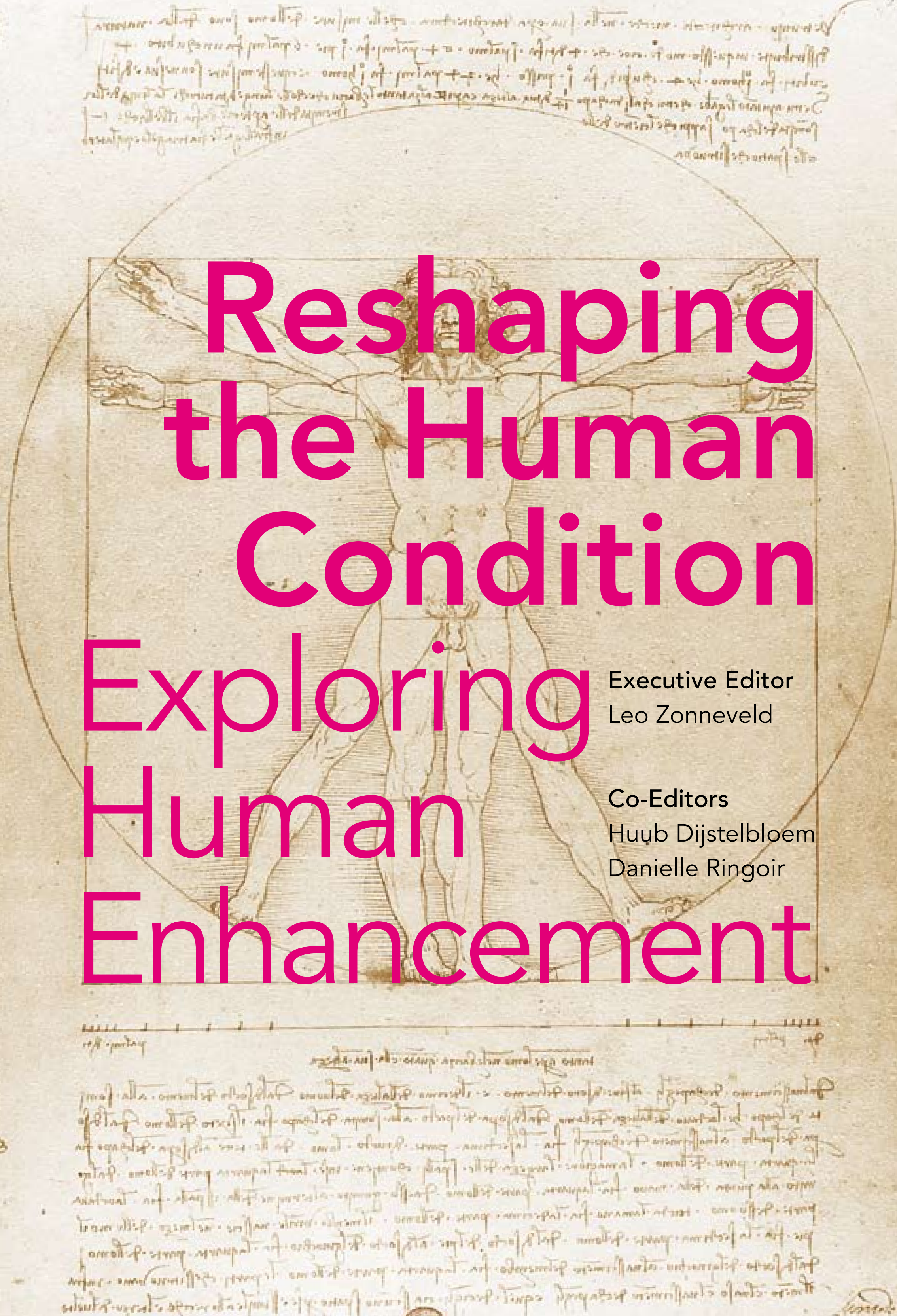


Reshaping the Human Condition

Exploring Human Enhancement

Executive Editor
Leo Zonneveld

Co-Editors
Huub Dijstelbloem
Danielle Ringoir

Reshaping the Human Condition
Exploring Human Enhancement

Rathenau Institute
Anna van Saksenlaan 51
P.O. Box 95366
2509 CJ The Hague
The Netherlands

Telephone: +31 70 342 15 42
Telefax: +31 70 363 34 88
E-mail: info@rathenau.nl
Website: www.rathenau.nl

Publisher: Rathenau Institute
Design & Layout: Smidswater The Hague / Breda
Print: Veenman Drukkers, Rotterdam

ISBN: 978-90-77364-24-6

Preferred citation:
Zonneveld, L., H. Dijstelbloem and D. Ringoir (eds.) (2008)
Reshaping the Human Condition: Exploring Human Enhancement
The Hague: Rathenau Institute, in collaboration with the British Embassy, Science and Innovation Network and the Parliamentary Office of Science & Technology, 2008.

Reshaping the Human Condition
Exploring Human Enhancement

Executive Editor
Leo Zonneveld

Co-editors
Huub Dijstelbloem & Danielle Ringoir

Rathenau Instituut

British Embassy The Hague
Science & Innovation Network

Houses of Parliament
Parliamentary Office of
Science and Technology

This is a joint publication by
Rathenau Institute (The Hague, The Netherlands)
The British Embassy, Science & Innovation Network (The Hague, The Netherlands)
Parliamentary Office of Science and Technology (London, United Kingdom)

Executive Editor: Leo Zonneveld
Co-Editors: Huub Dijstelbloem and Danielle Ringoir

Project Managers:
Leo Zonneveld, British Embassy, Science & Innovation Network
Huub Dijstelbloem, Rathenau Institute
André Krom, Rathenau Institute
Mireille den Otter, British Embassy, Science & Innovation Network

Acknowledgements:
The following texts in this volume are reproduced
by permission of the author, or their publishers:
'Neuroethics of Cognitive Enhancement', by Danielle C. Turner
and Barbara J. Sahakian. Reprinted with permission from Cambridge University Press.
Originally published in *BioSocieties*, **1**(1):113-123. 'The Cognition-enhanced Class-room' by Danielle C. Turner and Barbara J. Sahakian. Reprinted with permission from DEMOS. Originally published in *Better Humans*, DEMOS Collection **21**:79-85.
'Changing Expectations of Life', by Tom Kirkwood by kind permission of the author.

Table of Contents

Part 2 Applications and Expectations

Appendices

Contributing organisations

Foreword

by Lyn Parker

► Lyn Parker is British Ambassador to The Netherlands.

The human drive to better ourselves is nothing new. There is something very seductive about the idea of making ourselves stronger, fitter, more beautiful, more alert or more intelligent. For thousands of years humans have explored ways of doing these things. Physical and mental training, the use of stimulants and other mind-altering substances, even physical modification for cosmetic or religious purposes: all these have very ancient and culturally diverse roots.

What is new today is the rapidly expanding range of possibilities for human enhancement that contemporary science now offers, as a direct result of our growing understanding of human physiology, biochemistry and cognition, and our increasing skill in manipulating these and other aspects of human life processes. At the same time, many of these developments potentially affect not just individual human performance but also how our whole society functions, confronting us with difficult and thought-provoking ethical and social choices.

This volume, based on a fascinating day of discussion between leading Dutch and British scientists in 2007, has a two-fold objective. The first is to give an overview of some of the key directions in which modern science is pushing out the boundaries of what is possible in the field of human enhancement. The second is to flag up some of the obvious ethical and societal issues which will need fuller discussion over the next few years.

Some of these debates have already begun. Concerns about how far it is permissible to go in pursuing new scientific possibilities are most prominent in the extensive public and political debates over genomics. In education, debate is still at an early stage over the use of cognitive enhancers, although evidence suggests that the unofficial use of such drugs is rapidly increasing in some Western countries. In sport, where the emphasis is on fair competition, a clear policy against the use of enhancing drugs has emerged, while the prolonged debate over whether disabled runners using 'blades' should be allowed to compete on equal terms with able-bodied athletes illustrates some of the dilemmas when potential enhancement is available only to some.

Physical and sensory enhancement and the development of more seamless man/machine interfaces have obvious potential too, for example in improving our capacity to manage physical disability or in providing enhanced capabilities to meet specific physical or perceptual needs. While military applications are one obvious driver for research, there is a wide range of possible civilian applications as well.

No discussion of human enhancement would be complete without some consideration of longevity. The question of the natural limits to human lifespan remains open, and the ethical and social implications of efforts to extend life further are complex. However it is already clear that, while an increasing number of people are living longer, many of them are spending their final years in poor health. Finding ways to increase the length of time for which we can expect a good quality of life is likely to be at least as important as the search for greater longevity.

There is no doubt that the science of human enhancement offers exciting possibilities whose full potential we are only beginning to realise. While the potential opportunities and benefits are obvious, so are the problems and risks. We can expect an increasingly lively public debate over how to ensure that scientific progress works to the overall advantage of both individuals and society at large, while meeting ethical standards.

In the process, we will be forced to think harder about what defines us as human beings, and how far we really want to go in reshaping how we are. I hope that the discussions in this volume, bringing together the views of leading Dutch and British scientists in the field, will contribute to a better understanding of where current scientific research is heading, and to a better-informed debate about the ethical and societal implications.

Introduction

by Leo Zonneveld, Huub Dijstelbloem and Danielle Ringoir

▶ The Editors

Philosophically and culturally engaged intellectuals that are concerned by the present state of humankind traditionally form the professional elite who reflect on the human condition. They reconsider the hopes, dreams, weaknesses and sorrows of people that try to make the best of their lives. The scientific and technological developments that can be gathered together under the common denominator of 'human enhancement' change all that. Not only do they open the door to a new group of experts to think about the human condition, most of all they make clear that this condition is not only a social, cultural or philosophical topic but a scientific topic as well. Who we are, who we can be and how we may reach that are no longer exclusive philosophical and existential questions: they have entered the science domain.

Various technologies to improve our bodies and our life emerging from the fields of pharmacology, the neurosciences, biotechnology and man-machine interactions are being developed in laboratories. But they are also reaching different domains of application already. Contemporary societies adopt and transform technological innovations at an enormous speed. Today's scientific developments may reach the market and the consumer by tomorrow. As a consequence, human enhancement is rapidly becoming a societal issue. Existential questions and their scientific exploration are now reaching the public.

Where do we go from here? Cultural and technological development, in parallel with biological evolution, have enabled our species to progress at a vastly accelerated pace. Although the engines of evolutionary change are still running at nature's own pace, the human organism is speeding up its own progress by creating access to future pathways for improving its mental and physical architecture. Tools to achieve this are created by converging accomplishments in evolutionary biology with newly derived insights offered by biotechnology, the cognitive sciences, genetics, ICT, molecular biology, nanotechnology, and pharmacology. Exploration of the human boundaries of future science has finally culminated into the crucible of human enhancement.

Scenarios for promising vistas on the re-conceptualisation of the human phenomenon are written while new transhumanist paradigms verge on the horizon. Human enhancement explores the current demarcations of the human brain and body and seeks further potential for improvement. Our ancestral line and natural order do not demand us how we will evolve in future. Evidently, we will. Education, the process of learning from our tireless investigations in exploring, mimicking and copying nature, continues to have the greatest cognitive enhancing effect on humans.

Re-conceptualisation of the human phenomenon comes accompanied with pressing questions about our future. In a world of continuous change, how will human enhancement develop, influence and blend with the organic sensitivities of the human species and affect our health, cognitive abilities, life expectancy, intellectual and educational skills in the coming century? Will the ethical and social implications of techno-centred, human-induced cognitive and organic change lead to symbiotic transformation? What form should regulation take?

This blend of ethical and research questions was tabled and discussed by a group of expert scientists in human enhancement from centres of excellence in Britain and the Netherlands, united in a conference hosted by the British Ambassador in the Hague. This book presents a series of essays written by neuroscientists, life science and cybernetic specialists and experts in some of the different social domains where human enhancement technologies are already having an impact, sharing their visions and works at the *Human Enhancement Colloquium*. The essays complement their scientific presentations on the advantages and dangers of enhancement.

In providing further anchoring ground to the interested reader, essays published in this book come with two interviews on human enhancement. Human fertility expert Professor the Lord *Robert Winston* stresses the uniqueness of each human being and the decisive role played by the environment in genetic inheritance. According to Lord Winston, epigenetics and looking at the ways genes function will be the most important development in the next ten years. Cognitive neuroscientist Professor Dr *Peter Hagoort* looks from his considerable experience in brain imaging technologies to expected future developments in brain research and limitations to cognitive perfection. Both interviews divide the book into two sections of which the first looks more particularly at the ethics and impact of human enhancement, and the second at applications and expectations.

Virtually all authors in this volume are simultaneously looking at the ethical and social implications of human enhancement as part of their contribution. *Nick Bostrom* goes deeply into the specifics of human enhancement and offers arguments for more public funding for research in determining optimal pre- and parinatal nutrition. He recommends further funding of research in the safety and efficacy of cognitive enhancers, and, most importantly, to expand the disease-focused regulatory framework for cognitive enhancing substances into a health – and well-being framework. Using the disease-focused regulatory framework implies that human enhancement technology – based products such as neuro-enhancers and memory-enhancers are only allowed to reach the consumer market when they offer therapeutic relief to a well-defined disease. The unintended consequence of this is that more and more expressions of psychological and physiological behaviour are being defined as diseases. Is that what we want?

A particularly full account of ethical considerations in the field of psychopharmacological research is given in the contribution by *Danielle Turner and Barbara Sahakian* on the neuroethics of cognitive enhancement. They encourage scientists to take moral responsibility for their research and to monitor and foresee, as far as possible, the consequences of their work.

