responses.[13] Because of this effect, the compounds can improve communication in complex networks and, hence, can alter the encoding and organization of information in normal brains. In primate studies, the ampakine CX717 was shown to enhance cognitive performance under normal alert conditions and also proved effective in alleviating impairment of performance due to sleep deprivation.[98]

Lastly, pharmaceuticals that target the inorganic milieu of the brain can also significantly impact cognitive function. For example, research has shown that by simply elevating the amount of magnesium present in the brain, a range of cognitive abilities can be enhanced. Slutsky and colleagues show that a newly developed magnesium compound, called magnesium-L-threonate, can enhance learning abilities, working memory, and both short- and long-term memory in rats.[99]

Ethical Issues in Pharmacological Cognitive Enhancement

With new, rapidly developed technology, comes the need to rapidly develop policies for the use and control of such technologies. Inevitably, the rules—whether governmentally, institutionally, or just socially imposed—are forced to keep pace with advancements. And the social change that results from such rapid advancements can vary widely, from the outright banning of performance enhancements in athletics to the relative acceptance of cosmetic surgery as a personal choice. As demonstrated by the statistics, pharmacological means of enhancement are by far the most rapidly growing method of cognitive enhancement. Already in use in a variety of ways and settings, pharmaceutical cognitive enhancement presents the most real-time concerns—ones that

will likely induce rapid social and policy change. We are approaching a time when the wide range of issues surrounding cognitive enhancement as a whole—issues in fairness, coercion, safety, and so on—must be dealt with.

It becomes an issue of if and how to control the off-label enhancement use of both already available drugs and chemicals and soon-to-be marketed "smart drugs". There is a reason pharmaceuticals are required to have FDA approval for a particular use prior to prescription. Having such approval indicates that the drug has been tested for that purpose and is at least relatively safe. On the other hand, there is also a reason for allowing physicians' latitude in prescribing drugs for off-label use. It is impractical and arguably not feasible to test every drug for every possible use in every possible user demographic. Is the current balance sufficient enough to handle the increasing off-label use of various drugs for enhancement purposes?

Furthermore, the use of pharmaceutical cognitive enhancements solely for their instrumental value may create a particularly salient social justice problem in a variety of settings. The motives of students for using drugs such as Adderall or methylphenidate to enhance cognition will vary. While some students may just want to learn better or focus better, others may just want to make the grade to better their GPA and resume. Pharmaceutical cognitive enhancements have the potential to confer unfair advantages to users. Those who can't afford to buy the drugs or those who simply choose not to take them may be at an immediate disadvantage to their peers. Just as calculators were once banned in the classroom because high costs precluded many students from owning them, pharmaceutical cognitive enhancements may face the same fate. However, the ultimate decision of whether to permit the use of such enhancements will come down to the

priorities of individual institutions. In schools, it may become a question of what is important—the final grades or the cumulative knowledge that students obtain. Similar priorities will also need consideration in the workplace.

The Moral Permissibility of Pharmacological Cognitive Enhancement

A lack of serotonin in the brain is related to several psychiatric impairments, including depression, anxiety, and poor self-confidence. Psychiatrists often prescribe drugs that act to adjust levels of serotonin to correct these impairments. However, there are other methods that can correct such impairments that may be just as effective in many cases. Therapy can be used to treat depression. Meditation and other spiritual practices can calm a person and reduce anxiety. Working out to improve physique, classes in public speaking, and other endeavors can help to improve a person's self-confidence. In any case, the options can achieve similar results and are, in general, equally acceptable therapeutic methods.

The same concept applies when the tables turn and the reason for intervention shifts toward improvement in healthy individuals. People regularly enter into psychotherapy as a means of altering behavior and personality, to work through issues and, hopefully, come out an improved person. This serves as an external and indirect method for enhancing oneself. Taking a pill that can allow the individual to realize similar improvement serves as a quicker and possibly even more effective method.

For example, a healthy person experiencing trouble with maintaining attention and focus at work could enter into therapy to get at and ultimately address issues causing this problem. Alternatively, a person could begin taking a stimulant medication such as

methylphenidate. Both methods can affect behavior in a desired manner and ultimately enhance cognition. The difference lies in directness, timing and preference. The former—entering into psychotherapy—is less direct and more time-consuming, likely taking on the order of months to years to be effective; however, it also has the potential to eliminate the underlying cause. The latter—taking a drug—is more direct and near instantaneous, with results being noticed with the first tablet; however, taking a drug may not solve an underlying cause and a person may be required to take the drug indefinitely; there may also be side effects associated with drug use. It also becomes a matter of choice as to whether weekly therapy sessions are preferable to daily medication. Both options have trade-offs. In some cases, a quick method, such as popping a pill, may be preferable; say, for example, if a lack of focus is affecting one's job performance to a detriment, then taking methylphenidate to fix the problem quickly and improve job performance would be preferred. In other cases, therapy may be preferable. Hence, both methods reach a similar result and both are tools we can and should be able to employ to enhance cognition.

