Lecture 1: "The New Science of the Mind and Brain"
SFU Harbour Centre, 28 February 2007

The notice for this series of three lectures gives a brief statement of the main theme of each one: **[Slides 1/2]**

1. Tonight I explore the idea that the meaning of scientific progress changes for us, once it begins to reach inside our genes and, especially, into our minds.

2. The second lecture focuses on the long historical trajectory of the relation between science and society, using the idea of Enlightenment.

3. The third suggests that all of us must get much more deeply involved in the discussion of the achievements of science in relation to traditional structures of ethics and values, as the choices confronting us about the manipulation of life become more and more significant.

When Science "Gets Personal" [Slide 3]

Tonight I begin with what may appear to you to be a trivial notion – the idea that the busy enterprise we know as the modern sciences of nature has begun, quite suddenly, to touch our lives in very personal ways. This was not always the case, if we think back in time about 250 years, which was when the so-called "scientific revolution" really started to gain momentum – when it started to demonstrate, consistently, a relevance for technological applications that promised to improve the everyday life of people. **[Slide 4]** Chemistry was the first in line. Antoine Lavoisier, known as the "father of modern chemistry," lived in the second half of the eighteenth century. By the early years of the twentieth century – only about one century after Lavoisier's tragic death, at the age of 51, during the Reign of Terror in France – chemistry was being used by industry to turn out an endless stream of useful consumer products.

Then it was the turn of physics, the revolutionary science of the first half of the twentieth century, producing not only a radical new form of energy, from atomic fission, but also, of course, weapons of almost unimaginable destructiveness. **[Slide 5]** But in all of the industrial technologies based on the sciences of chemistry and physics, one would be hard-pressed to locate any type of personal significance: They touched the lives of individuals by a very indirect route, through new forms of energy and new types of commodities, including new medical therapies.

Biology, however, is different. Already in the second half of the nineteenth century it had shown itself to be a different type of science, so far as its social impact was concerned. This was, of course, the era of Darwin and Mendel, the era of evolutionary biology and the early clues as to how living things reproduce. **[Slides 6/7]** Society's reaction to the idea of animal evolution was instantaneous and vociferous. It goes on, even today. But it was not until the coming of molecular biology – the branch of biology that focuses on the DNA molecule – that the long trajectory of modern science arrived at the point where we can say that science is, truly, "up close and personal."

"Genomics" is the study of genomes, the so-called "templates of life" for all plants and animals, including humans, of course. Genomes are information systems: The human genome can be represented as a barcode made up of some three billion lines of code, called nucleotides or base-pairs. Just four chemical compounds, abbreviated A, C, G, T, are needed in order to write the code; they occur in two pairs, A/C and G/T. (The name of the film "Gattaca" contains these four letters.) **[Slides 8/9/10]** When we say that a genome has been "sequenced," we mean that we have figured out the order in which those sets of base-pairs follow one another. The readout of a stretch of DNA, therefore, gives us something like: GGAAAATTCCTTTAAG (and it goes on and on, just like that, for three billion letters!).

We usually think of genomes at the species level, that is, what we have in common with all other humans, and what differentiates us from other animals, especially our closest relatives, the chimpanzees. **[Slide 11]** But even the genomes of species become personal when we realize that each of us carries slight differences – in that long sequence of four letters – from everyone else. This small variation, which is referred to as "alleles," turns out to be highly significant in terms of, for example, our risks for contracting inherited diseases, or how well certain drug or other therapeutic interventions work on any of us. So human genetics turns out to be a science that is involved with extracting and using information of a very special kind, with intensely personal significance.

"Well, so what?" you might reply. Or: "That's good, my doctors might need such knowledge if I happen to become seriously ill." In this first lecture I will be offering some thoughts on what larger implications this form of knowledge might hold for us. I will be suggesting that it changes fundamentally the meaning of modern science, and what it is accomplishing. The changes to which I refer do not occur within the practice of science itself; in that respect, nothing that molecular biologists do in their research programs is, or indeed could be, different from what chemists and physicists do. (The reason is that the DNA molecule, which is a chemical structure, necessarily obeys the more general "laws" describing the behaviour of all chemical compounds; and, in turn, all chemical compounds are forms of matter that have atomic structures and thus obey the "laws" of physics.)