Present-day ‘brain-based’ education lacks understanding of cerebral interconnectivity and prevents neuroscience-based approaches to pedagogy and remedial interventions according to *John Geake*. fMRI centres, neuroscientists and educationists should jointly contribute to the educational cognitive research agenda. An internationally accessible database of available functional brain images of children could significantly increase the present results of neuroscientific research in human learning endeavour.

In sharing his participatory experience in criminal investigations, *Willem Wagenaar* discusses the prospects for enhancement for each of the three stages at which memory is created and retrieved. He points to the time-induced fragility of memory traces observed in executing retrieval techniques and gives rules that apply to the process of encoding, storing and retrieval of memory traces.

Gangani Niyadurupula’s contribution expects improvement of our understanding of cognitive enhancement in the next 20 years. She reviews existing methods of enhancement along with likely future developments and considers the regulatory and ethical questions they pose.

Innovative strategies to postpone and even prevent some aspects of age-related frailty, disability and disease are presented in this volume by *Tom Kirkwood*. Scientific research on ageing has enormous potential for positive synergy with developments in medicine, technology and social science, finance and industry. Ageing arises from the gradual accumulation of damage in cells and tissues which can be modulated by lifestyle, nutrition and environment. His two major challenges are to reveal the specific kind of damage that contributes to individual degenerative conditions of ageing, and to identify and exploit possible pathways to ensure that our extra expectation of life is as long as possible.

In their second contribution to this volume *Danielle Turner and Barbara Sahakian* report about positive results in enhancing cognition pharmacologically with minimal side effects in healthy volunteers using, amongst others, modafinil and methylphenidate in several of the tests at their laboratory in Cambridge.

An overview of substances, known or expected to achieve cognitive enhancement, is presented in this publication from the hand of *Wim Riedel*. In his conclusion he mentions the importance of identifying truly effective cognitive enhancers and the necessity of their validation through translational research in the field.

Current success in exchanging signals between human nervous systems, and the successful use of a microelectrode array implant in human median nerve fibres to steer robotics over the Internet, might lead to further research in enhancing and upgrading human mental abilities according to *Kevin Warwick*. Short-term prospects for application of his research include the development of unique therapeutic devices. While very much involved in further experiments by using his own body, Kevin believes brain enhancement could be augmented to a level of thought communication at long-term.

Human cognition is not limited to the biological brain since humans employ external parts of the environment to enhance cognition, according to *Catholijn Jonker* in her presentation about intelligent (software) agents from an artificial intelligence perspective. Humans, extended with intelligent software agents, profit from their sophisticated reasoning and knowledge applications to specific tasks. A reduced need for organic strength in perception speeds up interaction and scales up human performance.

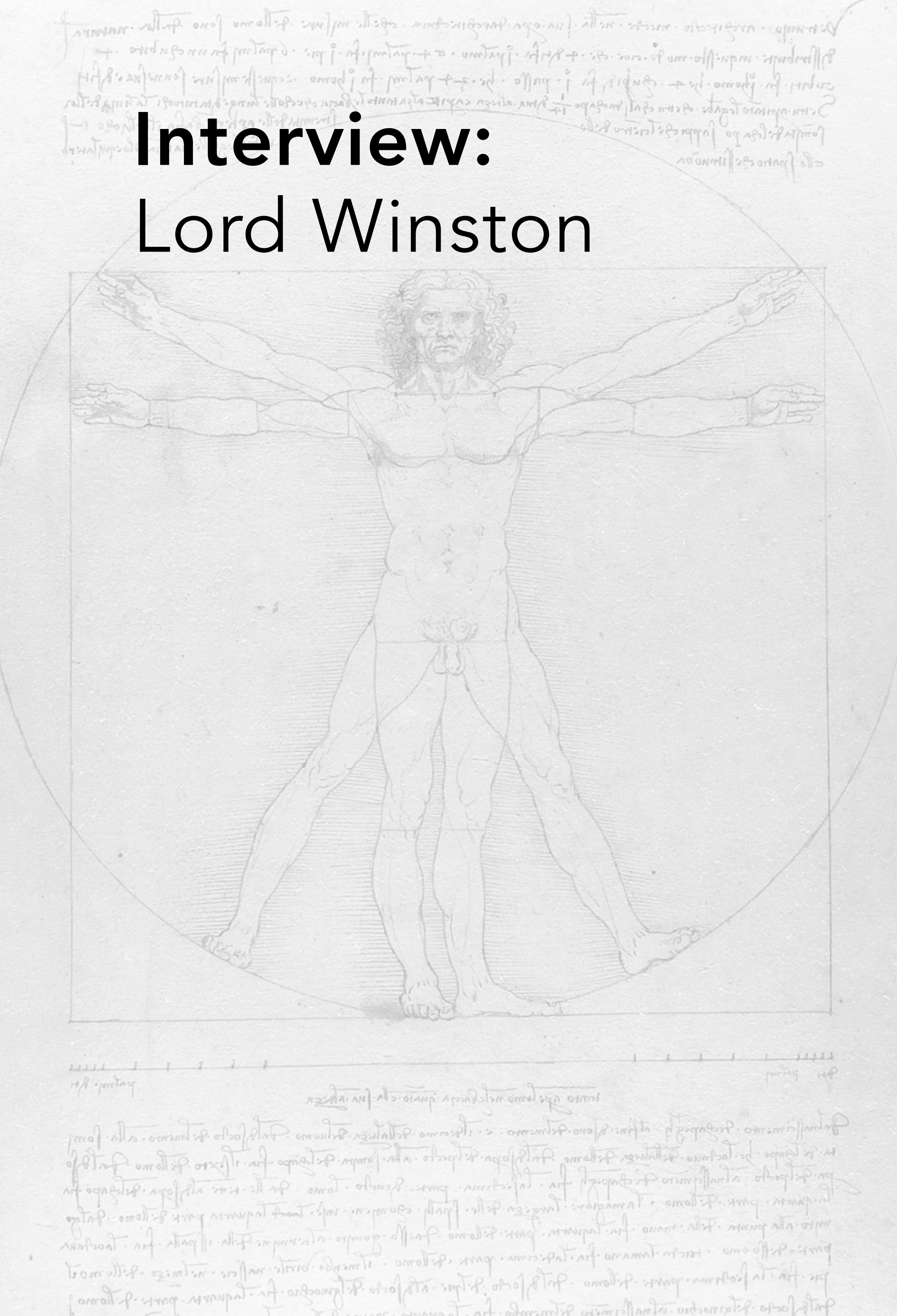
Soldier systems replace the classic soldier model and offer enhancing capabilities through networked soldier operations. The cognitive aspects of combat and research in the human emotional domain are highlighted by *Wouter Lotens*.

Interconnection technologies, including battlefield management systems and the newly introduced network enabled capability (NEC) bring in a host of new technologies, amongst which the possible introduction of exoskeletons for soldiers and future co-operation between soldiers and robots.
It is beyond doubt that humanity will go through a radical socio-cultural and technical change in the coming decades. Cognitive enhancement has already proved to be a great good in medical and psychiatric therapeutic treatment. Its further exploration in the domain of human wellbeing is slowly moving out of the experimental phase. Continued scientific research into the inevitability of the ageing process, and the limitations on human intellectual endeavour will, as all contributors to this volume aspire, be instrumental to effectively improve the human condition and its behavioural expression. The questions that exploration in human enhancement pose will need to be addressed by political decision-makers, regulators and of course the public at large.

To identify these questions and the various groups of people who are involved in this topic is not a matter of armchair-philosophy. In this book we will read the contributions of a wide variety of experts who are working in the field of human enhancement, irrespective whether they would chose to use that term themselves or not. These contributions sketch the current state of affairs in specific scientific domains and in specific domains of application. The reason to bring these authors together, however, was not only to give an impression of the state-of-the-art of human enhancement. Reasons were also to use their contributions as a starting point to discover where developments will lead us, what type of questions they pose, which groups of people will be affected by future use of human enhancement technologies and how they will transform the self-perception of people and the image of society.

It is impossible to give final answers to these questions. That would prove to be as much a case of *hubris* as human enhancement itself is sometimes being accused of. But these contributions may help us to better understand what is going on in the laboratories, and what the ulterior roots are that drive these developments. With that knowledge in mind we should be better able to anticipate on the societal impact of human enhancement and we may see more clearly in what way it will affect the human condition of our times.

Interview: Lord Winston



Cognition and its Environment: the Limitations of Genomic Intervention

► Professor the Lord Winston is Professor of Science and Society and Emeritus Professor of Fertility Studies at the Imperial College, London, United Kingdom.

Professor the Lord Winston in conversation with Leo Zonneveld accompanied by Danielle Ringoir, Science & Innovation Officer, British Embassy, The Hague.

House of Lords, Tuesday 5 February 2008

LZ: *Recognising that in the Western world, as some biologists believe, the human body in terms of evolutionary development has been optimised where do you expect future research to go in human perfectibility, and what are its drivers?*

"I hate the question because first of all, I do not believe that we are 'optimised' through evolution. If we were, we would not, for example, have a menopause. The latest data surely show that *homo sapiens* is substantially different from our nearest primate relative, the chimpanzee, in having a female menopause. This is a good example of our not being adapted to the environment in which we now find ourselves, because it would be perfectly appropriate for women, given their current state of good health by the age of 40 – 50 years old, to consider reproduction later in life. Neither do I like the idea of human perfectibility.

The notion of human perfectibility presupposes a number of issues with which I have a problem. First of all it argues a kind of certainty about what is perfect and what is imperfect. Scientists who are certain are ultimately almost as dangerous as people who have a fixed idea and unchangeable view of God.

The wonder of being human is essentially the unique and random nature of each person, produced by chance as a result of meiosis, environment and various developmental fortunes and constraints. The notion of perfectibility belittles this natural biological mystery. However, I think I can understand and live with the term 'improvement'. But do not forget, whilst a given 'improvement' may be desirable now in our society, that same trait, which we considered an 'improvement' at the time may well be thought to be undesirable in a hundred years'.

An example: we might decide today that we would want to see a generation of blonde people with blue eyes who are six foot two tall, because those features presently typify our 'ideal' human being. Yet in a different society, with a different environmental influence in a hundred years time it might be that people who are short, dark and fast-footed have become preferable. Therefore we should be very careful about what we see as perfection or improvement. I think that applies to all the issues of enhancement.

I also believe that any scientist who does not recognise the serious risks presented by your question should consider very carefully. Any form of manipulation of the human, in whatever capacity, may produce greater inequalities in our society. Although some people are very ready to ignore that argument by declaring all societies are unequal for certain people to have special enhancement which others do not increases a real problem and is likely to present a massive issue for the future of our society."

LZ: *Perhaps I may turn the question round by saying that various improvements in brain development are possible which do not directly effectuate cognitive inequality, or present a danger in producing classes in society, or a drive for competitive advance in knowledge. OECD studies have appeared, under the chairmanship of Sir Christopher Ball in 2002 (OECD 2002) and 2007 (OECD 2007), drawing attention to organic methodologies which make it possible for learning to be optimised through nutrition, nurture, training and adapted teaching processes all taking full advantage of developments in educational neuroscience.*

"Of course that is true, but equally that any time we try to 'perfect' ourselves by improving access to our education, we imply degrees of inequality in society. There is a point, I think, where your question leaves the issue of better ways of learning. Take, as an example, what we mostly regard as completely unsatisfactory human enhancement – those in the sports arena. Most people regard artificial enhancement to increase sporting prowess as undesirable. And of course, our society is ridden with inequalities and divisions but, as I asserted, we would do well not to increase them. In well-to-do Holland and well-to-do England there are fairly wealthy middle class people who can afford a bit extra for the further learning experience for their children. Governments have consistently argued about what is a desirable level of education. Regrettably, it seems that in the UK we tend to level education down, where state education is often giving the basic minimum rather than exploring the potential. Although education has improved considerably in Britain, there is a very worrying study in a report from UNICEF. Admittedly it may not be totally statistically relevant in all respects but it should give pause for reflection. It was published last year and looks at how children are nurtured in our respective societies in OECD countries (UNICEF 2007). It turns out that Britain and America have some of the worst deprivation of children, the most serious child poverty, often a very poor learning experience, the lowest standards in some aspects of school work, the poorest relationship with other children and a worsening relationships with their parents. It shows a whole range of tensions within our society. If we then added in a practice of cognitive enhancement we could end up in a potentially inflammatory situation. By the way, Holland scored well in the UNICEF study and Denmark and Sweden scored higher than anywhere else. The Netherlands, scored in this report as being in the first five or six countries, is giving a better living experience to children. And ultimately, these things really matter at an early age, so we should first have the needs and happiness of primary school children in mind."

LZ: *Apart from the educational spectrum, you may wish to address primary and pre-natal care for humans and their brains, with respect to your research into embryology and genetics. There is evidence, for instance, that increased maternal DHA intake, and the use of Omega 3 supplements in prenatal and perinatal nutrition, could have a significant and positive lifelong impact on cognition.*

"I am aware of some 450 scientific publications about the effect of Omega 3 fatty acids on the brain. At least about 20 or so of them are concerned with children, and one or two examine the effects on babies during pregnancy when these fatty acids are taken by the mother or during feeding with breast milk. Omega 3 is a naturally occurring fat, which is not readily catabolised in the human body and needs to be incorporated in the diet. As you rightly say, the evidence seems that administering extra Omega 3 in the diet may result in producing children whose behaviour is better, whilst their risk of attention deficit is less. More importantly, there is some evidence that their learning is often better too. But this, at its most pronounced, is only a very minor form of enhancement. Even if this effect is statistically proven, it is likely to be not a very major one. It would not help producing Nobel Prize winners, but what it might do somewhat is improve brain development. Of course, it is worth remembering that this kind of 'cognitive enhancement' is hardly new – who can forget taking repulsive cod liver oil as a child sixty years ago because one's parents believed it was 'good for the brain'?"