There are also reasons that exist for cognitive enhancement that may not necessarily be achieved with alternative means. Pilots, military personnel, and medical residents are often required to work long hours with little or no sleep. In these cases, drowsiness can have devastating effects. Shift workers must work against their circadian rhythms and, as such, often have trouble staying awake at night and sleeping during the day. In both cases, cognitive enhancers that can improve wakefulness and other cognitive function in light of sleep deprivation would be particularly valuable. Other alternatives, like psychotherapy and meditation, will not produce any useful result for

people in such positions. It is important, then, that cognitive enhancers be an available option.

Summary and Conclusions

Pharmaceutical cognitive enhancement has existed for quite some time. Caffeine, nicotine, and glucose are compounds that have been used for years, and all are compounds known to have positive effects on cognition. More recently, drugs developed for the treatment of various disorders, such as ADHD and Alzheimer's disease, have also shown promise in enhancing the cognitive abilities of healthy individuals. Drugs are also being developed without a treatment purpose in mind. Statistics demonstrate that pharmacological enhancement of cognition is a practice that is already occurring in many settings, including the workplace and the classroom. Because of this, ethical concerns have rapidly arisen. With rapid advancement, comes rapid social change. Issues including those of social justice and unfair advantage must be considered by society, including the scientists making advances in the field. While some oversight may be required at the individual institution level—based on priorities of individual institutions—pharmaceutical cognitive enhancement is morally permissible.

CHAPTER V

THE MORAL PERMISSIBILITY OF COGNITIVE ENHANCEMENT

Enhancement Methodologies and the Principle-Based Approach to Bioethics

Each of the potential methods of achieving cognitive enhancement presents unique ethical concerns. However, just like the general arguments presented for and against cognitive enhancement in chapter one, methodology-specific arguments presented in the subsequent chapters also fall within Beauchamp and Childress's four principles—respect for autonomy, beneficence, nonmaleficence, and justice.

Respect for autonomy plays an important role. Freedom of personal choice is a critical component of the arguments in favor of all forms of cognitive enhancement. Each of the methods of achieving cognitive enhancement is similar in kind, to other practices already being undertaken. Making a genetic change, such as inserting a gene for improved focus, is not that different than using methylphenidate or employing reward and punishment to correct inattentive behavior. Using methylphenidate is arguably no different than entering into intensive psychotherapy. Having a memory chip implanted is not much different than carrying around a smartphone. Each option achieves a similar end. It simply comes down to personal preference in how one goes about achieving a desired enhancement. Issues in autonomy also arise on the negative side of the debate. Personal responsibility may become questionable in the case of mechanical cognitive enhancements. The autonomy of one's decisions may be called into question, since one's decisions may be misinterpreted by technology or instigated by an outside source controlling the technology.

Beneficence, like the principle of respect for autonomy, also plays an important role, particularly in arguments favoring cognitive enhancement in all forms. Methylphenidate and Adderall can be used to improve focus. DBS can be used to stimulate the reward pathways and can reinforce desired behaviors. Memory chips can confer a seemingly endless capacity to remember. Inserting additional NMDA receptors can lead to quicker learning. Each form of cognitive enhancement has the potential to benefit those who use them.

Nonmaleficence underlies many of the arguments against each form of cognitive enhancement. The off-label, and hence unapproved, use of pharmaceuticals to enhance cognition immediately opens up issues of safety. If drugs haven't properly been tested for a particular use, such as enhancement, then there is no way to know if a drug is safe. This could lead to major harms to those using unapproved pharmaceuticals to enhance. Similarly, harms can also come about from manipulating our genetics in way as to surpass our cognitive limits. It is possible, perhaps even likely, that humans have particular limitations for a reason. Remembering some information while forgetting other information may be necessary from a mental health standpoint. Bypassing these limits by manipulating genes to improve memory could irreparably harm the individual. Furthermore, these harms could become exponential with germline genetic manipulations.

Lastly, justice plays a similarly critical role in the methodology-specific arguments. Concerns about social justice surround all forms of cognitive enhancement. Particularly salient, are issues with pharmacological cognitive enhancements being used solely for their instrumental value, and hence, conferring a competitive edge to users.

Taking an Adderall to cram the night of an exam lends an advantage in that it may result in a better grade. Although pharmaceutical cognitive enhancement most readily presents an issue of justice—mostly because it is the one method already being used—the other forms will likely lead to similar concerns.

It is important to reiterate that all of the arguments presented thus far are insufficient to stand alone in either promoting or deterring the use of cognitive enhancements. Instead, it is the balance of these arguments that is in favor of proceeding with all forms of cognitive enhancement.

The Human Identity

While referring to questionable medical practices and the idea of multiculturalism, Ruth Macklin claims that a human condition merely being considered "…statistically normal implies nothing whatever about whether an obligation exists to seek to alter the statistical norm for the betterment of those who are affected."[100] Death due to malaria may be considered statistically normal in Africa, but the mere fact that this is normal implies nothing about whether such a norm should be accepted. In fact, this norm is one that is actively undergoing a presumably positive change with the introduction of protective bed nets and anti-malarial medications. An even more dramatic example can be noted in the drastic change over time that has occurred in what is considered to be normal human life expectancy. A hundred years ago, the normal human life expectancy from birth in the United States was less than 50 years; today this norm has shifted nearly 30 years, making the normal life expectancy now just over 78 years old.[101]

The concept of what is normal is constantly shifting. It can be argued that a philosophy such as this also applies to cognitive enhancement. Simply because a particular IQ, attention span, or ability to retain a certain quantity of information is statistically normal across humans, does not imply that norms such as these should be left alone. In fact, given the changing nature of human norms, one might assume that these norms will eventually shift.