Instead, the changes in meaning I refer to occur in science's social context, that is, in the wider social order within which all scientists work. In becoming "up close and personal," science now touches directly on many of the most sensitive and meaningful domains of human cultures. These domains include sex, gender and reproduction; the evolution of species; how we distinguish right from wrong; and, more generally, all of the traits that make up our behaviour as well as the degree to which we are responsible, as individuals, for what we do. Looming over all of these domains is a question posed to us that we have never had to answer before during all of human history to date: Would you like to change any of this? And if so, would you like to make such changes not just for yourselves, but for your children, and all of your descendants, while you are at it? **[Slide 12]** Finally, with respect to these questions, do you believe that such decisions are rightfully yours alone to make, without oversight or interference by others or by governments?

The Science and Technology of the Mind and Brain [Slide 13]

For the remainder of this first session I will focus on the personal sphere, primarily on the sphere of the brain, that truly remarkable natural organ that each of us carries around; in its activity arises what we call our minds. **[Slide 14]**

We usually regard the mind as an instrument which we can apply to various tasks, such as thinking about problems. But it is much more than that; in fact, most of what our mind does is spontaneous and inner-directed. Most of its activity takes place below the threshold of consciousness. Here's an example: One of the things our minds are really good at is free-association. One of my personal quirks is that I read and think a lot about our closest relatives, the bonobos and chimpanzees, and I spend time with them at zoos whenever I can. Two years ago I had a chance to visit the large and opulent new chimp enclosure at the zoo in Sydney, Australia. The females and infants were mostly grouped directly across from the viewing platform, observing the tourists. But far off in the distance, against the back wall, were a group of males, hanging out (you can tell because the males are much larger than females). These were common chimps, not bonobos, and in this species the males are known for aggressiveness. They looked for all the world like the members of an outlaw urban gang, bonding with each other and considering mischief. This image stuck in my mind. **[Slide 15]**

A few weeks ago I was performing exercise rituals in a gym at my local Y in Ottawa. The weights are in one corner of a large room. At one point I glanced up and noticed that there was a group of young males who happened to be working together on the weights. Instantly – literally in a matter of milliseconds – the mental image of the band of male chimps flashed into my conscious mind. In effect, my mind was asking me: "Is what you now see like that other image, by any chance?" As this happened, I just stopped what I was doing and stood there for a few moments in utter amazement.

Broadly conceived, the trajectory of modern development moves from the enhanced capacity to manipulate matter and energy in our external environment – the world "out there" – to the world of our personal space, that is, our own bodies and minds. Phrased otherwise, we who seek to turn everything else in the world into "stuff" to manipulate, in order to better satisfy our needs and whims, become such stuff ourselves. Neuroscientists want to know, for example, how the mass of tissue in our heads carries out its amazing, complex functions, such as the little act of free-association I just mentioned – the brain functions that we otherwise refer to as mental activity. And once we know how it works, we are on the way to being able to play around with it – to repair it, say, when it's damaged, or perhaps even to upgrade its performance.

This is a perfectly "logical" development, when one stops to think about it. Our technologies are intended to serve our needs and desires. We like bodily comforts, stimulating experiences, movement, erotic and sexual pleasures, personal safety, regular doses of psychoactive substances (caffeine and beyond), social interactions with others, emotional bonding with infants, and on and on. This is nothing new: It was Plato who first remarked, "We all have many needs." But it was inevitable that, sooner or later, the technological imperative would move toward the source of all those needs, as it were. After all, we are mammals, and more specifically primates. Recall the list of needs I just mentioned – bodily comforts, sexual pleasure, psychoactive substances, challenging activities, emotional bonding: Over the last few decades we've discovered that monkeys too like those same things, more or less. **[Slide 16]**

The sources of our manifold needs and desires are, in short, our bodies and minds. So why not just manipulate the sources directly? That is exactly what we have set out to do. Already a great deal of attention has been focused on manipulating bodily attributes, of course, especially in the area of competitive athletics (blood doping is an example). I want to leave that area aside and concentrate just on the mind, because it is in that realm where we approach what is most personal and intimate for all of us.