LZ: *US and European governments are introducing programmes for the convergence of nano- bio- and cognitive technologies all aiming to improve human performance (Roco and Bainbridge 2003). How do you feel about these new trends, which connect studies in neuroscience to technological aims?*

"Well, I don't think we should necessarily trouble ourselves with nanotechnology in this regard. Its possible impact is probably not yet relevant to mainstream neuroscience and therefore difficult to judge. Yes, the technological tools we now have to image the brain include functional magnetic resonance imaging, additional advances in brain magnetometry, better recordings of electrical activity and, sometimes, even the ability to do single neuron analysis. These are some of the most exciting advances in the whole of biology. There has been quite an extraordinary change in neuroscience. In the last few years neuroscientists have remarkably been trying to actually measure our humanity. Scientists now evaluate the relationship between brain activity, brain function and our emotions in a way never done before. Previously, we might interrupt the projections between the prefrontal cortex and the rest of the cortex in a rather crude way or various operations could be conducted on a rat's brain to disturb the integrated activity of the CNS. Now neuroscientists are making detailed studies of the function of the amygdala, of what is sometimes called the limbic system, or, for example, mirror neurons, the cingulate gyrus and nucleus accumbens.

To take one area: some interesting research has concentrated on empathy. Tania Singer's work for example, and work like it in social neuroscience, is really fascinating. In the Institute of Neurology at University College London, she amongst others has investigated the mechanisms underlying our capacity to understand the pain and love of others. Scientists there are researching the intentions, desires, and the capacity to share the feelings of others, known as empathy

(Singer 2007). It makes me think about what makes science truly human. So one question to be assessed, before we think of enhancement, is to consider who we are. One of the arguments might be: Is it better to enhance cognitive ability, or is it better to enhance one's emphatic ability to understand and live with other people?"

LZ: *This leads me to a frank question about your personal stance on the concept of enhancement. Do you consider cognitive enhancement a legitimate chain in the history of human physical and social evolution?*

"Well, we have always 'indulged' in cognitive enhancement, of course. The history of the human from birth is one of cognitive enhancement. The ultimate scientist is the new-born baby; as he or she is learning constantly from his environment at a faster rate than at any point later in human development. The issue that is a concern, and which scientists sometimes may seem to neglect, is that we continue to think of all sorts of ways in which we might try enhance human beings. The best way to enhance a human being is surely something we can, and should, all do. It is to improve the environment in which we bring up our children. The old issues such as love, giving appropriate rewards, treating them with respect, listening to their concerns, providing them with a stable background, avoiding conflict, all that is crucial. Those things are more important than anything we can do to enhance the human artificially and which are not strictly environmental. But, if I understand you correctly, your questions are asking about enhancements which are not environmental. My answer would be that we probably should not try to enhance humans by more biological means, whilst we give them such an imperfect environment to live in. What we should do is to look at our surroundings, improve processes during human development, and guide young people as best as we can through life's influential processes during all aspects of their cognitive environment and experience."

LZ: More and more I understand your emphasis on the environmental factors of cognition, which makes me slightly hesitant whether I should go forward in asking you about developments in the field of psychopharmaceutical research and intervention in which the University of Cambridge excels.

"One of the issues you have not addressed is the question of human happiness. Would it be desirable to enhance happiness if we could? Your question includes the issue of the use of drugs like Ritalin™ and other cogno-active substances tested in psychopharmaceutical research. There are probably all sorts of ways in which we can make people more content, more relaxed or more at ease, and just possibly, happier. It is possible to enhance 'happiness' with cannabis, for example. Surely this is what Aldous Huxley was trying to address in his Brave New World; the notion that one might give a drug that would make people content with their imperfect environment (Huxley 1932). What Huxley was exposing in his book, often, I think, misunderstood, is essentially that pleasure and happiness are not the same. Making a population happy, as Huxley describes, is also quite likely to make them relatively unproductive. So an interesting question is: if you gave Ritalin™ to Beethoven would he still compose the Kreutzer Sonata, and the answer is, possibly not... Equally, I guess, had Franz Schubert been on any of the anti-depressive drugs, or mood-enhancing drugs, would he have been able to produce some of the most sublime chamber music that has ever been composed? Does not the same apply to Vincent van Gogh, one of the most disturbed of great modern painters? In fact the same must apply to pretty well every aspect of the highest activity of humans. There is this mixture of suffering and triumph so often at the basis of our best endeavours. Are we to take these natural ingredients away? And if so, to what purpose? This aspect of cognitive enhancement is not straight forward and brings us into genetics in due course about which I know you are going to ask. We should be careful with the presently alarming consumption of Ritalin™, our 'best' pharmaceutical solution to combat effects in ADHD-diagnosed children. When too frequently prescribed, it might lead to simply controlling them, to make the lives of adults easier, rather than theirs. The effect and abuse of Ritalin™ as a performance enhancer is equally known. We should realise that we have not still yet discovered enough, and there is still much research to be done."

LZ: *Pre-implantation diagnosis allows human fertility experts to influence reproductive scenarios. In what respect and within what limits can genetic manipulation become an instrument for cognitive improvement. Are there any candidate genes?*

"My own research is currently to try finding methods to modify large animals genetically. Ideally we wish to manipulate the reproduction of animals which are roughly of the same size and physiology as humans such as pigs. One of the goals is to produce large transgenic animals whose organs, after genetic modification, might be used for human xenograft transplantation. This work involves assessing various viral vectors and modifying germ stem cells, and a range of ways of getting targeted integration into the genome. Now such technology, if it were perfected, could be used to modify human offspring. One uncomfortable possibility involving this kind of technology could eventually be to attempt to improve intelligence. We already have a handful of candidate genes that seem to affect mammalian cognitive ability. One example is the gene producing synaptosomal-associated protein [SNAP25]. This is involved in the machinery of neurotransmitter release. It has been shown in rats to improve memory, and possibly cognitive ability.
Mutations in that gene changes the protein, which seem to change ability to remember. But I must immediately add that one of the problems with that particular one-sided approach about genetics is our having simplistic ideas about the relationship between genetics and the phenotype. I doubt that genetic remodelling of such genes will be particularly profitable.

Knowing the mere sequence of the human genome does not really get us much closer to any practical ability to be able to improve human genetics. Genomics focuses very much on the 'printing' of the DNA, the 'spelling' of different genes and so on. That, I think, may be relatively unimportant given improvement in our understanding of gene function.

What may be more important is the relationship between genes, the relationship between other genes, and regulators upstream and downstream. This kind of technology may be quite beyond our control for a long time to come, so its unpredictability presents real dangers. And, most intriguing of all, something which is rapidly becoming of considerable significance, is the field of epigenetics. The study of heritable changes in genome function that occur without a change in DNA sequence is a relatively new area. Present day concepts involve the conventional thinking that we might be able to modify sequences within a few genes and change their function. But we could change gene function more effectively and safely, possibly by changing the environment which affects gene function. Moreover, we should no longer be merely considering the concepts of heredity and environment as two interlinked, but separate issues. We should also be considering what happens during an organism's development. Environment immediately after conception and during early embryonic and foetal growth may be very important in what finally makes us what we eventually become."

LZ: *Are there any major advances to be gained in genomics research bearing in mind the environmental factor? Are such views sufficiently developed to allow scientists to combine human genetics, epigenetic processes and environmental impacts, particularly with regard to early and adult brain and cognitive developments?*

"Epigenetic modifications do not change the DNA code itself. Let me give you one or two examples. But before I do so, I should stress that it is likely that the gene is not really the only unit of heredity. Now this may seem something of a heresy but it may well be that there are proteins, histones, microRNAs, and possibly even hormones which can influence heritability.

Take, for example, the Mongolian gerbil *Meriones unguiculatus*, a friendly little pet that you may give your children. As a parent one may be horrified to find, one morning, that your child's innocent-looking pets have increased their family size overnight by twelve. This is the average litter size for these gerbils; usually six males and six females. That ratio can be manipulated so that there can be, say, eight males and four females. After they are born, the females, which have been living in a predominantly male uterine environment, tend to have a later-onset sexual maturation, are more likely to be infertile and tend to show male patterns of aggression. More significantly, their children show similar trans-generational effects; female grandchildren showing male patterns of aggression. What seems to happen is an in-utero epigenetic effect as a result of the female foetuses having been exposed to excessive testosterone. This results in a change in their usual developmental environment affecting gene function, possibly for some generations to come. It seems that some epigenetic effects may certainly persist for five generations, but this may be longer.

Another example which seems to indicate an epigenetic effect, are the observations of Bygren, in Skellefteå, Sweden (Bygren, Edvinsson and Bostrom 2000). He studied birth records of children born in this particular parish in the north of Sweden from the late 18th Century onwards. This was a farming area with records of good and bad harvests. Bad harvests in early pregnancy followed by good harvests immediately before birth (or for that matter, the reverse, good harvests in early pregnancy, followed by bad harvests) resulted in very high chance of cardiovascular disease in the offspring in later life, with a doubled chance of premature death. This implies some kind of environmental metabolic programming of the foetus by its early environment. Another study followed the lives of all the children who were born in that parish. Any paternal grandsons of boys who were aged between 8 to 9 years old at the time of a very good harvest were more likely to have a shorter longevity than other grandchildren from the same parish. These male grandchildren seem to have been more prone to disease, possibly diabetes. What may be happening here?

Well, nobody knows for sure. The possibility is that this is an effect caused by something inherited through the male germ line, presumably only through the Y-chromosome. At some point something happened which, although presumably the DNA remained the same, changed the genetic programming – a change caused by the environment. As it happens a little boy's testes are producing his spermatogonia, non-differentiated germinal stem cells, for the first time between 8 and 9 years. Spermatogenesis will follow an elaborate process of cell differentiation during which time gene methylation is happening. The process of maturation, of course, ends with the production of fully differentiated, highly specialised motile cells called spermatozoa. So possibly, if during this process, the developing sperm cells are presented with an environment which has a plentiful carbohydrate source it is possible they will end up signalling the need for altered metabolic programming. An interesting observation is that it seems that a good harvest produced the undesirable effect, not a bad harvest."

LZ: *Surely you will wish to tell me what happens at times of a bad harvest?*

"As I explained, it is possible that bad harvests may also have an adverse effect in other ways. To get back to pure experimental work where the environment can be carefully controlled, we know when rats are starved during pregnancy by giving them 30 per cent less carbohydrate than normal, the cognitive function of at least some offspring may be affected. Whether these changes of cognitive function continue to affect subsequent generations to come is not, as far as I know, recorded, but this is not unlikely. This seems not to be a genomic effect, not a change in the DNA or a 'genetic' effect; it is epigenetic. This is something much more subtle than those changes which are identified by exploration of the sequence of the genome only. In fact, research into epigenetics is beginning to argue that our rather determinist and somewhat simplistic view of genetics leaves much to be answered. Eva Jablonka, an Israeli scientist from Tel Aviv, has written about this extensively. In her scholarly but popular account on epigenetics called *Evolution in Four Dimensions* (2005) there is a gentle rebuke to the determinist view which is I am afraid is very frequently pedalled.

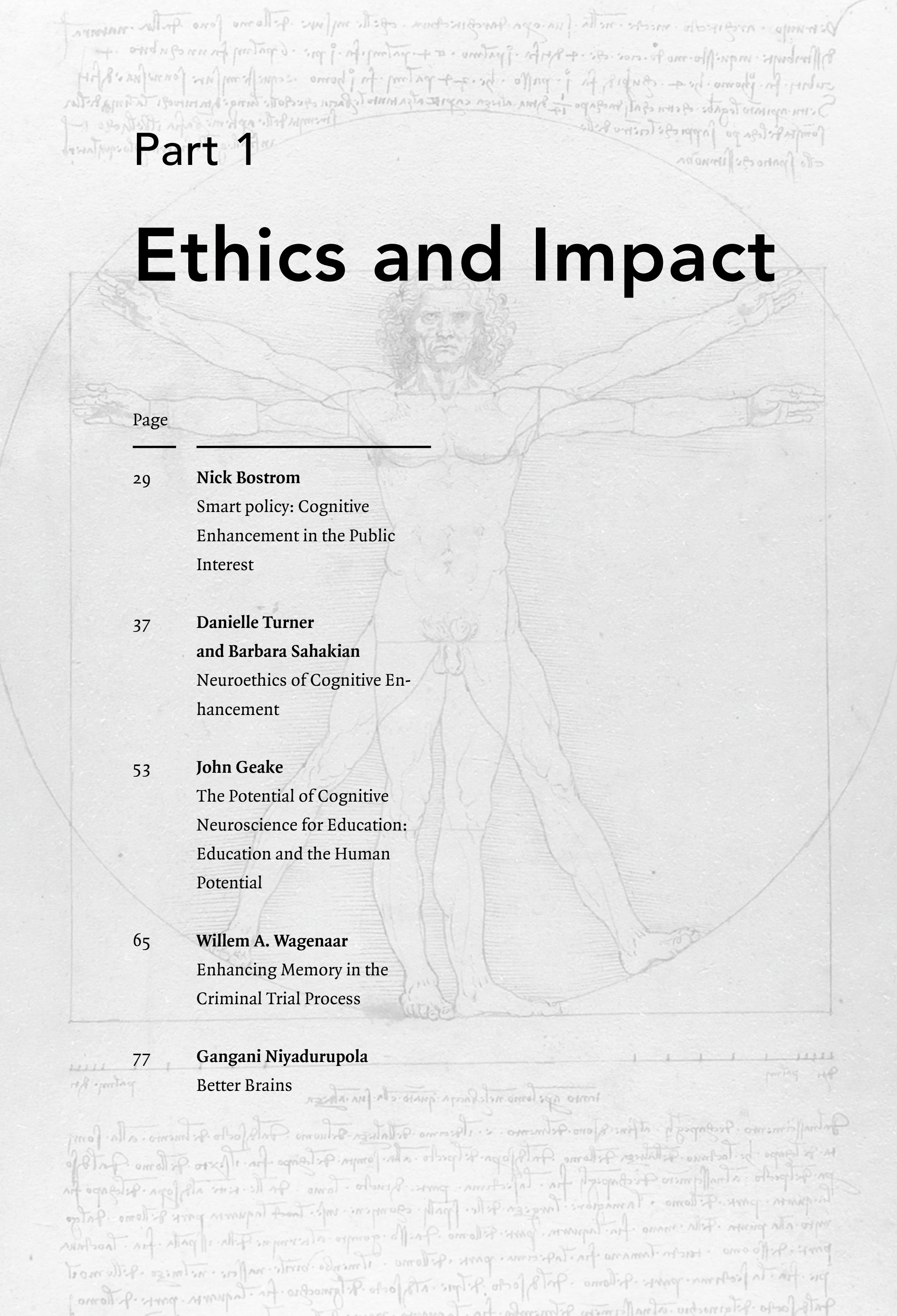
This is one reason at least why it would be totally wrong for humans to suddenly decide to change genes involved in cognition. We know, for example, SNAP25 is one such candidate. But to alter it to give a 'favourable' mutation or manipulate it otherwise, because this might enhance cognitive ability, would be foolish. The results are likely to be highly unpredictable. Far better to find environmental factors, which might be changed resulting in understanding the effect of these on development. I think we have to be very careful about genetic manipulation. This is not merely a moral stance but also a practical one.