It is this change—the constant shifting of what is means to be normal—that is at the very core of what it means to be human. Humans have never been nor are they now stagnant creatures. Human identity rests upon the ability to adapt and the drive to alter ourselves and the world around us. As a species and as individuals, our identities constantly evolve. As a species, we have developed, and are steadily developing, new tools to make our lives better. As individuals, we make countless choices, from the mundane to the monumental, in every aspect of our lives, each of which plays some role, small or large, in our individual identities. On both levels—species and individual—cognitive enhancement falls right in line with the natural progression of human identity.

Evolving the Species: The Use of Tools as Part of Human Identity

One of the fears of cognitive enhancement is that it will prove deleterious to human identity—that by enhancing ourselves we are becoming something that is no longer human. However, I argue that all forms of cognitive enhancement are morally permissible, and serve to establish our identity. Cognitive enhancement as a tool to improve our lives is an extension of human nature. Our tools—ranging from remarkably simple to incredibly complex—define who we are as a species.

We, as humans, have always used tools and technologies to improve nearly every facet of our lives. For example, humans are perfectly capable of living outdoors without constructed shelter—just as other primates; however, we use tools, such as hammers and nails, and our knowledge to construct homes to protect us and make our lives more comfortable. Likewise, we can walk to our destinations, but we instead use cars or airplanes to make the trips easier. We wash our clothes by machine rather than by hand. As a species, we live by our tools. Putting to use our knowledge of chemistry, genetics, and engineering as a tool to improve our lives—by improving our mental abilities and capacities—is the next logical step in our progression as a species.

Not only do we regularly use tools, but we also regularly assume the risks associated with our tool use so that we may reap their associated benefits. The houses that we build have the inherent, albeit rare, risk of collapse. The use of cars—the tools that we rely so heavily upon for transportation—results in numerous injuries and fatalities worldwide on a daily basis. Yet, people assume these risks because the benefits are perceived to be worth it. The use of cognitive enhancements will likely have some imposition of risk upon users, just as is the case with many other tools we have developed. And just as with other tools, an individual should be able to decide if the benefits, in this case of enhanced cognition, are worth the risks involved in doing so.

Using cognitive enhancement, irrespective of methodology, as a tool to improve our lives also makes sense from the perspective of science. Science is reaching a point where life expectancy is reaching a plateau. Even with extensive advancements in cleanliness and medical interventions in the last 30 years, the average life expectancy of a person living in the United States has increased only a matter of a few years. Science

provided the information necessary to rid ourselves of disease from poor sanitation, and then humans died from polio and smallpox. Science eradicated polio and smallpox and now humans die from cancer and heart disease. It is unlikely that enhancing human cognition will increase lifespan.

However, even if cognitive enhancement does allow for prolonged lives, it is entirely possible that it will just allow humans to live long enough to encounter new ways to die. We will never truly master everything in our world, including ourselves. Science will never be able to fix all of the problems humans will encounter. With a limited amount of years, we should be able to enhance the years we do have, maximizing our life experiences. As previously mentioned, using tools and finding ways to improve our relatively short lives is inherent to our nature.

Evolving the Individual: Altering Identity by Choice

Not a single person maintains the same personality, beliefs, values, or goals from birth to death. A toddler's priorities are appropriately quite different from the priorities of a middle-aged man. A single woman's values will likely shift when she begins a family. A college student's goals will evolve once he or she graduates. Correspondingly, a person's cognitive functions and abilities also change and evolve throughout the course of one's life.

As these functions and abilities change, so to does the chemistry of our brains. For example, each time we learn something, or reinforce something we have already learned, our synapses change. Receptors, like the NMDA receptors previously mentioned, are trafficked in and out of the cell membrane at the synapse, leading to the

strengthening or weakening of individual synapses. These changes can affect the release of and response to various neurotransmitters in the brain. Hence, as we learn and remember, the chemistry of our brains changes.

To the extent that we constantly alter our brain chemistry, identity is self-made. It is the decisions we make or don't make that affect our very character and nature. We adjust our chemistry every time we attend a lecture, take an aspirin for a headache, or even tie a shoe. Human identity, while being somewhat dependent on genetics and chemistry, is also dependent on choices, which in turn affect our genetics and chemistry. Take, for example, the case of musicians. Perhaps as a consequence of focused training, musicians have been shown to exhibit superior working memory task performance and an enhanced ability to exert sustained cognitive control.[102] In undergoing musical training, an individual is also choosing to alter their brain chemistry and, in turn, their cognitive abilities.