What are some of these "personal and intimate" aspects of the brain and mind that are now the subject of intensive and systematic investigation in the neurosciences? First, the broad category of "higher cognitive functions" – the apparatus we have for learning, reasoning, and making judgments. These include memory, of course, plus attention, motivation, language, calculation, multi-tasking, and many others. There is a suite of traits we refer to as "mood" or "affect," which is a kind of crossover zone between thinking and emotion: Neuroscience tells us that the brain is first and foremost an emotional organ; for example, children's capacity to learn is strongly link with feelings of emotional security.[1] Falling in love? Studies of the mental circuitry of people involved in a new sexual relationship show how the brain's reasoning powers are literally hijacked and taken off-line temporarily.[2]

Then there are a whole set of mental traits that, when they are dysfunctional, cause so much grief for individuals, their families, and society. Things like aggression, violence, and psychopathology; also addiction, depression, schizophrenia, anxiety, and fear. With respect to this entire list, both the good and the bad, what we have learned falls into two categories. **[Slide 17]** One is the biochemistry of signal transduction in the brain: The brain works by using chemicals known as neurotransmitters to send electrical impulses, and we can intervene in these processes. The most familiar case is the Prozac-type drugs, which work by influencing the production of serotonin, for treatment of depression. The second is gene expression: Scientists have begun to discover the specific genes involved in many of the mental traits I have referred to, for example, memory.

I will give a few examples in a moment. First I want to distinguish two broad categories of therapeutic interventions in brain function. The first might be called "repair and rehabilitation." As already mentioned, we can influence the brain's supply of chemical neurotransmitters in order to deal with certain types of illnesses. We also hope to be able, one day, to repair defective genes, the ones responsible for inherited single-gene disorders, such as those which cause severe mental retardation ("Fragile-X Syndrome" and others).[3] Or, at the very least, we hope to be able to identify such disorders through genetic diagnostics, giving us the option of screening out early-stage embryos that carry defective genes.

The other category is a more problematic one, namely, interventions designed to enhance specific brain functions in otherwise healthy individuals. Let's take memory as an example. Neuroscientists have discovered how the brain stores and retrieves our memories, as well as the supremely important process, carried out by chemicals and directed by a number of genes, whereby the brain converts short-term to long-term memories. (The area of our brain known as the hippocampus is the principal site of this activity.[4]) There is a huge amount of interest in therapeutic interventions, of course, since many kinds of neurodegenerative diseases, most famously Alzheimer's, involve permanent and severe memory impairment. **[Slide 18]** A number of privately-controlled companies, one of which has the charming name of Memory Pharmaceuticals, are now vying for the prize of developing drug therapies designed to restore impaired memory. It is routine for scientific articles on this type of brain functions to include references to potential therapeutic strategies based on the latest findings, for example: "Our observations reveal an endogenous function of [the hormone] ghrelin that links metabolic control with higher brain functions and suggest novel therapeutic strategies to enhance learning and memory processes."[5]

Who else might be interested in such drugs? How about students? If you put the phrase "memory enhancers" into your search engine, you will find some interesting links to news articles about recent scientific discoveries in this area. On the right-hand side of the page, under "sponsored links," you will find drugs offered for sale under the following headings:

- Pregnenolone, the brain and memory enhancer, 50mg, 60 pills, $9.95;
- "Get a photographic memory – remember names, facts and numbers! Get higher grades with less effort!";
- Nonprescription drugs that may inhibit age-related memory decline in your dog or cat (why not try some yourself while you're at it?);
- At www.brainquicken.com, order the "world's first neural accelerator," based on "clinically supported science used by students at Harvard, Princeton, Yale, Oxford, and Tokyo universities," as well as by world-champion athletes, which will increase short-term memory by 35% in just 30 minutes or less. **[Slide 19]**

Of course, if you are in a hurry, you might miss the little news item about another scientific finding, based on experiments with aged rats, reporting that some drugs touted as long-term memory enhancers actually worsened considerably the operation of short-term "working memory" in another part of the brain, the prefrontal cortex. (For some reason I enjoy discovering that we can obtain reliable guidance about how our own minds work by studying the brains of rats.) **[Slide 20]** At any rate, eventually it will all work out, and such unfortunate side effects will be eliminated.