There is the concern that frankly all of us would be tampering with a system that we hardly understand. We are not likely to understand it well enough soon, and I do not think it is going to be possible in the near future to consider systems whereby many of these complexities can be unravelled. It has been argued by the molecular biologist, Lee M Silver (1998), at the University of Princeton that appropriate predictions could be arrived at by complex computing but I disagree. I think we have a long way to go.

When it comes down to human enhancement, we need to address the questions with which we started. If we change humans we run the risk of redefining our humanity, and with it essential questions such as the sanctity of human life. If we end by having 'superhumans', what value are humans – and what value human life? Fears on this front are real, and we must temper our zest for exploration with a mature and sober understanding of what is at stake. As humans, I think we have to have considerable humility about what we are able to do. I think that if we lose that humility, we may lose our humanity."

References

- Bygren, L.O., Edvinsson S., and Bostrom, G. (2000). Change in food availability during pregnancy: Is it related to adult sudden death from cerebro – and cardiovascular disease in offspring? *American Journal of Human Biology* **12**(4):447-453.
- Huxley, A. (1932). *Brave New World.* (London: Chatto & Windus Publishers Ltd).
- Jablonka, E. and Lamb, M. (2005). *Evolution in four dimensions.* (Boston: MIT Press).
- OECD (2002). Understanding the Brain: Towards a New Science of Learning.
- OECD (2007). *Understanding the Brain: The Birth of a Learning Science.*
- Roco, M.H. and Bainbridge W.S. (Eds.). *Converging technologies for improving human performance: Nanotechnology, biotechnology, information technology and cognitive science.* Arlington: NSF/DOC 2002. (Springer, 2003).
- Silver, L. M. (1998). Remaking Eden. (London: Weidenfield and Nicholson).
- Singer, T. (2007). *The Neuronal Basis of Empathy and Fairness.* Novartis Found Symp. 2007;**278**:20-30. discussion 30-40, 89-96, 216-21.
- UNICEF (2007). *An overview of child well-being in rich countries. Child poverty in perspective: A comprehensive assessment of the lives and well-being of children and adolescents in the economically advanced nations.*



Part 1

Ethics and Impact

Smart Policy: Cognitive Enhancement in the Public Interest

by Nick Bostrom

▸ Nick Bostrom is the director of Oxford Future of Humanity Institute, Faculty of Philosophy & James Martin 21st Century School, Oxford University, United Kingdom.

Introduction

Cognitive enhancement may be defined as the amplification or extension of core capacities of the mind through improvement or augmentation of internal or external information processing systems. Cognition refers to the processes an organism uses to organise information. These include acquiring information (perception), selecting (attention), representing (understanding) and retaining (memory) information, and using it to guide behaviour (reasoning and coordination of motor outputs). Interventions to improve cognitive function may be directed at any of these core faculties.

Many methods for enhancing cognition are of a quite mundane nature, and some have been practiced for thousands of years. The prime example is education and training, where the goal is often not only to impart specific skills or information but also to improve general mental faculties such as concentration, memory, and critical thinking. Other forms of mental training, such as yoga, martial arts, meditation, and creativity courses are also in common use. Caffeine is widely used to improve alertness. Herbal extracts reputed to improve memory are popular, with sales of Ginkgo biloba alone in the order of several hundred million dollars per year in the US (van Beek 2002). In an ordinary supermarket or health food store we can find a veritable cornucopia of energy drinks and similar preparations, vying for consumers hoping to turbo-charge their brains.

As cognitive neuroscience has advanced, the list of prospective biomedical enhancements has steadily expanded (For a recent review of various cognitive enhancement methods, see Bostrom and Sandberg 2007; Farah and Illes *et al.* 2004). Yet to date, the most dramatic advances in our effective cognitive performance have been achieved through non-biomedical means. Progress in computing and information technology has vastly increased our ability to accumulate, store, analyse, and communicate information. External hardware and software supports now routinely give human beings effective cognitive abilities that in many respects far outstrip those of our biological brains. Another important area of progress has been in 'collective cognition' – cognition distributed across many minds. Collective cognition has been enhanced through the development and use of more efficient tools and methods for intellectual collaboration. The World Wide Web and e-mail are among the most powerful kinds of cognitive enhancement developed to date. Non-technological approaches to enhancing collective cognition have also made important advances: it is possible to view institutions such as academic peer-reviewed journals, and social conventions such as limitations on the use of *ad hominem* arguments in discussions, as part of the cognitive enhancement spectrum.

It is useful to bear in mind this wider perspective on the various forms that cognitive enhancement can take. Such a wide perspective helps us see just how important advances in cognitive and epistemic functioning are to individuals and to modern societies. It also helps us avoid a myopic fixation on biological paths to enhancement to the exclusion of other ways of achieving similar goals, which in many cases may be more feasible. Nevertheless, biomedical forms of cognitive enhancement are worthy of serious consideration, not only because of their novelty but because they could eventually offer enormous leverage. Consider the cost-benefit ratio of a cheap pill that safely enhances cognition compared to years of extra education.

Assessment

'Conventional' means of cognitive enhancement (such as education, mental techniques, neurological health, external information technology, and epistemic institutions) are quite uncontroversial, while 'unconventional' means (such as drugs, implants, and direct brain-computer interfaces) are more likely to evoke moral concerns. However, the boundary between these two categories will become increasingly blurred. It seems plausible that the controversy surrounding unconventional means of cognitive enhancement is largely due to the fact that they are currently novel and experimental, rather than to any intrinsic problem with the technologies themselves. As, through scientific research and practical experience of their use, we learn more about the strengths and weaknesses of these unconventional methods for improving cognitive performance, they are likely to become normalised. Enhancement discourse might become absorbed into the ordinary discourse of tools, technologies, medicine, and practices.

At present, biomedical enhancement techniques produce at most modest gains in cognitive performance. Improvements of 10-20% in some test task are typical. More dramatic results can be achieved through training and human-machine collaboration. Mental techniques (e.g. mnemonic tricks) can achieve upwards of 1,000% improvement in narrow domains such as specific memorisation tasks (Ericsson, Chase and Faloon 1980). However, while pharmacological enhancements do not produce dramatic improvements on specific tasks, their effects are often broad. A drug might, for instance, enhance performance on all tasks that rely heavily on working memory, or on long-term memory. External tools and cognitive techniques such as mnemonics, by contrast, are usually task-specific, producing potentially huge improvements in relatively narrow abilities. A combination of different methods can be expected to achieve greater results than individual methods used in isolation, especially in everyday or workplace settings where a wide variety of cognitive challenges have to be met.

Even small improvements in general cognitive capacities can have important positive effects. Individual cognitive capacity (imperfectly measured by IQ scores) is positively correlated with income. One typical study estimates the increase in income from one additional IQ point to 2.1% for men and 3.6% for women (Salkever 1995). Higher cognitive abilities are associated with avoidance of a wide array of social and economic misfortunes (Gottfredson 1997; Gottfredson 2004) and appear to promote health (Whalley and Deary 2001). At a societal level, the sum of many individual enhancements may have an even more profound effect. Economic models of the loss caused by small intelligence decrements due to lead in drinking water predict significant effects of even a few points change (Salkever 1995; Muir and Zegarac 2001). Correspondingly significant benefits can be expected if a similarly small amount of intelligence were gained instead of lost (Bostrom and Ord 2006).

Policy implications

Many forms of extant regulation are intended to protect and improve cognitive function. Regulation of lead in paints and in tap water; requirements of boxing, bicycle, and motorcycle helmets; bans on alcohol for minors; mandatory education; folic acid fortification of cereals; legal sanctions against mothers taking drugs during pregnancy: these all serve to safeguard or promote cognition. To some extent, these efforts may be motivated by a concern to promote general health; yet greater efforts appear to be made when cognitive function is at risk. One may also observe that mandated information duties, such as labelling of food products, were introduced to give consumers access to more accurate information in order to enable them to make better choices. Given that sound decision-making requires both reliable information and the cognitive ability to retain, evaluate, and use this information, one would expect that enhancements of cognition would also promote rational consumer choice. By contrast, there exists no public policy that is intended to limit or reduce cognitive capacity. Insofar as patterns of regulation reflect social preferences, therefore, it seems that there is at least an implicit commitment to promote better cognition.

There are, however, a number of obstacles to the development and use of cognitive enhancements. One major obstacle is the present system for licensing drugs and medical treatments. This system was created to deal with traditional medicine, which aim to prevent, detect, cure, or mitigate diseases. In this framework, there is no room for enhancing medicine. Drug companies would find it difficult to get regulatory approval for a pharmaceutical whose sole use was to improve cognitive functioning in the healthy population. To date, every pharmaceutical on the market that offers some potential cognitive enhancement effect was developed to treat some specific disease condition, such as attention-deficit hyperactivity disorder (ADHD), narcolepsy, or Alzheimer's disease. The enhancing effect of these drugs in healthy subjects is a serendipitous unintended benefit. Progress would almost certainly be accelerated if pharmaceutical corporations could focus directly on developing nootropics for use in non-diseased populations rather than having to work indirectly by demonstrating that the drugs are also efficacious in treating some recognised disease.

One of the perverse effects of the failure of the current medical framework to recognise the legitimacy and potential of enhancement medicine is the trend towards medicalisation and 'pathologisation' of an increasing range of conditions

that were previous regarded as part of the normal human spectrum. If, for example, a significant fraction of the population could obtain certain benefits from drugs that improve concentration, it is currently necessary to categorise this segment of people as having some disease (in this case ADHD) in order to get the drug approved and prescribed to those who could benefit from it. This disease-focused medical model is increasingly inadequate for an era in which many people will be using medical treatments for enhancement purposes. Academic research is also hampered by the disease framework, in that researchers find it difficult or impossible to secure funding to study potential cognitive enhancers except in contexts where the study can be linked to some recognised pathology (Danielle Turner and Barbara J Sahakian, personal communication).
The medicine-as-treatment-for-disease framework creates problems not only for pharmaceutical companies, but also for individual users ('patients') whose access to enhancers is often dependent on being able to find an open-minded physician who will prescribe the drug. This creates inequities in access. People with high social capital and good information get access while others are excluded.

Given that all medical interventions carry some risk, and that the benefits of enhancements may often be more subjective and value-dependent than the benefits of being cured of a disease, it is important to allow individuals to determine their own preferences for tradeoffs between risks and benefits. It is highly unlikely that one size will fit all. At the same time, many will feel the need for a limited degree of paternalism that would protect individuals from at least the worst risks. One option would be to establish some baseline level of acceptable risk in approved interventions. This could be done through comparison with other risks that society allows individuals to take, such as risks from smoking, mountain climbing, or horseback riding. Enhancements that could be shown to be no more risky than these activities would be allowed, with appropriate information and warning labels when necessary. Another possibility would be 'enhancement licenses'. People willing to undergo potentially risky but rewarding enhancements could be required to demonstrate sufficient understanding of the risks and the ability to handle them responsibly. This would both ensure informed consent and enable better monitoring. A downside with enhancement licenses is that people with low cognitive capacity, who may have the most to gain from enhancements, could find it hard to gain access if the license requirements were too demanding.

Public funding for research does not yet reflect the potential personal and social benefits of many forms of cognitive enhancement. There is public funding (albeit, arguably, at inadequate levels) for research into new education methods and information technology, but not for pharmacological cognitive enhancers. In view of the potentially enormous gains from even moderately effective general cognitive enhancements, the field deserves large-scale public funding. It is clear that much research and development is needed to make cognitive enhancement medicine practical and efficient. As discussed above, this requires – in addition to funding – a change of the paradigm according to which medicine is only about restoring, but not enhancing; and a concomitant change in the regulatory framework for medical trials and drug approval.

There are also regulatory changes could be useful without being complicated or disruptive. The evidence on prenatal and perinatal nutrition suggests that infant formulas containing suitable nutrients may have a significant, positive, life-long impact on cognition. Because of the low cost and extremely large potential impact of enriched infant formula if applied at a population level, it should be a priority to conduct more research to establish the optimal composition of infant formula. Regulation could then be used to ensure that commercially available formula contains these nutrients. Public health information campaigns could further promote the use of enriched formula (or breast feeding practices) that promotes mental development. This would be a simple extension of current regulatory practice, but a potentially important one.