"Artificially" enhancing our cognitive abilities—via genetics, pharmacological or mechanical means—doesn't affect our human identity any more than the decisions we make everyday. Decisions about things like education and religion can shape the brain. Literacy changes how our brains function and, as such, the physical layout of our synapses and circuits.[71] A decision to get a doctorate can have drastically different affects on cognitive function and abilities than a decision to drop out of high school. Similarly, a decision to follow one faith over another can dramatically change one's morals, values and beliefs—and in turn brain chemistry also changes.

Decisions make us who we are. Someone who chooses not to be religious is not any less human than someone who engages in religious practice. Likewise, a person

who has enhanced his or her memory would be no less or more of a human being than a person who has Alzheimer's disease; in fact, it would be morally indefensible to call someone with such a disease a lesser human. It would be equally problematic to claim that an enhanced person is anything but human. And it is morally permissible, and possibly even considered a moral duty, to treat a person with a disease; it is also permissible to cognitively enhance ourselves.

Whether a decision is deliberate or not, it still changes the chemistry of our brains. Every activity we do—whether consciously or not—serves as an external means of altering the chemistry of our brains, and in turn our bodies. In pursuing cognitive enhancements, we are simply pursuing desired changes in more direct—a more conscious and deliberate—manner.

Implications of Allowing Cognitive Enhancement

First and foremost, the perspective I have taken here is one of incrementalism. That is, I make the claim that cognitive enhancement, regardless of methodology, is a morally permissible next step in our progression as a species. We have come this far, therefore it makes sense to continue our progression into the realm of cognitive enhancement. However, what is incremental to some may seem like a slippery slope to others. While we can't necessarily undo existing practices that have come about with our progress thus far, we can choose to stop building upon and furthering these practices. Essentially, we could say this far, but no farther. The balance of ethical issues I present is somewhat tipped in favor of cognitive enhancement in part by questionable practices—

socially accepted inequalities, the human drive to master, the parental aspiration to push their children to perfection.

While some of our social norms do deserve reconsideration and even restructuring, it does not follow that cognitive enhancement should be disallowed. My view of human nature is considerably more plastic than that of scholars who argue that cognitive enhancement is unnatural. It is central to my argument that I do not consider cognitive enhancement different in kind to other human tool-making endeavors, but only different in degree. Enhancing cognition is a progression of degree, directly in line with performance enhancement and cosmetic enhancement. Drawing an arbitrary line and, as such, singling out cognitive enhancement as impermissible is not the answer. Doing so does nothing to solve the underlying moral concerns. Ultimately, there must be a good reason to draw that line. There must be a good reason to stop our progression. As I have laid out, the harms and the benefits weigh out in favor of pursuing cognitive enhancements. Unless there is a shift in the calculus, there is not yet a good reason to say stop. Therefore, when balancing potential benefits and risks of harms, I can only conclude that cognitive enhancement is morally permissible and that there is no logical point beyond which we should not go.

This is not to say, however, that the moral concerns associated with cognitive enhancement be ignored. Proclaiming moral permissibility and allowing cognitive enhancement has its own implications. But the ethical issues that arise can be monitored as the technology progresses and addressed appropriately at the necessary level. Just as we monitor other technologies, so too should we monitor cognitive enhancement technologies. The oversight needed for each form of cognitive enhancement is no

different than the oversight required for other advancements. Regulation may be needed at a variety of levels depending on the particular issues that come to fruition.

Such regulation can begin at the research level. At the research level, decisions to move forward or to regulate can be made based on safety concerns. Safety is one concern that resounds across all forms of cognitive enhancement. Some enhancements may present risks, side effects, and detrimental outcomes that are just too great to justify the use of those enhancements. As the research advances the potential applications of cognitive enhancement, the research also needs to advance the safety of each form of cognitive enhancement. Thorough research will also provide valuable information to allow for well-informed decisions by individuals with regard to cognitive enhancement. Both newly developed medications, and drugs already available being used off-label, merit extensive research to ensure that these drugs do not harm those who choose to use them. Methods of delivering genetic interventions need further research to ensure that adverse reactions are avoided. Similarly, methods for implanting mechanical devices in the brain also need further development. As previously stated, safety concerns are paramount and research should especially focus on ensuring that harms are minimized. Beyond the research stage, a proper physician-patient relationship can help mitigate many concerns that arise. In such a relationship, a physician can monitor the individual undergoing cognitive enhancement for unexpected or negative outcomes, such as personality changes—changes in moral agency, self-destructive behaviors and so on—and detrimental physiological side effects.

Concerns over germline genetic manipulation and genetic manipulations in children may be an area requiring further consideration moving forward. The policies

and regulations developed for the use of genetic cognitive enhancement will need to be based on the safety of such interventions, as determined by properly conducted research studies. Decisions about the extent to which parents can decide for their children, and future children, will likely need to be decided on a societal level. However, depending on how far the research goes, the government may also need to step in and implement policies on parental authority. In any case, this may very well be the form of cognitive enhancement where each particular intervention is assessed on individual merits and policies are then instituted as such.

With regard to pharmaceutical enhancements, the issues in social justice and the use of cognitive enhancers purely for their instrumental value is one area that we need to think about moving forward. If this truly becomes problematic, rather than just theory, individual institutions can then address the concerns by implementing their own policies. The use of drugs such as methylphenidate and Adderall is already becoming prevalent in academic settings. Universities, and perhaps even secondary schools, may need to develop and institute policies—such as post-exam drug testing—to control such drug use. Various workplaces may also need to consider such policies. However, in both cases, policies should be instituted based on the ultimate goals of the particular institution.