Since we are on the subject of cognitive enhancement, I should note that many of the techniques under experimental development deal with what is called the "machine – brain interface." In general, this refers to connecting mechanical supports directly to a neural interface. Such interfaces are in advanced development for prosthetics, moving an artificial limb, for example, in response to a thought-command in the brain. In a newsworthy series of experiments, researchers at Duke University first developed a computer program that correlated neuronal firing patterns in the brain with the movements of a robotic arm, by implanting hundreds of tiny electrodes in the brain regions where arm movements are controlled, and recording the output signals from the brain. **[Slide 21]** In 2003 they used this technique with two female macaque monkeys, as they operated a joystick that moved a cursor on a computer screen.[6] Then they incorporated a robotic arm into the sequence, removed the joystick, and watched as the monkeys learned that they could "grasp" and move the cursor just by waving their arms in the air. After a few more days of practice, the monkeys had learned that they could perform these functions just by thinking about doing so, with their arms hanging by their sides. Two years later, the researchers reported a more astonishing result: The monkey's brain seems to have changed as a result of this experience, distinguishing between its own arms and the new device, in effect treating the prosthetic device as its own "third arm."

Other experiments under way now are, for example: linking two persons using a neural interface (the researcher and his wife both had electrodes implanted in their arms, and one can feel when the other moves an arm); a brain prosthesis – an artificial hippocampus or "memory bank" to be implanted in the brains of Alzheimer's sufferers; a direct interface between a brain and a computer; and a pacemaker-like device from which wires lead into the brain, designed to treat and control everything from Parkinson's symptoms to migraines, chronic pain, depression, addiction, and obsessive-compulsive disorder.[7]

So, to repeat, we have two broad categories of intervention, namely, repair and enhancement. At present, both are conceived as a one-time alteration, of course. In the longer term, however, genomics holds out the possibility of inter-generational changes through alterations made in what is called the "germline," something already routine in the cases of plants and laboratory rodents. This is of particular interest where particular traits are strongly linked with specific genes, thus suggesting that a gene modification would substantially reconfigure an individual's behaviours or capacities. Let me give a few examples.

Acts of violence, and especially the type of predatory violence that is associated with psychopaths, are common in human societies, causing profound harms to people and communities. Neuroscientists have found that genetic anomalies play an important role here. You will recall an earlier mention of "alleles," the tiny variations – sometimes a single nucleotide (one in three billion, remember) – in the genomes of all of us. **[Slide**

22] Well, it turns out that such infinitesimally-small changes can have enormous implications:[8]

> It is unlikely that genes directly code for violence; rather, allelic variation is responsible for individual differences in neurocognitive functioning that, in turn, may determine differential predisposition to violent behavior. Genes regulating serotonergic neurotransmission ... have been highlighted in the search for a genetic predisposition to violence.

Misfunctioning involving the neurotransmitter serotonin shows up in many mental disorders (I have already mentioned depression). There is another gene, known as the human serotonin transporter gene, that is active in the brain region known as the amygdala, where our fear response is located. **[Slide 23]** Allelic variation here causes huge differences in levels of anxiety and fear, both innate and learned, as experienced by individuals. Polymorphisms in another gene altogether have been shown to explain differences among individuals in anger and aggressivity.[9] Progress is being made in isolating the genes whose misfunctioning may be important for the etiology of affective disorder (psychosis) and schizophrenia.[10]