While access to medicine is regarded as a human right constrained by cost concerns, it is less clear whether access to all enhancements should be regarded as a positive right. The case for at least a negative right to cognitive enhancement based on cognitive liberty, privacy interests, and the important interest of persons in protecting and developing their own minds and capacity for autonomy, seems very strong. (It can certainly be argued as a negative right, cf. Sandberg 2003; Boire 2001). Proponents of a positive right to (publicly subsidised) enhancements could argue for their position on grounds of fairness or equality, or on grounds of a public interest in the promotion of the capacities required for autonomous agency. The societal benefits of effective cognitive enhancement may turn out to be so large and unequivocal that it would be economically efficient to subsidise enhancement for the poor, just as the state now subsidises education.*

* I am grateful to Anders Sandberg for research collaboration and Rebecca Roache for excellent research assistance.

Recommendations

- Conceptualise pharmacological cognitive enhancers as part of a wider spectrum of ways of enhancing the cognitive performance of groups and individuals.
- Expand the disease-focused regulatory framework for drug approval into a health – or wellbeing – focused framework in order to facilitate the development and use of pharmaceutical cognitive enhancement of healthy adult individuals.
- Provide public funding for academic research into the safety and efficacy of cognitive enhancers, for the development of improved enhancers, and for epidemiological studies of the broader effects of long-term use.
- Increase public funding for research aimed at determining optimal nutrition for pregnant women and newborns to promote brain development.
- Disseminate information to the public about optimal pre- and perinatal nutrition.

References

- Boire, R. G. (2001). On Cognitive Liberty. *The Journal of Cognitive Liberties* **2**(1):7-22.
- Bostrom, N. & Ord, T. (2006). The Reversal Test: Eliminating Status Quo Bias in Applied Ethics. *Ethics* **116**(4):656-680. Preprint at: *http://www.nickbostrom.com/ethics/statusquo.pdf.*
- Bostrom, N., & Sandberg, A. (2007). Cognitive Enhancement: Methods, Ethics, Regulatory Challenges. *Science and Engineering Ethics,* in press. Preprint at: *http://www.nickbostrom.com/cognitive.pdf.*
- Ericsson, K. A., Chase, W. G., & Faloon, S. (1980). Acquisition of a Memory Skill. *Science* **208**(4448):1181-1182.
- Farah, M. J., Illes, J., Cook-Deegan, R., Gardner, H., Kandel, E., King, P., Parens, E., Sahakian, B.J., & Wolpe, P. R. (2004) Neurocognitive enhancement: what can we do and what should we do? *Nature Reviews Neuroscience* **5**(5):421-425.
- Gottfredson, L. S. (1997). Why g matters: The complexity of everyday life. *Intelligence* **24**(1):79-132.
- Gottfredson, L. S. (2004). Life, death, and intelligence. *Journal of Cognitive Education and Psychology* **4**(1):23-46.
- Muir, T., & Zegarac, M. (2001). Societal costs of exposure to toxic substances: Economic and health costs of four case studies that are candidates for environmental causation. *Environmental Health Perspectives* **109**:885-903.
- Salkever, D. S. (1995). Updated estimates of earnings benefits from reduced exposure of children to environmental lead. *Environmental Research* **70**(1):1-6.
- Sandberg, A. (2003). Morphologic Freedom. Eudoxa Policy Studies. Available from *http://www.eudoxa.se/content/archives/2003/10/eudoxa_policy_s_3.html.*
- van Beek, T. A. (2002). Chemical analysis of Ginkgo biloba leaves and extracts. *Journal of Chromatography* **A 967**(1):21-55.
- Whalley, L. J., & Deary, I. J. (2001). Longitudinal cohort study of childhood IQ and survival up to age 76. *British Medical Journal* **322**(7290):819-822.

Neuroethics of Cognitive Enhancement

by Danielle C. Turner and Barbara J. Sahakian

▸ Danielle C. Turner is a postdoctoral research associate in the Department of Psychiatry, University of Cambridge and a Fellow of the Center for Cognitive Liberty (CCLE), USA. Barbara J. Sahakian is Professor of Clinical Neuropsychology at the University of Cambridge, United Kingdom.

Introduction

The prospect of being able to take safe and effective drugs to improve mental functioning is becoming a reality. With the potential for widespread use of cognitive enhancers by large sectors of the population, this article discusses the rationale behind the development of these drugs and how society might benefit from them. Important ethical questions and scenarios are also raised. Scientists are urged to explore the implications of their work and engage in active debate with a wide range of interested stakeholders about the ethical and moral consequences of these new technologies to ensure maximal benefit with minimal harm.

Cognitive Enhancement

The social implications of pharmacologically improving the brain functioning of healthy, normal individuals are numerous. Neuroethics is a new and expanding area concerned with the benefits and dangers of modern research on the brain. In 2002, the Dana Foundation defined neuroethics as 'the study of the ethical, legal and social questions that arise when scientific findings about the brain are carried into medical practice, legal interpretations and health and social policy' (Marcus 2002). Recent advances and trends in neuroscience raise some important ethical questions that are demanding the attention of scientists, ethicists, policy-makers and the public. In particular, this article will focus on developments in the pharmacological enhancement of cognition. One framework in which to discuss the ethical implications of cognitive enhancement is by commencing at a relatively tangible starting point, namely by describing the scientific basis of these discoveries, their potential and the motivations behind their development.

The need for cognitive enhancers

Major psychiatric illnesses are extremely common and their effects on behaviour, perception, emotion and cognition constitute an enormous contribution to worldwide disability (see *www.who.int*). Numerous neuropsychiatric disorders, such as attention deficit hyperactivity disorder (ADHD), schizophrenia, frontal dementia, Alzheimer's disease, Huntington's disease and Parkinson's disease are characterized by cognitive impairments. Patients frequently struggle with many everyday activities requiring concentration, memory, problem-solving and planning. The potential public health benefit of improving current treatments for cognitive disabilities in patients is largely undisputed (Meltzer 2003).

The disorder of schizophrenia provides a particularly good illustration of the potential benefits to be had from exploring new options for the treatment of cognitive dysfunction. It is estimated that 24 million people worldwide suffer from schizophrenia, with schizophrenia ranking third in terms of the global burden of neuropsychiatric conditions, following depression and alcohol dependence (Murray and Lopez 1996). The economic impact alone of the disorder is enormous: in the United States the direct and indirect costs of schizophrenia were estimated to have been as much as $40 billion in the year 2000 (Fuller Torrey 2001). In many patients with schizophrenia, cognitive difficulties are the main factor limiting full rehabilitation (such as returning to work) and quality of life, particularly after the clinical symptoms have remitted (Goldberg *et al.* 1993; Mitchell *et al.* 2001). Indeed, it has been proposed that in certain patients with schizophrenia even small improvements in cognitive functions, such as enhancing the ability to adapt efficiently to new situations and to plan effectively, could help patients make the transition to independent living outside a psychiatric institution (Davidson and Keefe 1995). The relatively recent shift in clinical emphasis, away from a restricted targeting of the more overt psychotic symptoms of this disorder, serves to emphasize the debilitating long-term effects that cognitive impairments can have, and the need to identify effective treatments.

The pharmacological enhancement of cognition

Cognitive enhancement is commonly considered in terms of improving memory and attention, largely through the use of pharmacological agents (Stahl 2000). Effective cognitive functioning typically involves numerous neuronal pathways and neurotransmitter systems, with several distinct neurotransmitters being implicated in the enhancement of cognitive function (Robbins *et al.* 1997). In particular executive functions, such as attention, planning, problem-solving and adapting behaviour, are crucial for the successful performance of many everyday procedures like prioritising tasks and remembering important information for completion of a task while engaging in other necessary task activities (Stuss and Levine 2002). Frontal neural networks in the brain have been shown to subserve many of these crucial functions and to be modulated by neurochemicals such as the catecholamines dopamine and noradrenaline (Solanto *et al.* 2001).

It is now known that many of these functions are susceptible to intervention with pharmacological agents. Agents that target these catecholamine neural projections include conventional stimulants such as amphetamine and methylphenidate (Ritalin™), both of which have been shown to have cognitive enhancing properties (Elliott *et al.* 1997; Halliday *et al.* 1994; McKetin *et al.* 1999), and also more novel compounds such as modafinil (Provigil™) (Turner *et al.* 2003) and the ampakines (Ingvar *et al.* 1997; Lynch, 2002). Work in our own laboratory has shown that a single dose of modafinil, a drug originally licensed for the treatment of narcolepsy, consistently improves short-term memory and planning abilities in healthy, young volunteers, adults with ADHD and patients with schizophrenia (Turner *et al.* 2003, 2004a, 2004b).

The neural mechanisms by which many of these drugs exert their effects are also becoming clearer. For example, neuroimaging in healthy volunteers has shown that methylphenidate (a drug primarily used to treat ADHD) enhances efficacy within certain neural networks in the brains of young, healthy volunteers, including the important frontal areas that are implicated in many executive functions (Mehta *et al.* 2000b). Much work of this type has helped define the neural pathways and neurotransmitters that are closely associated with the different psychiatric disorders.

Through an increased understanding of neurochemical mechanisms, it is becoming increasingly possible to identify drugs that are intended to help patients lead lives unhindered by cognitive impairments. Short-term administration of pharmacological agents can improve certain aspects of cognition in ADHD (Aron *et al.* 2003; Mehta *et al.* 2000a; Turner *et al.* 2004a 2005), schizophrenia (Turner *et al.* 2004b) and frontotemporal dementia (Rahman 2001), as well as in patients with cognitive impairments resulting from traumatic brain injury (Cardenas *et al.* 1994; McDowell *et al.* 1998). The longterm effects that these drugs have on cognition, and the extent to which changes in laboratory measures of functioning will translate into improvements in everyday performance, are currently being explored. It is important that work of this kind continues if we are to help improve the suffering of thousands of patients and their families, as well as to reduce the financial burden of these disorders on society.

Much of this research work necessarily involves studies using healthy volunteers. Indeed, many of the advances in understanding cognition would not have reached the current state without research in healthy adults. Volunteer studies enable a comprehensive understanding of the effects of pharmacological cognitive enhancement, relatively free from the problems of interpretation posed by underlying pathology. This work is vital in furthering our understanding of cognition and deepening our knowledge of underlying brain mechanisms. It is also the most contentious because of the ethical issues inherent in enhancing the healthy brain. Until recently, psychotropic medications had significant risks and side effects that made them attractive only as an alternative to disorder or illness. However, the body of evidence demonstrating that it is possible to pharmacologically enhance cognition with minimal side effects in healthy volunteers is growing (Elliott *et al.* 1997; Ingvar *et al.* 1997; Turner *et al.* 2003). Executive functions and memory seem particularly susceptible to improvement. As a result, many drugs are increasingly being used off-label (Farah *et al.* 2004).

Thousands of normal, healthy adults and children have on their own discovered the benefits of cognitive enhancement (Farah 2002) with many people already selfmedicating, using over-the-counter remedies such as herbal stimulants, tonics and caffeine, to improve performance at work, school and leisure. Increasingly, people are turning to pharmaceutical cognitive enhancers. Cognitive enhancement is thus no longer just a theoretical possibility (Farah 2002). Many agents, such as methylphenidate and modafinil, are readily available through the Internet. With their worldwide availability, ethical discussions need to consider the effects of these drugs on all sectors of society.

Ethical considerations of cognitive enhancement

The brain, with its higher cognitive processes, demands unique ethical consideration. One of the reasons why ethical dilemmas regarding enhancement of the brain are so much more complex than, for example, enhancement of one's appearance, is that we primarily define and distinguish ourselves as individuals by our behaviour and personality. There are two main discussion points regarding the use of cognitive enhancers in healthy people. The first is the definition of what is considered a 'normal' healthy brain (and the distinction between treatment and enhancement) and the second relates to the consequences that widespread use of 'smart drugs' could have.

Defining normal

It is generally accepted that, because of natural human diversity, 'normal' encompasses a distribution of abilities. In psychiatric terms, 'normal' implies an absence of any psychiatric diagnosis. However, it can often be difficult to categorically determine whether an individual is 'normal' or suffering from a psychiatric condition requiring treatment, with many psychiatric diagnoses presenting as spectrum disorders. For instance, despite attempts at standardising criteria using tools such as the *Diagnostic and statistical manual* (American Psychiatric Association 1994) and the *International classification of diseases* (World Health Organization 2004), cross-cultural studies on the rating of symptoms of ADHD show major, significant differences in the diagnosis of childhood ADHD amongst raters from different countries (Mann *et al.* 1992), in the diagnosis of children from different cultures (Sonuga-Barke *et al.* 1993), and even in the diagnosis of children from within the same culture (Rappley *et al.* 1995). As an illustration, in the United States, ADHD is conservatively estimated to occur in 3.0–7.5% of school-age children, although some estimates are as high as 17%, and up to 20% of boys in some private schools have been found to be receiving psychostimulant treatment (reviewed by Castellanos and Tannock 2002). Sociological factors can thus play a highly prominent role in clinical deliberations when considering treatment.

In order to overcome discrepancies due to the lack of objective diagnostic tools, often a patient's symptoms must be seen to significantly impair everyday functioning before a diagnosis is made (American Psychiatric Association 1994). Yet impaired cognition and alertness also chronically affect millions of otherwise healthy people, frequently as a result of jet lag, shift work, sleep deprivation or even old age. Cognitive performance and alertness deficits that result from monotonous activities or sleep loss are recognised as a considerable threat to productivity and safety in both industrial and military settings (Wesensten *et al.* 2002). Furthermore, a disadvantaged educational background might put a person on the lower end of the 'normal' distribution curve, while low cognitive reserve is known to be a risk factor for the adverse effects of stressors such as head injury, dementia and psychiatric disorder (Orrell and Sahakian 1995; Salmond *et al.* in submission; Stern 2002). Could these be justifications for enhancement? It might seem easier to justify the use of pharmacological cognitive enhancement to enable someone to enter employment for the first time, than to help an ambitious student overcome weeks of sleep deprivation. Is there a moral distinction between self-induced and inherent deficits, when deciding whether it is appropriate to offer treatment? However, if everybody has the right to fulfil their potential, this surely must also include 'already-clever' people who choose to enhance. The medical profession has a duty to service those in need. But it is not inconceivable that limited healthcare resources could mean that, in the future in the UK, certain people would be able to receive cognitive enhancement on the National Health Service while others would be urged to 'go private'.