As far as mechanical enhancements, issues of mind control and responsibility will all need consideration. Concerns such as these may require oversight at higher levels, likely above that at individual schools and workplaces. Perhaps at the federal or state legislature levels, for example, policies may need to be implemented to ease concerns over mind control. The criminal justice system will need to adjust to the potential for cases of questionable responsibility; however, this adjustment will likely be similar to

what occurred when genetic discoveries led to similar questionability. At present, mechanical enhancements are not approaching the point of allowing total brain replacement; however, as the technology advances, this will likely be an area that merits further evaluation—perhaps to the extent of regulating how much enhancement is appropriate or allowable.

Moving forward with cognitive enhancements seems inevitable, and is morally permissible. Because these developments are happening in so many areas, case-by-case monitoring is necessary; however, because the developments are incremental, review and assessment of their effects is possible.

REFERENCES

1 Fair, J. D. Isometrics or Steroids? Exploring New Frontiers Of Strength in the Early 1960s. *Journal of Sport History* **20**, 1-24 (1993).

2 *World Anti-Doping Code*. 1-135 (World Anti-Doping Agency, 2009).

3 WADA. The 2010 Prohibited List International Standard. 1-9 (2009).

4 Shea, L. *Rosemary Essential Oil & Hair Loss*, <http://www.livestrong.com/article/81806-rosemary-essential-oil-hair/> (2010).

5 Bear, M. F., Conners, B. W. & Paradiso, M. A. *Neuroscience: Exploring the Brain*. Second edn, (Lippincott, Williams & Wilkins, 2001).

6 Floresco, S. B. & Jentsch, J. D. Pharmacological Enhancement of Memory and Executive Functioning in Laboratory Animals. *Neuropsychopharmacology* **36**, 227-250 (2011).

7 *Executive Function Fact Sheet*, <http://www.ncld.org/ld-basics/ld-aamp-executive-functioning/basic-ef-facts/executive-function-fact-sheet> (2009).

8 Bostrom, N. in *Reshaping the Human Condition: Exploring Human Enhancement* (eds Leo Zonneveld, Huub Dijstelbloem, & Danielle Ringoir) 29-36 (Rathenau Institute, 2008).

9 Bailey, R. in *Liberation Biology: The Scientific and Moral Case for the Biotech Revolution* Ch. 7, 223-238 (Prometheus Books, 2005).

10 Tang, Y. *et al.* Genetic Enhancement of Learning and Memory in Mice. *Nature* **401**, 63-69 (1999).

11 MachielVanDerLoos, H. F. Design and Engineering Ethics Considerations for Neurotechnologies. *Cambridge Quarterly of Healthcare Ethics* **16**, 303-307 (2007).

12 Chatterjee, A. The Promise and Predicament of Cosmetic Neurology. *Journal of Medical Ethics* **32**, 110-113 (2006).

13 Lynch, G. & Gall, C. M. Ampakines and the threefold path to cognitive enhancement. *Trends in Neurosciences* **29**, 554-562 (2006).

14 Larriviere, D., Williams, M. A., Rizzo, M. & Bonnie, R. J. Responding to Requests from Adult Patients for Neuroenhancements. *Neurology* **73**, 1406-1412 (2009).

15 Allhoff, F., Lin, P., Moor, J. & Weckert, J. Ethics of Human Enhancement: 25 Questions & Answers. 1-50 (US National Science Foundation, 2009).

16 Wolpe, P. R. Treatment, Enhancement, and the Ethics of Neurotherapeutics. *Brain and Cognition* **50**, 387-395 (2002).

17 Bostrom, N. & Sandberg, A. Cognitive Enhancement: Methods, Ethics, Regulatory Challenges. *Science and Engineering Ethics* **15**, 311-341 (2009).

18 Beauchamp, T. L. & Childress, J. F. *Principles of Biomedical Ethics*. 6th edn, (Oxford University Press, 2009).

19 Dees, R. H. Better Brains, Better Selves? The Ethics of Neuroenhancements. *Kennedy Insititute of Ethics Journal* **17**, 371-395 (2008).

20 Warren, O. J., Leff, D. R., Athanasiou, T., Kennard, C. & Darzi, A. The Neurocognitive Enhancement of Surgeons: An Ethical Perspective. *Journal of Surgical Research* **152**, 167-172 (2009).

21 Cakic, V. Smart Drugs for Cognitive Enhancement: Ethical and Pragmatic Considerations in the Era of Cosmetic Neurology. *Journal of Medical Ethics* **35**, 611-615 (2009).

22 Bush, S. S. Neurocogntive Enhancement: Ethical Considerations for an Emerging Subspecialty. *Applied Neuropsychology* **13**, 125-136 (2006).

23 ThePresident'sCouncilonBioethics. Beyond Therapy: Biotechnology and the Pursuit of Happiness. 1-347 (Washington DC, 2003).