I want to tell just one more story from the record of recent neuroscience, because it prompted a good deal of media notice and commentary about the wider implications of the scientific findings. One fine day in a laboratory in Germany, a research team noticed something strange and later published a note about unusually violent behaviour in lab mice which were missing a gene, named "tailless," that was well known from research on the fruit fly. **[Slide 24]** This gene is active in very early stages of embryonic development; a spontaneous mutation in the mouse colony in the German lab had deleted it entirely. Another scientist, now at UBC, bred a hybrid line of mice with the missing gene in order to study their behaviour more thoroughly. She called her mutants "fierce mice" for straightforward reasons: They not only had abnormalities in the eye, the limbic system of the brain, and the olfactory bulb, but also exhibited astonishingly violent aggressive behaviour – the researchers themselves labeled it "pathological" – in both sexes (such aggressiveness is very rare in normal female mice). They chewed off their own tails; moreover, "fierce mice" routinely attacked and killed their siblings, including mating partners, and the females also lacked maternal behaviour, simply abandoning their pups in the nests.[11]

This was interesting enough to attract the attention of newspaper reporters, including Carolyn Graham of the *Globe and Mail.*[12] In interviews the researchers expressed their own surprise at their findings: "Even in a mouse, it's quite a surprise that a single gene would do this and be able to change the brain that much," said UBC Professor Elizabeth Simpson, one of the lead scientists. In her interviews the reporter unearthed the information that this gene also exists in humans, and she commented: "The finding also suggests that medicine might one day concoct a gene-therapy treatment – or even a cure – for extreme aggression." (The gene sits on human chromosome 6.) Her comment may have been prompted by Professor Simpson's other remark: "There is a growing field recognizing the potential of mice to study human brain disorders." So the reporter called Margaret Somerville at McGill, a frequent commentator on bioethics issues, who took the matter in a different direction altogether: "We have to be terribly careful about these things because humans are different from animals," she said. "It's fascinating research, but scary if it turns out to be true for us." Actually, I find it quite comforting to learn that we carry a gene so strongly conserved in evolution that it's in the genome of the fruit fly, from which we diverged about 600 million years ago. **[Slide 25]**

But news about the team's second publication, in 2005, was good enough for the newspaper's front page. The research objective was stated as follows:[13]

> Determining the subset of observations from mice that generalize to humans remains challenging because of differences between the species. From this perspective, we reasoned that establishing a paradigm in which one could functionally evaluate the ability of a human gene to shape behavior ... would be powerful. Toward this end, we generated transgenic mice expressing the human form of orphan nuclear receptor 2E1 ... and evaluated the ability of this human gene to modulate the behavior of mutant mice, which in its absence would have demonstrated pathological violence.

The researchers first created transgenic mice which carried copies of the cloned human version of the target gene, then crossed them with the "fierce" mice in which the comparable mouse gene is absent. In the offspring all the abnormalities were absent: The human gene had "cured" the mutant mice. They concluded: "Our data support the hypothesis that variation at *NR2E1* may contribute to human behavioral disorders."

Can you see in the passage a clue as to why this piece of research could be found on the front page of the *Globe and Mail*?[14] This is Carolyn Abraham's opening sentence: "A breakthrough experiment has used a human gene to turn vicious mice into very gentle creatures – holding out the prospect of doing similarly sweet things to violent people." Good journalists get right to the point, don't they? It gets better. A few paragraphs later came the real zinger: "As such, the experiment raises the possibility of designing a gene therapy to counter aggression – as well as the eerie spectre of enhancing it." This apparently tangential development of the issues seems to have been prompted by the reporter's second conversation with Margaret Somerville, who told her, as paraphrased by Abraham, that "concerns already have been raised that some country or group might try to use such research to design perfect soldiers whose genes are manipulated to make them fearless killers." **[Slide 26]** But Professor Simpson had the last word and sought to dampen the effects of such alarmist discourse with a physiologist's perspective. In her own words, as quoted by Abraham: "For some reason we think the brain is different from your liver, yet we should see the brain as no different than any other part of our body."