If we are going to posit differences between treatment and enhancement, we need a clear conceptualisation of the point at which treatment becomes enhancement. As mentioned previously, this hinges on the definition of normal. 'Normal' is traditionally defined as typical, or not deviating from the standard (*The Chambers dictionary* 1993). However, diversities in culture, wealth and economic status make it difficult to envisage an ideal 'standard' for human cognition in a global environment. Besides, no human can perform 'typically' (or indeed, optimally) all the time—are we therefore all entitled to occasional 'treatment'? There are countless examples of lifestyle habits that result in less-than-ideal performance (such as excessive alcohol consumption or a lack of sleep). Drugs such as caffeine are already used widely to target temporary deficits in performance in 'normal' individuals. Indeed, there might be situations in which clinicians might wish to use cognitive enhancement for rehabilitation purposes, such as in the case of substance abuse (Duka *et al.* 2005). However, even if it is difficult to categorically define treatment and enhancement, many are still concerned about the potential harms that could accompany widespread use of cognitive enhancers.

Concerns and limitations

Ethicists have already begun grappling with some of the potential effects on society of the use of these technologies. For example, some people are concerned about what would happen if the level of 'normal' cognitive performance was increased, while at the same time only the wealthy had the means of attaining this new level (Caplan 2002). Others, however, point out that unequal distribution is not a reason to reject neurocognitive enhancement outright, as there are countless examples in our society of the unfair distribution of education, wealth and resources that are accepted as inevitable (Farah 2002). Indeed, an alternative fear is that the opposite might become true, where the widespread use of cognitive enhancers leads to the creation of population homogeneity and loss of diversity (Butcher 2003). Along a similar vein, some are concerned that if we substantially improve our overall cognitive functioning, we may alter fundamental aspects of our identity by eliminating the need to strive for success (Parens 2002). Is it likely that virtues such as motivation, applying oneself and working hard could potentially become outdated as society becomes more productive, fuelled by the ability to perform optimally for extended periods?

Many of these predictions and fears rely on the assumption that a range of 'ideal' psychotropic drugs will be developed with robust and predictable effects. We are already considerably nearer this goal and it is conceivable that, in the future, we will have a sufficient understanding of the interactions between the neural, pharmacological, and genetic. Thus, these fears should not be summarily dismissed. It is worth considering whether we are capable of creating a homogeneous society in which members lose all personal and individual identity, and diversity disappears. For this to happen we would have to attend to all facets of human psyche. Some people will always work harder, whether enhanced or not. Thus, for the moment, these technologies are neither so advanced, nor so predictable, that we are in danger of an Orwellian existence.

Perhaps more pressing is the need to concern ourselves with the current acceptability of drug use for cognition. One of the predominant concerns of widespread cognitive enhancement is safety (Butcher 2003). Patients with severely debilitating symptoms will often tolerate the side effects of drug treatment because improvements in symptoms outweigh the negative aspects. It is very difficult to be certain about the potential for subtle, rare or long-term side effects, particularly in relatively new pharmaceuticals, and thus a full exploration of the long-term implications of any treatment that might be used by the healthy population is imperative. Children, especially, are at risk if drugs are discovered to adversely affect brain development. It would be devastating to learn that a dazzling youth of successful cognitive enhancement meant a middle age of premature memory loss and cognitive decline (Farah 2002). Scientists, pharmaceutical companies and the government must commit resources to the development of robust predictive and long-term detection methods. Research and development organisations should be encouraged to improve on preclinical screening methods for drugs.

Another concern is the extent to which purported beneficial effects of certain drugs are neither predictable nor guaranteed. Our understanding of pharmacogenomics, whilst growing (Roiser *et al.* 2005), is not yet fully developed. At the moment, our knowledge of the effects of cognitive enhancers is largely based on small-scale proof-of-concept studies and more work is required before we can understand the full effects of these drugs. For example, when healthy adults are given methylphenidate, improvements are typically seen in performance on novel cognitive tasks and impairments seen when a task is familiar (Elliott *et al.* 1997). It is possible that inverted U-shaped functions that illustrate the Yerkes–Dodson principle of optimal levels of arousal for effective performance (Yerkes and Dodson 1908) are implicated in these different effects. Similarly, baseline levels of performance, particularly on working memory tasks, may have some predictive value in determining the cognitive enhancing effects of certain drugs. Mehta *et al.* (2000b) showed that the beneficial effects of methylphenidate on working memory in normal adult volunteers were greatest in those subjects with a lower baseline working memory capacity. However, the opposite effect was observed in children with ADHD, where this time it was those with the highest baseline digit span scores who demonstrated the greatest improvement in spatial working memory following methylphenidate (Mehta *et al.* 2004).

Given the enthusiasm with which society tends to embrace new technologies, some might argue that it is advantageous to encourage paternalism within appropriate authorities in order to minimize harm. Pharmaceutical companies, scientists and the media must avoid unwarranted claims of efficacy, and perhaps government regulators should restrict availability of drugs until their full effects are understood. We only need to look at the explosion in the use of botulinum toxin type A (Botox™) for beauty enhancement, or sildenafil (Viagra™) for sexual performance, to realize that many people are not hindered by the potential for long-term risks if there is immediate, tangible benefit (Boshier *et al.* 2004; Vartanian and Dayan 2004).

However, many would argue against such restrictions. Sententia (2004), for example, points out that public policy decisions about cognitive enhancement should be guided by the democratic right to what she terms 'cognitive liberty' and the principle of safeguarding one's own thought processes, rather than by moralism or paternalism. Moral and safety precautions will inevitably have a place in determining appropriate uses of drugs, but she argues that what is paramount is that each individual should have access to the information necessary in order to determine for him or herself what is an acceptable personal risk.

This idealistic libertarianism assumes that all people exposed to such developments live in democratic societies with access to education and the freedom of information. It also supposes that people will be educated to a high enough standard to be able to make informed personal decisions. If we adopt this libertarian approach, we have to consider that many of the freedoms enjoyed in our society are not universal, and that many of these drug developments will impact on people living in less democratic or in less educated societies, and in poorer situations. Furthermore, the majority of safety-orientated drug trials are funded by the pharmaceutical industry and access to the full results by individuals and independent scientists is often not possible (Lexchin 2004, 2005). This has already been tackled to some extent, with a European Union directive (Clinical Trials Directive 2001/20/ EC) intended to ensure greater access to information about clinical trials. Similar measures are also encouraged by the Food and Drug Administration (FDA) in the United States, with the FDA Modernization Act of 1997. In addition, independent government-funded trials with widespread dissemination of the results should be encouraged. To ensure this information is utilized effectively, healthcare professionals should be encouraged to acquire the skills to analyse scenarios on a case-by-case basis, bringing together an understanding of science and public policy in collaboration with social scientists, legislators, insurance companies, employers and educational authorities. Due to the increase in information sources and the Internet, patients are already considerably more educated about treatment options than during the last century (Porter 1997), and it is likely that this trend will continue. The media is essential in the dissemination of ideas and we should not underestimate people's ability to make informed decisions.

Even if we are able to embrace the above principles so that the majority of individuals can make fully informed decisions, widespread availability of cognitive enhancers could bring with it the more sinister prospect of compulsory or forced drug administration to individuals unable to give informed consent. Forced drug administration is already a part of our healthcare system. At present, in extreme circumstances, individuals whose behaviour is considered to be dangerous to themselves or to others can be treated with psychotropic medication under the UK Mental Health Act 1983 (Dale *et al.* 2001). In the United States authorities are increasingly attempting to order individuals in criminal proceedings to take psychotropic medication to improve their competence to stand trial (Boire and Ruiz-Sierra 2003) or even to be executed (Randall 2004). Children, in particular, are also very vulnerable to overzealous drug administration. As described earlier, the diagnosis of many disorders such as ADHD still involves some degree of subjectivity, which can make it very difficult to ensure that children are not being unnecessarily medicated as a result of misleading accounts by enthusiastic parents who want to give their child the edge at school, or frustrated teachers who desire a better-behaved classroom (Farah 2002). Even relatively poorly defined forces, such as social pressures, could be driving the unnecessary increase in the use of cognitive enhancers. The pressure to take a cognitive enhancer, when all of one's peers are pharmacologically enhanced, is great. Perhaps we should be asking how many of these ethical quandaries would still exist, if expectations of ourselves and others were more reasonable.

Future decisions

We need to decide if it is the practicalities of cognitive enhancement that worry us – the risks and harms – or the outcomes. History has shown that many of the concerns that people have had in the past about new technologies, such as heart transplants and in vitro fertilisation, no longer worry the vast majority of citizens as these technologies are perfected. Concerns may always remain topical when human brain function and performance is under consideration. However, if we imagine the perfect cognitive enhancer and ask ourselves how we would proceed, will this provide us with a clearer moral picture? We could then examine what aspects of the current limitations might affect our opinion and whether these can be reconciled or overcome. Alternatively, we could approach these questions in the context of currently available drugs, with the assumption that we may never develop the 'perfect' cognitive enhancer and thus there is no point in considering the 'perfect' situation.

There are many reasons to strive to identify the ideal cognitive enhancer. Already countless patients have benefited from advances in neuropsychopharmacology. We must not shy away from new developments on the grounds of conservatively fearing change. However, scientists should be encouraged to take moral responsibility for their research and to monitor and foresee, as far as possible, the consequences of their work. It can be very difficult for scientists to anticipate the implications of their work, particularly at the discovery stage. Nevertheless, consideration for the ethical implications of research could be further encouraged by funding bodies, in the same way that scientists have been urged to engage in the public dissemination of their results. Funding bodies will often be the main determinants of the type of research carried out, and are certainly in a position to encourage much greater collaboration between scientists, social scientists, philosophers and ethicists. Furthermore, many scientists, due to the international, collaborative nature of their research work, are in a position, through these networks, to monitor and assess the consequences of their work in many different social groups.

Only time will determine the true impact of these enhancing technologies. Ultimately, however, many people believe (e.g. Sententia 2004) that, as long as a person's behaviour does not harm others, they should be free to take any substances they wish to, and equally, as long as a person's behaviour does not endanger others, individuals should not be compelled against their will to use technologies that will affect their cognitive liberty.

Clearly, these developments in cognitive neuroscience will improve the quality of life for patients and their families and reduce the economic burden on society. We must, therefore, rationally consider and debate the implications of these new developments so that strategies can be put in place to ensure these advances support maximal benefit to the individual person and society, with minimal harm.

Acknowledgements

This work was completed within the MRC (UK) Centre for Behavioural and Clinical Neuroscience, and our research work cited was funded by the Wellcome Trust and the Medical Research Council. The authors would particularly like to thank Andrew Blackwell and Simon Redhead for very helpful discussions regarding this paper.

References

- American Psychiatric Association (1994). *Diagnostic and statistical manual of mental disorders*, 4th edn. Washington, DC: American Psychiatric Press.
- Aron, A.R., Dowson, J.H., Sahakian, B.J., & Robbins, T.W. (2003). Methylphenidate improves response inhibition in adults with attention-deficit/hyperactivity disorder. *Biological Psychiatry* **54**:1465–1468.
- Boire, R.G., & Ruiz-Sierra, J. (2003). Supreme court upholds right to refuse mind-altering drugs. URL (accessed 31 August 2004): *http://www.cognitiveliberty.org/news/US_v_Sell_decision.htm*
- Boshier, A., Wilton, L.V., & Shakir, S.A. (2004). Evaluation of the safety of sildenafil for male erectile dysfunction: Experience gained in general practice use in England in 1999. *BJU International* **93**(6):796–801.
- Butcher, J. (2003). Cognitive enhancement raises ethical concerns: Academics urge pre-emptive debate on neurotechnologies. *Lancet* **362**(9378):132–133.
- Caplan, A. (2002). No-brainer: Can we cope with the ethical ramifications of new knowledge of the human brain? *Neuroethics: Mapping the field. Conference Proceedings, May 13–14 2002, San Francisco, California, 95–106*. New York: The Dana Press.
- Cardenas, D.D., McLean, Jr, A., Farrell-Roberts, L., Baker, L., Brooke, M., & Haselkorn, J. (1994). Oral physostigmine and impaired memory in adults with brain injury. *Brain Injury* **8**(7):579–587.
- Castellanos, F.X., & Tannock, R. (2002). Neuroscience of attention-deficit/hyperactivity disorder: The search for endophenotypes. *Nature Reviews Neuroscience* **3**(8):617–628.
- Dale, J.R., Appelbe, G.E., & Wingfield, J. (2001). *Dale and Appelbe's pharmacy law and ethics*, 7th edn. London: Pharmaceutical Press.
- Davidson, M., & Keefe, R.S. (1995). Cognitive impairment as a target for pharmacological treatment in schizophrenia. *Schizophrenia Research* **17**(1): 123–129.
- Duka, T., Sahakian, B.J., & Turner, D.C. (2005). Experimental psychology and research into brain science, addiction and drugs. URL (accessed 14 July 2004):
- *http://www.foresight.gov.uk/Brain_Science_Addiction_and_Drugs/Reports_and_Publications/ScienceReviews/Experimental%20Psychology.pdf*
- Elliott, R., Sahakian, B.J., Matthews, K., Bannerjea, A., Rimmer, J., & Robbins, T.W. (1997). Effects of methylphenidate on spatial working memory and planning in healthy young adults. *Psychopharmacology (Berl)* **131**(2): 196–206.
- Farah, M.J. (2002). Emerging ethical issues in neuroscience. *Nature Neuroscience* **5**(11):1123–1129.
- Farah, M.J., Illes, J., Cook-Deegan, R., Gardner, H., Kandel, E., King, P., Parens, E., Sahakian, B., & Wolpe, P.R. (2004). Neurocognitive enhancement: What can we do and what should we do? *Nature Reviews Neuroscience* **5**(5): 421–425.
- Fuller Torrey, E. (2001). *Surviving schizophrenia: Manual for families, consumers, and providers,* 4th edn. New York: Perennial-HarperCollins Publishers.