24 Jaffe, H. *ADD & Abusing Adderall*, <http://www.washingtonian.com/articles/education/1729.html> (2006).

25 Harrell, E. *Q&A: Nick Bostrom on the Future of Human Enhancement*, <http://www.time.com/time/health/article/0,8599,1921027,00.html> (2009).

26 DeGrazia, D. in *Prozac as a Way of Life* (eds Carl Elliott & Tod Chambers) 33-47 (The University of Chapel Hill Press, 2004).

27 Sandel, M. J. The Case Against Perfection. *The Atlantic Monthly* **293**, 51-62 (2004).

28 Butcher, J. Cogntive Enhancement Raises Ethical Concerns. *The Lancet* **362**, 132-133 (2003).

29 Bostrom, N. & Roache, R. Ethical Issues in Human Enhancement. *New Waves in Applied Ethics*, 1-27 (2007).

30 Watson, J. D. & Crick, F. H. C. Molecular Structure of Nucleic Acids: A Structure for Deoxyribose Nucleic Acid. *Nature* **171**, 737-738 (1953).

31 *Human Genome Project Information*, <http://www.ornl.gov/sci/techresources/Human_Genome/home.shtml> (2010).

32 Pan, F., Aldridge, G. M., Greenough, W. T. & Gan, W.-B. Dendritic Spine Instability and Insensitivity to Modulation by Sensory Experience in a Mouse Model of Fragile X Syndrome. *PNAS*, 1-6 (2010).

33 Flint, J. The Genetic Basis of Cognition. *Brain* **122**, 2015-2031 (1999).

34 Lee, Y.-S. & Silva, A. J. The Molecular and Cellular Biology of Enhanced Cognition. *Nature Reviews Neuroscience* **10**, 126-140 (2009).

35 Knight, W. *Dolly the Sheep Dies Young*, <http://www.newscientist.com/article/dn3393-dolly-the-sheep-dies-young.html> (2003).

36 Obasogie, O. K. *Ten Years Later: Jesse Gelsinger's Death and Human Subjects Protection* <http://www.geneticsandsociety.org/article.php?id=4955> (2009).

37 Barnett, M. W., Fisher, C. E., Perona-Wright, G. & Davies, J. A. Signalling by Glial Cell Line-Derived Neurotrophic Factor (GDNF) Requires Heparan Sulphate Glycosaminoglycan. *J Cell Sci* **115**, 4495-4503 (2002).

38 Gale, E. & Li, M. Midbrain dopaminergic neuron fate specification: Of mice and embryonic stem cells. *Molecular Brain* **1**, 8 (2008).

39 Kordower, J. H. *et al.* Neurodegeneration Prevented by Lentiviral Vector Delivery of GDNF in Primate Models of Parkinson's Disease. *Science* **290**, 767-773 (2000).

40 Messer, C. J. *et al.* Role for GDNF in Biochemical and Behavioral Adaptations to Drugs of Abuse. *Neuron* **26**, 247-257 (2000).

41 Airaksinen, M. S. & Saarma, M. GDNF Family: Signalling, Biological Functions and Therapeutic Value. *Nature Reviews Neuroscience* **3**, 383-394 (2002).

42 Cunha, C., Brambilla, R. & Thomas, K. L. A Simple Role for BDNF in Learning and Memory? *Frontiers in Molecular Neuroscience* **3**, 1-14 (2010).

43 Gorski, J. A., Balogh, S. A., Wehner, J. M. & Jones, K. R. Learning deficits in forebrain-restricted brain-derived neurotrophic factor mutant mice. *Neuroscience* **121**, 341-354 (2003).

44 Nakajo, Y. *et al.* Genetic Increase in Brain-Derived Neurotrophic Factor Levels Enhances Learning and Memory. *Brain Research*, 103-109 (2008).

45 Wang, D. *et al.* Genetic Enhancement of Memory and Long-Term Potentiation but not CA1 Long-Term Depression in NR2B Transgenic Rats. *PLOS One* **4** (2009).

46 Fukiyama, F. in *Foreign Policy* (The Slate Group, Washington, DC, 2004).

47 Hanna, K. E. *Genetic Enhancement*, <http://www.genome.gov/10004767> (2006).

48 Wei, F. *et al.* Genetic Enhancement of Inflammatory Pain by Forebrain NR2B Overexpression. *Nature Neuroscience* **4**, 164-169 (2001).

49 Mauron, A. *Ethical Aspects of Gene Therapy*, <http://www.gfmer.ch/Endo/Lectures_09/ethical_aspects_of_gene_therapy.htm> (2008).

50 Lappé, M. Ethical Issues in Manipulating the Human Germ Line. *Journal of Medicine and Philosophy* **16**, 621-639 (1991).

51 Hansson, S. O. Implant ethics. *Journal of Medical Ethics* **31**, 519-525 (2005).

52 McGee, E. M. & Maguire, G. Q. *Ethical Assessment of Implantable Brain Chips*, <http://www.bu.edu/wcp/Papers/Bioe/BioeMcGe.htm> (1998).

53 Coffey, R. J. Deep Brain Stimulation Devices: A Brief Technical History and Review. *Artifical Organs* **33**, 208-220 (2008).