Well, perhaps. First let's ask: Is the reference to soldiers really appropriate here? It turns out that one agency that is very much interested in the results of neuroscience reasearch goes by the acronym DARPA – the U. S. government's Defense Advanced Research Projects Agency. A new book has just been published on this subject, and I will give you just one example from it. One very important area of brain research these days, in the general area of memory, is the desire to help people who are repeatedly traumatized by recurring memories of acts of violence which they have suffered. As I mentioned earlier, our brain is highly sensitized to emotion, and it is the fate of such persons to be forced by their own brains to relive regularly the traumatic event that occurred earlier. A treatment regime has been developed, on the basis of the research, using the beta-blocker propranolol, because it appears to interrupt the biochemical process involved in the consolidation of long-term memory in the brain. So far, so good. On the other hand, DARPA is interested in the question as to whether propranolol could be administered successfully as a prophylactic – in other words, if it were given in advance to soldiers who are about to enter into combat, whether it would inhibit the formation of long-term memories associated with the horrific scenes that they would be encountering there.[15]

A Truncated Dialogue [Slide 27]

How many of you here tonight remember hearing about the fierce mice discussions in the media? Not very many, I suspect, nor even if you did recall the publicity would you necessarily remember what had been said. As you can tell from the summary I gave you, very serious issues of ethics and social policy were raised in the excellent article that Carolyn Abraham wrote for the *Globe and Mail*. And yet, after the day of publication, the concerns addressed in her piece pretty much vanished, perhaps to resurface again in a few academic articles of severely limited circulation – until the occurrrence of the next episode of one-day media attention elicited by a scientific journal article that happens to strike the journalists' fancy.

I have been referring to neuroscience research as just the most dramatic instance of the culminating point in time, during the long trajectory of modern science, at which science becomes "up close and personal." My main argument is that the meaning of science for the future of individuals and societies changes radically, and qualitatively, at that point in time. Why? Because modern science asks, not what nature "is" in any metaphysical or religious sense, but only *how it works*. What happens – in terms of effects that can be measured and repeated – when we understand enough about natural processes, such as protein synthesis, to intervene in them and manipulate the sequence of steps and thus influence the outcomes? **[Slide 28]** Through its experimental methods and its inherent orientation toward technological applications, science shows us how to adapt natural processes more precisely and efficiently to human purposes.

The first stages of discovery, in chemistry and physics, revealed to us how the world outside, our physical environment, functions – that is, through precisely what causation chains specific effects are produced. Beginning in the nineteenth century, these insights, and the technologies built upon them, brought forth entirely new materials (such as steel) and sources of energy (electricity). By the end of that century, department stores and merchants' catalogues were chock-full of new commodities; together with amenities such as public health and sanitation regimes, these goods began to change the conditions of life in ways previously neither imagined nor feasible. The one constant in this revolutionary transformation of human life, however, was the human being itself, now disposing over vast new resources in material wealth, cultural monuments, and popular entertainments, but also busily perfecting the savage exploitation of foreign colonies, new forms of political oppression, and ominous technologies of warfare. Amidst all that was innovative and different, the average representatives of the human species were fully recognizable as the natural heirs of earlier historical epochs. In other words, they continued to behave a lot like their predecessors, except that now they were wielding exceptionally potent technologies. And so, by the time the twentieth century drew to a close, it had attained the status of being the bloodiest hundred years in recorded history. **[Slide 29]**

As I mentioned toward the beginning, there is something eminently "logical" in the latest phase of development: The lens of science, focused for so long on the world outside, turns 180 degrees and now peers inside us. Every last aspect of the natural environment has been successfully analyzed, manipulated and steered toward the satisfaction of human purposes – and now it is our turn. On what basis could we claim an exemption? We too are made of the same materials as everything else, a bit of nitrogen, hydrogen, oxygen, and carbon (and not very much at that, as the ash residue from the crematorium indicates). So far as our precious brains are concerned, they're a lot bigger than every other mammal's, in terms of the ratio of brain to body mass; but in structural terms what we carry around in our skulls is not all that different from what's inside a rat's head. Yes, I know, we have special brains, capable of religious ecstasy, mystical meditation, mathematical proofs, and other things we're pretty sure your average rat can't do. But *in neurological terms* these operations have *exactly* the same characteristics as the rat's ratiocinations: the firing of neurons in response to chemical neurotransmitter cascades and the generation of patterns of electrical discharges in all directions across the regions of the brain.