- Goldberg, T.E., Greenberg, R.D., Griffin, S.J., Gold, J.M., Kleinman, J.E., Pickar, D., Schulz, S.C., & Weinberger, D.R. (1993). The effect of clozapine on cognition and psychiatric symptoms in patients with schizophrenia. *British Journal of Psychiatry* **162**:43–48.
- Halliday, R., Naylor, H., Brandeis, D., Callaway, E., Yano, L., & Herzig, K. (1994). The effect of D-amphetamine, clonidine, and yohimbine on human information processing. *Psychophysiology* **31**(4):331–337.
- Ingvar, M., Ambros-Ingerson, J., Davis, M., Granger, R., Kessler, M., Rogers, G.A., Schehr, R.S., & Lynch, G. (1997). Enhancement by an ampakine of memory encoding in humans. *Experimental Neurology* **146**(2): 553–559.
- Lexchin, J.R. (2004). Clinical trials register. *Lancet* **364**(9431):330.
- Lexchin, J.R. (2005). Implications of pharmaceutical industry funding on clinical research. *Annals of Pharmacotherapy* **39**(1):194–197.
- Lynch, G. (2002). Memory enhancement: The search for mechanism-based drugs. *Nature Neuroscience* **5 Suppl.**:1035–1038.
- Mann, E.M., Ikeda, Y., Mueller, C.W., Takahashi, A., Tao, K.T., Humris, E., Li, B.L., & Chin, D. (1992). Crosscultural differences in rating hyperactive-disruptive behaviors in children. *American Journal of Psychiatry* **149**(11): 1539–1542.
- Marcus, D. (2002). *Neuroethics: Mapping the field conference proceedings, May 13–14 2002, San Francisco, California.* New York: The Dana Press.
- McDowell, S., Whyte, J., & D'Esposito, M. (1998). Differential effect of a dopaminergic agonist on prefrontal function in traumatic brain injury patients. *Brain* **121** (Pt 6):1155–1164.
- McKetin, R., Ward, P.B., Catts, S.V., Mattick, R.P., & Bell, J.R. (1999). Changes in auditory selective attention and event-related potentials following oral administration of D-amphetamine in humans. *Neuropsychopharmacology* **21**(3):380–390.
- Mehta, M.A., Calloway, P., & Sahakian, B.J. (2000a). Amelioration of specific working memory deficits by methylphenidate in a case of adult attention deficit/hyperactivity disorder. *Journal of Psychopharmacology* **14**(3):299–302.
- Mehta, M.A., Goodyer, I.M., & Sahakian, B.J. (2004). Methylphenidate improves working memory and set-shifting in AD/HD: Relationships to baseline memory capacity. *Journal of Child Psychology and Psychiatry* **45**(2):293–305.
- Mehta, M.A., Owen, A.M., Sahakian, B.J., Mavaddat, N., Pickard, J.D., & Robbins, T.W. (2000b). Methylphenidate enhances working memory by modulating discrete frontal and parietal lobe regions in the human brain. *Journal of Neuroscience* **20**(6):RC65 (61–66).
- Meltzer, H.Y. (2003). Beyond control of acute exacerbation: Enhancing affective and cognitive outcomes. *CNS Spectrum* **8**(11, Suppl. 2):16–18, 22.
- Mitchell, R.L., Elliott, R., & Woodruff, P.W. (2001). fMRI and cognitive dysfunction in schizophrenia. *Trends in Cognitive Sciences* **5**(2):71–81.
- Murray, C.J.L., & Lopez, A.D. (1996). *The global burden of disease: A comprehensive assessment of mortality and disability from diseases, injuries and risk factors in 1990 and projected to 2020.* Geneva: World Health Organization.

- Orrell, M., & Sahakian, B. (1995). Education and dementia. *British Medical Journal* **310**(6985):951–952.
- Parens, E. (2002). How far will the term enhancement get us as we grapple with new ways to shape ourselves? *Neuroethics: Mapping the field. Conference Proceedings May 13–14 2002 San Francisco, California*, 152–158. New York: The Dana Press.
- Porter, R. (1997). *The greatest benefit to mankind: A medical history of humanity from antiquity to the present*. London: HarperCollinsPublishers.
- Rahman, S. (2001). Executive and mnemonic functions in the frontal lobe dementias. PhD thesis, University of Cambridge.
- Randall, K. (2004). Mentally ill inmate put to death after medical 'treatment' prepares execution. URL (accessed 31 August 2004): *http://www.cognitiveliberty.org/dll/singleton_executed.html*
- Rappley, M.D., Gardiner, J.C., Jetton, J.R., & Houang, R.T. (1995). The use of methylphenidate in Michigan. *Archives of Pediatrics & Adolescent Medicine* **149**(6):675–679.
- Robbins, T.W., McAlonan, G., Muir, J.L., & Everitt, B.J. (1997). Cognitive enhancers in theory and practice: Studies of the cholinergic hypothesis of cognitive deficits in Alzheimer's disease. *Behavioural Brain Research* **83**(1–2):15–23.
- Roiser, J.P., Cook, L.J., Cooper, J.D., Rubinsztein, D.C., & Sahakian, B.J. (2005). Association of a functional polymorphism in the serotonin transporter gene with abnormal emotional processing in ecstasy users. *American Journal of Psychiatry* **162**(3):609–612.
- Salmond, C.H., Menon, D.K., Chatfield, D.A., Pickard, J.D., & Sahakian, B.J. (in submission). Cognitive reserve as a resilience factor against depression following moderate/severe head injury.
- Sententia, W. (2004). Neuroethical considerations: Cognitive liberty and converging technologies for improving human cognition. *Annals of the New York Academy of Sciences* **1013**:221–228.
- Solanto, M.V., Arnsten, A.F., & Castellanos, F.X. (2001). The neuroscience of stimulant drug action in ADHD. In M.V. Solanto, and A.F. Arnsten, and F.X. Castellanos, (Eds), *Stimulant drugs and ADHD: Basic and clinical neuroscience*. New York: Oxford University Press, 355–379.
- Sonuga-Barke, E.J.S., Minocha, K., Taylor, E.A., & Sandberg, S. (1993). Inter-ethnic bias in teacher's ratings of childhood hyperactivity. *British Journal of Developmental Psychology* **11**:187–200.
- Stahl, S.M. (2000). *Essential psychopharmacology*. Cambridge: Cambridge University Press.
- Stern, Y. (2002). What is cognitive reserve? Theory and research application of the reserve concept. *Journal of the International Neuropsychological Society* **8**(3):448–460.
- Stuss, D.T., & Levine, B. (2002). Adult clinical neuropsychology: Lessons from studies of the frontal lobes. *Annual Review of Psychology* **53**:401–433.
- The Chambers dictionary (1993). *The Chambers dictionary*. Edinburgh: Chambers Harrap Publishers.
- Turner, D.C., Robbins, T.W., Clark, L., Aron, A.R., Dowson, J., & Sahakian, B.J. (2003). Cognitive enhancing effects of modafinil in healthy volunteers. *Psychopharmacology (Berl)* **165**(3):260–269.

- Turner, D.C., Clark, L., Dowson, J., Robbins, T.W., & Sahakian, B.J. (2004a). Modafinil improves cognition and response inhibition in adult attention-deficit/hyperactivity disorder. *Biological Psychiatry* **55**(10):1031–1040.
- Turner, D.C., Clark, L., Pomarol-Clotet, E., McKenna, P., Robbins, T.W., & Sahakian, B.J. (2004b). Modafinil improves cognition and attentional set shifting in patients with chronic schizophrenia. *Neuropsychopharmacology* **29**(7):1363–1373.
- Turner, D.C., Blackwell, A.D., Dowson, J.H., McLean, A., & Sahakian, B.J. (2005). Neurocognitive effects of methylphenidate in adult attention-deficit/hyperactivity disorder. *Psychopharmacology (Berl)* **178**(2–3):286–295.
- Vartanian, A.J., & Dayan, S.H. (2004). Facial rejuvenation using botulinum toxin A: Review and updates. *Facial Plastic Surgery* **20**(1):11–19.
- Wesensten, N.J., Belenky, G., Kautz, M.A., Thorne, D.R., Reichardt, R.M., & Balkin, T.J. (2002). Maintaining alertness and performance during sleep deprivation: Modafinil versus caffeine. *Psychopharmacology (Berl)* **159**(3): 238–247.
- World Health Organization. (2004). *The international statistical classification of diseases and health-related problems ICD-10*, 2nd edn. Geneva: World Health Organization.
- Yerkes, R.M., & Dodson, J.D. (1908). The relation of strength of stimulus to rapidity of habit-formation. *Journal of Comparative Neurology and Psychology* **18**:459–482.

The Potential of Cognitive Neuroscience Research for Education: Education and Human Potential

by John Geake

► John Geake is Professor of Education at the Westminster Institute of Education, Oxford Brookes University, United Kingdom.

Introduction

A potentially informative contribution to the enhancement of human potential through education lies in the application of research in educational neuroscience: cognitive neuroscience concerned with learning, memory, motivation, and development. For example, an understanding of learning through synaptic reinforcement suggests that spiral models of curriculum would be more efficacious than present lock-step syllabi. Understanding cerebral interconnectivity as a necessary operationalisation of brain modularity has implications for new approaches to pedagogy and remedial interventions. Unfortunately, over-simplistic misunderstandings of brain function have spawned a plethora of neuromyths, which threaten the potential benefit of these scientific endeavours through engendering misdirected and non-achievable expectations in teachers and students. It is important, therefore, that educationists contribute to the cognitive neuroscience research agenda.

Education is the most traditional means of human enhancement. However, despite its ubiquity as a legislated agency for prosecuting social reform and associated political agendas, education has often disappointed its practitioners by its limited effectiveness to enhance human potential. This is not for want of putative educational reforms, but rather because the complexity of educational issues has remained somewhat opaque to insights offered by educational research.

A significant handicap is our limited understanding of human learning, education's core concern, despite its extensive theorising for over a century. However, recent developments in neuroimaging technology have promoted cognitive neuroscience into a position of pre-eminence as the science of learning. Notwithstanding some post-modern hostility towards natural science expressed by the educational 'old guard', modern cognitive neuroscience offers good prospects of enhancing education as a human endeavour.

Some neuroscientific implications for education

There are in-principle implications for education that can be drawn from earlier neuroscientific conceptualisations about learning and the instantiation of memories at the neural level. It was conjectured by Canadian neuropsychologist (and former secondary English teacher) Donald Hebb in the 1940s (and experimentally confirmed in the 1990s) that learning through repetition is manifested as an increase in the efficacy of local inter-neuronal communications (specifically, synaptic functioning). The result is the well-known phenomenon of automaticity in much of our everyday behaviour – driving a car, riding a bicycle, speaking in one's native language. Hebb's account explains how babies as young as six months selectively babble in the phonemes of their mother tongue(s), when from birth they babble in all possible phonemes (due to random articulations of their larynx). Hebbian reinforcement of neural feedback from heard sounds reinforces the neural circuitry supporting those phonetic productions, while those neural connections not so reinforced are effectively pruned away. In fact, without such neural selection in the first 24 months or so of development, our brains would not be organised to process the myriad informational inputs that enable us to participate in our particular cultures.

There are two main implications of Hebbian learning for education. If reinforcement is a necessary condition for culture-based explicit learning, then spiral curricula where material is met over and over again in differing contexts could be predicted to be more efficacious than the linear stepwise curricula that prevail in education systems in the Western world. There is limited evidence from a few case studies of the effectiveness of a spiral curriculum, and consistent evidence that learning in blocks results in weaker long-term retention. A case in point is the resilience of children's naive science concepts to change. Despite universal secondary science education, a significant number of adults maintain naive science beliefs including that the Earth is flat, that the sun orbits the Earth, and that the moon changes shape during its phases. For the latter, it is not hard to imagine in Hebbian terms how a favourite children's book illustration of the moon as a crescent with a man sitting on the pointy end dangling a fishing line creates a far stronger reinforced brain circuit than the one lesson on the moon's phases when, as a 14 year old, one's mind was on other matters.

This raises another implication for education of Hebbian reinforcement: re-programming for errors. The brain is a poor judge of culture-based correctness. An error or misconception that has been neurally reinforced tends to stay that way, unless a more highly reinforced alternate is established that 'out-competes' the erroneous predecessor in terms of salience or value. Certainly a red cross on an assignment or exam paper is unlikely to afford the necessary neural change. Music teachers know that merely telling a student who has diligently practised the wrong note about this error is insufficient to prevent their playing that error in their exam performance – only diligent slow practice with the correct note will suffice. Consequently, a Hebbian account of learning implies that teachers need to spend more time on one-to-one feedback of errors, and supervision of re-mastery, if education outcomes are to improve across the board. This has obvious systemic resource implications.

Likelihoods for educational neuroscience

Neuroscience will offer more for education as we increase our understanding of brain function. This is especially true for understanding the most basic characteristic of brain function, neural functional interconnectivity. "Circuitry is the basis of all complex neural function" (Mind Map 2007). The thrust of neuroimaging over the coming decades, thanks to recent breakthroughs in neuroimaging technology and analysis, is to understand neural connectivity. "Without knowing the circuit, there is no way of knowing how the brain works" (Mind Map 2007).