54 Blomstedt, P., Sjöberg, R. L., Hansson, M., Bodlund, O. & Hariz, M. I. Deep brain stimulation in the treatment of depression. *Acta Psychiatrica Scandinavica*, 1-8 (2010).

55 Denys, D. *et al.* Deep Brain Stimulation of the Nucleus Accumbens for Treatment-Refractory Obsessive-Compulsive Disorder. *Arch Gen Psychiatry* **67**, 1061-1068 (2010).

56 Sassi, M., Porta, M. & Servello, D. Deep brain stimulation therapy for treatment-refractory Tourette's syndrome. *Acta Neurochirurgica*, 1-7 (2010).

57 Halpern, C. H. *et al.* Deep brain stimulation in the treatment of obesity. *Journal of Neurosurgery* **109**, 625-634 (2008).

58 Vergani, F. *et al.* Surgical, Medical, and Hardware Adverse Events in a Series of 141 Patients Undergoing Subthalamic Deep Brain Stimulation for Parkinson Disease. *World Neurosurgery* **73**, 338-344 (2010).

59 Burdick, A. P. *et al.* Do patient's get angrier following STN, GPi, and thalamic deep brain stimulation. *NeuroImage* **In Press, Corrected Proof** (2010).

60 Fasano, A. *et al.* Motor and cognitive outcome in patients with Parkinson's disease 8 years after subthalamic implants. *Brain* **133**, 2664-2676 (2010).

61 McFarland, D. J., Sarnacki, W. A. & RWolpaw, J. Electroencephalographic (EEG) control of three-dimensional movement. *Journal of Neural Engineering* **7**, 036007 (2010).

62 Krusienski, D. & Shih, J. Control of a Visual Keyboard Using an Electrocorticographic Brain-Computer Interface. *Neurorehabilitation and Neural Repair* (2010).

63 Vance, A. *Merely Human? That's so Yesterday*, <http://www.geneticsandsociety.org/article.php?id=5256> (2010).

64 Warwick, K. <http://www.kevinwarwick.com/index.asp> (2010).

65 Oshima, H. & Katayama, Y. Neuroethics of Deep Brain Stimulation for Mental Disorders: Brain Stimulation Reward in Humans. *Neurologia Medico-Chirurfica* **50**, 845-852 (2010).

66 Schermer, M. The Mind and the Machine. On the Conceptual and Moral Implications of Brain-Machine Interaction. *Nanoethics* **9**, 217-230 (2009).

67 Decker, M. & Flecher, T. Contacting the Brain--Aspects of a Technology Assessment of Neural Implants. *Biotechnology Journal* **3**, 1502-1510 (2008).

68 Clausen, J. Moving Minds: Ethical Aspects of Neural Motor Prostheses. *Biotechnology Journal* **3**, 1493-1501 (2008).

69 Glannon, W. Stimulating brains, altering minds. *Journal of Medical Ethics* **35**, 289-292, doi:10.1136/jme.2008.027789 (2009).

70 Clausen, J. Man, machine and in between. *Nature* **457**, 1080-1081 (2009).

71 Greely, H. T. *Enhancing Brains: What Are We Afraid of?*, <http://www.dana.org/news/cerebrum/detail.aspx?id=28786> (2010).

72 *Caffeine: Our Most Popular Drug*, <http://www.drugscope.org.uk/resources/drugsearch/drugsearchpages/caffeine> (2005).

73 Talbot, M. in *The New Yorker* (Condé Nast Digital, New York, 2009).

74 PBS. *Ritalin Abuse: Statistics*, <http://www.pbs.org/wgbh/pages/frontline/shows/medicating/drugs/ritalinstats.html> (2001).

75 Ehrlich, S. D. *Gingko Biloba*, <http://www.umm.edu/altmed/articles/ginkgo-biloba-000247.htm> (2009).

76 Snitz, B. E. *et al.* Ginkgo biloba for Preventing Cognitive Decline in Older Adults *JAMA* **302**, 2663-2670 (2009).

77 Solomon, P. R., Adams, F., Silver, A., Zimmer, J. & DeVeaux, R. Ginkgo for Memory Enhancement: A Randomized Controlled Trial. *JAMA* **288**, 835-840 (2002).

78 Morgan, A. Does Bacopa monnieri Improve Memory Performance in Older Persons? Results of a Randomized, Placebo-Controlled, Double-Blind Trial. *The Journal of Alternative and Complementary Medicine* **16**, 753-759 (2010).

79 Cunha, R. A. & Agostinho, P. M. Chronic Caffeine Consumption Prevents Memory Disturbance in Different Animal Models of Memory Decline. *Journal of Alzheimer's Disease* **20**, S95-S116 (2010).

80 Koppelstaetter, F. *et al.* Caffeine and Cognition in Functional Magnetic Resonance Imaging. *Journal of Alzheimer's Disease* **20**, S71-S84 (2010).

81 Adan, A. & Serra-Grabulosa, J. M. Effects of Caffeine and Glucose, Alone and Combined, on Cognitive Performance. *Human Psychopharmacology* **25**, 310-317 (2010).