Using brain-imaging techniques (fMRI scans), which give real-time readouts of the living brain's neural circuitry at work, scientists are well on their way to finding what the news media have happily named the "God spot." The experimental subjects are a group of elderly Montréal nuns:[16] **[Slide 30]**

> Brain scans of nuns have revealed intricate neural circuits that flicker into life when they feel the presence of God. The images suggest that feelings of profound joy and union with a higher being that accompany religious experiences are the culmination of ramped-up electrical activity in parts of the brain. The scans were taken as nuns relived intense religious experiences. They showed a surge in neural activity in regions of the brain that govern feelings of peace, happiness and self-awareness.

Alas, there is no single "spot": at least twelve different regions of the brain were recruited in response to the task. In another now-famous study, a different research team did MRI scans of the brains of Tibetan monks trained in meditation exercises, and of a control group of persons with no such training, and watched what happened inside their heads when they were asked to think about the concept of universal compassion. They found not only huge differences in the sheer scope of brain activity, as between the two groups, but also as between the youngest and the oldest monks.[17] This data provides a marvelous confirmation of the idea that we can change the way our brain works in accordance with the tasks we ask it to do over our lifetime.

But to the neuroscientist this mighty organ is still, in the end, just tissue. This is fair game for the research agenda, because it's sufficient to achieve the desired objective, namely, to find out how this organ works – first, for the sheer pleasure of knowing (and being the first to publish) and second, for the possibility of setting in motion a process of innovation leading to more effective medical therapies. Clinical depression, for example, is a widespread and terrible burden. Understanding precisely the nature of the deficits in neurotransmitter sequences and gene expression that are associated with this disease is an indispensable ingredient in the formulation of more effective therapies. This same formula holds for schizophrenia, severe anxiety, addiction, and many other mental disorders. There is almost no upper limit to the benefits that can be obtained by individuals, families, and societies generally from further advances in this area.

Certainly this category of treatment regimes is not free of ethical controversy by any means: We have to be careful in how far we go in converting traits associated with mental activity into therapeutic problems – just think about the process of defining "deviant behaviour" – for which treatment is either recommended or required. (In the United States, schools can require children classified as "hyperactive" to be treated with ritalin as a condition of attendance.) **[Slide 31]** Such responses are to be expected where the behavioural anomalies related to an individual's mental condition affect others in the social environment, for example in the classroom. Some of the other traits mentioned earlier, such as impulsive violence and psychopathology, result in very serious harms to innocent persons. To the extent to which they are confirmed to be strongly associated with specific neurological deficits, including genetic variation, it will be possible to identify a propensity toward such behaviours in advance of its actual manifestations. So we will have to consider whether compulsory therapeutic interventions, sanctioned by legal processes, can be justified on the basis of the identification of an innate psychopathic propensity. **[Slide 32]**

Neurocognitive enhancement therapies pose completely different types of social dilemmas.[18] Here we have to start by distinguishing a person's efforts to achieve peak performance of his or her natural abilities, on the one hand – say, by studying hard for school exams – from attempting to "boost" one's natural capacities themselves, intially by drug interventions and later by genetic ones. Methylphenidate is an amphetimine-like central nervous system stimulant which, oddly enough, has a "calming" effect; it is the active ingredient in Ritalin, used to treat ADHD (attention-deficit hyperactivity disorder) and is prescribed also for narcolepsy, chronic fatigue syndrome, and traumatic brain injury. In the United States it is also a Schedule II controlled substance, due to its addictive potential – which has not prevented it from being self-administered as a "brain-booster" by many students at upper-class prep schools.[19]

Such experiments in neurocognitive enhancement occur in a specific kind of highly-competitive social environment. Superior performance in schooling results in gaining access to "elite" institutions which, in turn, virtually guarantee success for their graduates in later life, as measured by high income, wealth, and social status. In Japan, South Korea, the United States, and some other countries, competition for entry begins in the preschool period and proceeds though stages to the university level. This process is a zero-sum game: The number of entrants is fixed for each targeted institution, with each successful candidate occupying a place denied to all others who aspire to it. Once it is demonstrated that a certain type of therapeutic intervention can provide enhanced performance at the cognitive skills required for academic work, every competitor will be under extreme pressure to avail himself of it. Then the new, higher performance level will become the norm, leading to searches for further therapeutic innovations, and so on *ad infinitum*.

We are only at the beginning of a flood of such developments. The great wave of new neuroscience research, made possible by MRI technology, is still relatively recent. **[Slide 33]** So far we have witnessed only the first tentative follow-on steps in both the legitimate therapeutic innovations and the private experimentations, using pharmaceutical products, but there is intensive activity on all fronts and much, much more can be expected, especially with respect to genetics. We already have genetic screening *in utero* of developing fetuses for inherited disorders such as cystic fibrosis.

Pre-implantation genetic diagnostics, using similar screening *in vitro* at the embryonic stage, before implantation of the fertilized egg in the mother's womb, is already available in a few countries. Further off are the genetic manipulations and further still, the promise of targeted gene alterations in early-stage embryos that can be inherited by all future generations and thus become part of the spectrum of allelic variation in the human gene pool. The range of potential manipulations will not stop at the point where the body meets the mind. Indeed, why should they?

A Concluding Question [Slide 34]

I would like you to think about a final image, in the context of tonight's lecture. **[Slide 35]** Is the brain like the engine of a Japanese automobile racing engine, lying on the floor of a dirty garage, surrounded by excited teenage males, who are in the process of fine-tuning its performance for the upcoming street race? Is that how we should think about the wish, already much in evidence and gathering strength, to "upgrade" the performance of the brain's various components? After tinkering with its parts, if we don't like the results, do you think we can just undo it again and go back to the way it was before?

Remember that your brain – the foundation of your mind – is the result of nature's tinkering over the course of half a billion years. It is exquisitely fine-tuned – and, also, prone to error, not surprising, given its extraordinary complexity. It is, in fact, the most complex natural structure that exists, by a long shot. (One cubic centimeter of brain tissue contains enough "wiring" (axons) that, if laid end-to-end, would stretch for 4 kilometers.) Do you think that we can just rewire it, and expect everything to be fine?

Remember the results of the remarkable experiments at Duke University, the ones with macaque monkeys. The researchers themselves were astonished at what had happened at the end of their series of experiments: The monkey's brain had rewired itself, *all by itself*! Of all the organs in your body, only the brain could do this, because it has evolved to be adaptive in response to its experiences in the world. It will be interesting, to say the least, to see whether we like the modifications our own brains make to the experiments we will be conducting on them.

Let's leave the matter there, for the time being; we will return to it in the next two lectures.

Thank you for attending tonight. **[Slide 36]** I have some copies for sale of a fictional, futuristic scenario that deals with some of these themes.

List of Slides

[Slide 1/2: WL Info]
[Slide 3: Subtitle]
[Slide 4: Lavoisier]
[Slide 5: Atom Bomb Test, Alamogordo, New Mexico, 1945]
[Slide 6: Darwin]
[Slide 7: Mendel]
[Slide 8: GATTACA (film)]
[Slide 9: DNA Readout]
[Slide 10: DNA Double Helix]
[Slide 11: Young chimpanzee]
[Slide 12: Baby in incubator]
[Slide 13: Subtitle]
[Slide 14: Human brain]

[Slide 15: Male chimpanzees]
[Slide 16: Monkeys]
[Slide 17: Human brain]
[Slide 18: Brain of Alzheimer's victim]
[Slide 19: home page: www.brainquicken.com]
[Slide 20: Lab rat]
[Slide 21: Macaque monkey]
[Slide 22: DNA strands]
[Slide 23: Amygdala region of the human brain]
[Slide 24: Lab mouse]
[Slide 25: Fruit fly]
[Slide 26: soldiers (Iraq)]
[Slide 27: Subtitle]
[Slide 28: Protein synthesis]
[Slide 29: World War I trench warfare]
[Slide 30: Nuns]
[Slide 31: Children in school playground]
[Slide 32: Minority Report]
[Slide 33: MRI machine]
[Slide 34: Subtitle]
[Slide 35: Auto racing engine]
[Slide 36: *Hera* Cover]

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