82 Singh, K. *et al.* Nicotine- and Caffeine-Mediated Changes in Gene Expression Patterns of MPTP-lesioned mouse striatum: Implications in Neuroprotection Mechanisms. *Chemico-Biological Interactions* **185**, 81-93 (2010).

83 Herman, A. I. & Sofuoglu, M. Cognitive Effects of Nicotine: Genetic Moderators. *Addiction Biology* **15**, 250-265 (2010).

84 Mumenthaler, M. S. *et al.* Psychoactive Drugs and Pilot Performance: A Comparison of Nicotine, Donepezil, and Alcohol Effects. *Neuropsychopharmacology* **28**, 1366-1373 (2003).

85 Yesavage, J. A. *et al.* Donepezil and Flight Simulator Performance: Effects on Retention of Complex Skills. *Neurology* **59**, 123-125 (2002).

86 CESAR. *Ritalin*, <http://www.cesar.umd.edu/cesar/drugs/ritalin.asp> (2005).

87 Agay, N., Yechiam, E., Carmel, Z. & Levkovitz, Y. Non-specific Effects of Methylphenidate (Ritalin) on Cognitive Ability and Decision-Making of ADHD and Healthy Adults. *Psychopharmacology* **210**, 511-519 (2010).

88 *Dextroamphetamine and Amphetamine*, <http://www.ncbi.nlm.nih.gov/pubmedhealth/PMH0000166> (2010).

89 Farah, M., Haimm, C., Sankoorikal, G. & Chatterjee, A. When we enhance cognition with Adderall, do we sacrifice creativity? A preliminary study. *Psychopharmacology* **202**, 541-547 (2009).

90 *Modafinil*, <http://www.ncbi.nlm.nih.gov/pubmedhealth/PMH0000196> (2008).

91 Caldwell, J. A., Caldwell, J. L., Smythe, N. K. & Hall, K. K. A Double-Blind, Placebo-Controlled Investigation of the Efficacy of Modafinil for Sustaining the Alertness and Performance of Aviators: A Helicopter Simulator Study. *Psychopharmacology* **150**, 272-282 (2000).

92 Killgore, W., McBride, S., Killgore, D. & Balkin, T. The Effects of Caffeine, Dextroamphetamine, and Modafinil on Humor Appreciation During Sleep Deprivation. *Sleep* **29**, 841-847 (2006).

93 Randall, D. C. *et al.* Does Modafinil Enhance Cognitive Performance in Young Volunteers Who Are Not Sleep-Deprived? *Journal of Clinical Psychopharmacology* **25**, 175-179 (2005).

94 Randall, D. C., Fleck, N. L., Shneerson, J. M. & File, S. E. The cognitive-enhancing properties of modafinil are limited in non-sleep-deprived middle-aged volunteers. *Pharmacology Biochemistry and Behavior* **77**, 547-555 (2004).

95 Killgore, W. D. S. *et al.* Effects of dextroamphetamine, caffeine and modafinil on psychomotor vigilance test performance after 44 h of continuous wakefulness. *Journal of Sleep Research* **17**, 309-321 (2008).

96 Wesensten, N. J., Killgore, W. D. S. & Balkin, T. J. Performance and alertness effects of caffeine, dextroamphetamine, and modafinil during sleep deprivation. *Journal of Sleep Research* **14**, 255-266, doi:10.1111/j.1365-2869.2005.00468.x (2005).

97 Killgore, W. D. S., Kahn-Greene, E. T., Grugle, N. L., Killgore, D. B. & Balkin, T. J. Sustaining Executive Functions During Sleep Deprivation: A Comparison of Caffeine, Dextroamphetamine, and Modafinil. *Sleep* **32**, 205-216 (2009).

98 Porrino, L. J., Daunais, J. B., Rogers, G. A., Hampson, R. E. & Deadwyler, S. A. Facilitation of Task Performance and Removal of the Effects of Sleep Deprivation by an Ampakine (CX717) in Nonhuman Primates. *PLoS Biol* **3**, e299 (2005).

99 Slutsky, I. *et al.* Enhancement of Learning and Memory by Elevating Brain Magnesium. *Neuron* **65**, 165-177 (2010).

100 Macklin, R. Ethical Relativism in a Multicultural Society. *Kennedy Insititute of Ethics Journal* **8**, 1-22 (1999).

101 Moody, E. F. *Life Expectancy Tables*, <http://www.efmoody.com/estate/lifeexpectancy.html> (2010).

102 Pallesen, K. J. *et al.* Cognitive Control in Auditory Working Memory is Enhanced in Musicians. *PLOS One* **5**, 1-12 (2010).

VITA

Kelly R Daigle completed her undergraduate work at North Carolina State University and received both a Bachelor of Science in Biology and a Bachelor of Science in Molecular and Structural Biochemistry. Following graduation, she completed a two year research appointment at the National Institute for Environmental Health Sciences in the laboratory of Dr. Serena Dudek. During this time, she studied synaptic plasticity and, more specifically, synapse elimination during development. In 2009, she enrolled at Wake Forest University in the Masters of Bioethics program. Following completion of the program, she will begin a global medical education program through the University of Queensland in January 2011.