There are common brain functions for all acts of intelligence, especially those involved in school learning. These interconnected brain functions (and implicated brain areas) include:

- Working memory (lateral frontal cortex);
- Long-term memory (hippocampus and other cortical areas);
- Decision making (orbitofrontal cortex);
- Emotional mediation (limbic subcortex and associated frontal areas);

- Sequencing of symbolic representation (fusiform gyrus and temporal lobes);
- Conceptual inter-relationships (parietal lobe);
- Conceptual and motor rehearsal (cerebellum).

Importantly, these neural contributions to intelligence are necessary for all school subjects, and all other aspects of cognition. Cerebral interconnectivity is necessary for all domain-specific learning, from music to maths to history to English or Dutch as a second language. There are no multiple intelligences; rather, there are multiple applications of the one general but multi-faceted intelligence.

An illustrative early example was provided by a functional magnetic resonance imaging (fMRI) study of repeated subtraction (100 minus 7, minus 7, minus 7...) which revealed over ten cortical areas to be significantly activated in performing such effortful arithmetic (Dehaene 1997). These areas were found in both the left and right hemispheres, anterior and posterior. From other neuroimaging studies it is possible to attribute specific functionality to these various areas: symbolic representation and decoding, quantity representation, working memory, and so on. Importantly, there is no single area of brain dedicated to subtraction, or to any specific arithmetical operation. It takes the combined effort of a set of interconnected brain modules, presumably evolved for other purposes, to do arithmetic. Yet, this arrangement usually works remarkably quickly and accurately, at least to certain limits. But given there are so many more connections between these functional areas it suggests that interconnectivity is likely to be of far greater importance in looking for neural explanations of individual differences in education performance. Certainly, there is converging neuroimaging evidence that the brains of young gifted children are characterised by enhanced interconnectivity. With a greater understanding of cerebral interconnectivity, a neuroscience-informed assessment of learning needs can be foreseen where learning difficulties due to critical connective bottlenecks might be diagnosed. SEN remediations could then target alternate areas of potential neural plasticity, rather as stroke patient rehabilitation is now conducted.

More generally, we might expect neuroscientifically informed pedagogies whereby the introduction of new topics would employ activities that better reinforce understanding rather than inadvertently establish misconcepts. By way of example, a topic that could benefit from such an approach is the mathematical watershed of fractions. It is an intriguing dissociation that any young child can divide half a birthday cake at the end of the party amongst the five remaining guests, yet most adults on the street cannot compute 1/5 of 1/2. Given that culturally relevant concrete knowledge and culturally relevant symbolic knowledge tend to be stored laterally in our brains (typically right vs. left fusiform gyri (FG)), I wonder if the problem with fractions could be due to a breakdown in transference between these concrete and symbolic representations of fractions, i.e., impoverished inter-modular functional connectivity between the RFG and LFG. The implication for educational orthodoxy is striking: expertise in fractions does not emerge from concrete experiences as per Piaget, but rather in parallel. There is only anecdotal evidence for such a claim, but a well-designed neuroimaging study could be informative, and possibly have practical applications for the teaching of primary school arithmetic.

Limits to educational neuroscience

Neuroscience is a laboratory-based endeavour, dependent upon sophisticated neuroimaging technology. Even with the best of intentions, extrapolations from the laboratory to the classroom need to be made with considerable caution. A crucial point that most of the media overlook or ignore is that neuroimaging data are statistical. The coloured blobs on brain maps representing areas of significant activation (so-called 'lighting up') are like the peaks of sub-oceanic mountains, which rise above sea level. In neuroimaging studies, the sea level, that is how much or how little activation to reveal, is determined by the researcher as a suitable level of statistical threshold. In fact, the most challenging aspect of neuroimaging experimental design is to determine suitable control conditions to contrast with the criterion activations to avoid showing that actually most of the brain is involved in the targeted cognitive task. In a classroom it would be quite silly to think that only a small portion of pupils' brains are involved in an activity just because a small area of brain was reported to be of significance in a neuroimaging study of a similar task.

Another limitation to educational neuroscience arises from individual differences in brain structure and function, which are not necessarily reflected in the pooled group data required to reach sufficient statistical power given the subtle changes in cerebral vasculature that are recorded during an imaging study. It can be stated without fear of contradiction that due to the nonlinearities of morphogenesis, and the uniqueness of subjective experiences, every human brain that ever was, and ever will be, is unique. This includes the brains of identical twins ... and human clones should any ever be developed. Consequently, excluding pathology, it is near impossible to predict educational performance from variance in brain structure, at least by current neuroimaging technology. What few data there are about group structural differences create their own challenges for prediction: reading deficits are correlated with both a higher than average hemispheric asymmetry, as well as with a lower than average hemispheric asymmetry – a classic Wundt inverted U curve.

Overcoming neuromythologies

However, the greatest challenge presently facing the application of neuroscientific findings to education is that posed by the pervasive influence of so-called 'brain-based' teaching strategies within school education. Among the most popular are 10% usage, L and R brain thinking, VAK learning styles, brain gym, Multiple Intelligences, and water as brain food. Incredibly, most of these neuromyths are in complete contradiction to the scientific accounts of brain function.

The absurdity of the myth that we only use 10% of our brains is best exposed by the facts that evolution does not produce excess, much less 90% excess, and that in the millions of neurological studies ever conducted, no one has ever found an unused portion of the brain! (Beyerstein 2004). The left and right-brain thinking myth seems to have arisen from misapplying laboratory studies which show that the semantic system is left-lateralised (language information processing in the left hemisphere; graphic and emotional information processing in the right hemisphere) by ignoring several important caveats. First, the left-lateralisation is a statistically significant bias, not an absolute. Language processing does stimulate some right hemisphere activation. Second, the subjects for such studies are extremely right-handed. In fact, the subjects for most neuroimaging studies are extremely right-handed – it's a way of maximising the probability that group maps have contributions from all participants (that is, that their functional modules will be in much the same place in their brains). As language researchers are at pains to point out: "It is dangerous to suppose that language processing only occurs in the left hemisphere of all people" (Thierry, Giraud and Price 2003). The largest neural interconnection to transmit information in the brain is the corpus callosum, the thick band of fibres that connects the two hemispheres. The left and right sides of our brains cannot help but pass information between them. There is some evidence that constrictions in the corpus callosum can predict deficiencies in reading abilities (Fine 2005), again highlighting that language, much less thinking, is not isolated to one half of the brain.

The most pervasive neuromyth is that children have a dominant learning style: Visual, Auditory or Kinaesthetic (VAK). VAK learning styles were proposed to explain individual differences in learning abilities. The suggestion that some people are primarily visual (or auditory or kinaesthetic) learners is based on an implicit assumption that these sensory modalities function independently within the brain. This assumption is wrong. Brain interconnectivity includes sensory inputs. "To perceive the world as a whole, our five senses have to team up in the brain – and in some cases they actually seem to fuse with one another" (Kayser 2007). Moreover, as primates our afferent brain processes are 50 – 60% visual. What we do with that information is to construct spatial and quasi-spatial conceptual maps of the world so that we understand our location, both physically and conceptually. This is even true for people who are congenitally blind. Obviously unsighted people do not get their initial information visually but by tactile and aural means instead. But just as sighted people do, they construct spatial maps of the world to understand where they are.

fMRI studies in Oxford which compared people looking at and listening to speech which was synchronised and unsynchronised with the speaker's lip movements found dedicated areas in both visual and auditory cortices that show both a super-additive and a super-subtractive effect (Calvert, Campbell and Brammer 2000). We pay special attention when visual and auditory information does or does not correlate. From an evolutionary perspective, the survival of our primate ancestors clearly depended on this ability; living in a dense jungle, coordination of visual, auditory and tactile information about prey and predators was critical.
We can demonstrate the interconnectivity of visual and auditory information processing by asking children to decide, by estimation, which is the larger of two groups of dots. Children as young as five years give a pretty accurate answer. Now if we replace one of the groups of dots with a series of rapid sounds that are too quick to count, the task becomes a visual – auditory comparison. What happens to the accuracy of the response? There is no change! However we receive information, we abstract it to make sense of it and to decide what to do. We do not learn through one sense alone.

VAK is just one of over 170 different learning style inventories available via Google. However, no *independent* research has found learning benefit for any of them (Coffield, Moseley, Hall and Ecclestone 2004). The widespread proliferation of neuromyths has itself become a matter for investigation. My speculation is that folk psychology has generated folk brain science: we experience our left and right sides, and five senses, so brain function is similarly divided. But, if our brains were that simple, then we wouldn't be here today.

Publications about educational neuroscience

There is a growing literature of educational neuroscience, with both academic and teacher professional articles. It is a pity that the promulgators of the many neuromyths and so-called brain-based teaching strategies seem not to have read or taken much head of this literature.

- Blakemore, S-J, & Frith, U. (2005). *The Learning Brain: Lessons for Education.* (Blackwell Publishing).
- British Neuroscience Association & European Dana Alliance For The Brain (2003). *Neuroscience: Science of the Brain: An Introduction for Young Students.* (Liverpool: BNA).
- Byrnes, J.P. (2001). *Minds, Brains, and Learning: Understanding the Psychological and Educational Relevance of Neuroscientific Research.* (Guilford Press).
- Byrnes, J.P. & Fox, N.A. (1998). *The educational relevance of research in cognitive neuroscience. Educational Psychology Review* **10**(3): 297-342 (and following commentaries to p.412).
- Geake, J.G. (2000). Knock down the fences: Implications of brain science for education. *Principal Matters.* April, 41-43.
- Geake, J.G. (2003). Adapting Middle Level educational practices to current research on brain functioning. *Journal of the New England League of Middle Schools* **15**(2):6-12.
- Geake, J.G. (2004). How Children's Brains Think: Not left or right but both together. *Education 3-13.* **32**(3):65-72.
- Geake, J.G. (2004). Cognitive neuroscience and education: Two-way traffic or one-way street? *Westminster Studies in Education* **27**(1):87-98.

- Geake, J.G. (2005). Educational neuroscience and neuroscientific education: In search of a mutual middle way. *Research Intelligence* **92**:10-13.
- Geake, J.G. (2006). The neurological basis of intelligence: A contrast with 'brain-based' education. *Education-Line.* *www.leeds.ac.uk/educol/documents/156074.htm*
- Geake, J.G. (2007). A Brainy School of the Future? *Learning Matters* (in press).
- Geake, J.G. & Cooper, P.W. (2003). Implications of cognitive neuroscience for education. *Westminster Studies in Education* **26**(10): 7-20.
- Goswami, U. (2004). Neuroscience and education. *British Journal of Educational Psychology* **74**:1-14.
- Goswami, U. (2006). Neuroscience and education: from research to practice? *Nature Reviews Neuroscience* **7**:406-413.
- Gura, T. (2005). Big plans for little brains. *Nature* **435**:1156-1158.
- OECD (2002). *Understanding The Brain: Towards a New Learning Science.*
- OECD (2007). *Understanding The Brain: Birth of a Learning Science.*

The potential of cognitive neuroscience research to enhance education

For educational neuroscience to progress as a field of research, the importance of involving educators in setting the educational neuroscience research agenda cannot be over-emphasised. The Oxford Cognitive Neuroscience Education Forum has been holding termly meetings since 2001 (Kratzig and Arbuthnott 2006). The Forum enables educationists and neuroscientists to sit around the table to consider both scientific research proposals in terms of their potential educational applicability, and issues arising from educational studies, which might be informed by neuroscientific investigation.

This collaborative process suggests a methodology for educational neuroscience based on an action research cycle (ARC). The starting point is a significant education concern, which then can be characterised by a specific education problem. This becomes the generator of a broad science research question, which then is focussed into a set of specific neuroscience research questions. Following the neuroscientific study, the findings are scrutinised for possible educational implications and applications. These form the basis of an education research program to investigate their impact on mitigating the original educational concern. Thus the first round of the ARC is completed.

Typical concerns from teachers that could shape the educational neuroscience research agenda include:

- Is there a critical period for learning a second language? Music? Physics?
- Should boys and girls be taught separately in some subjects?
- Are the brains of children today different from those of previous eras due to high levels of IT usage?
- Are there any predictive correlations between differences in brain structure and school outcomes?

Although funding to support research across the interdisciplinary boundary of the social and natural sciences has historically been very difficult to attract, there have been recent moves by two of the UK's funding councils (the ESRC and the MRC) to invite applications to conduct socially relevant neuroscience.

Concluding remarks

In terms of the objectives of this bilateral colloquium, education, as the most traditional means of human enhancement, could benefit from the exchange of expert knowledge about those areas of education which transcend cultural specifics. Neuroscientific research into human learning is an international endeavour, and could profitably become more so. At present, there is no comprehensive database on normal children's brain structures across the developmental period covered by formal education, say 5 to 25 years. Without such a database, studies of the neural effects of different educational interventions are necessarily constrained in their interpretation, and hence application. Such a database (requiring several thousand brain images to control for socio-economic factors) could be constructed through the cooperative efforts of the hundreds of fMRI centres now operating across Europe, North America, and Australasia. 'All' it would take is multilateral agreement by the governments of participating centres to fund the necessary imaging and analyses.

Several governments have taken steps towards establishing interdisciplinary research centres to enable educational neuroscience to gain a foothold that otherwise would be difficult in traditional discipline-based university departments. With six centres, and a quarantined 5-year budget, the Science Learning Centers program of the National Science Foundation in the USA is the most ambitious to date (Sharp, Byrne and Bowker 2007).

Clearly there are potential psychosocial and ethical aspects of this work, not least in school selectivity. However, the hope is that educational neuroscience research will ultimately improve the educational experience of all learners towards optimising their potential.

References

- Beyerstein, B.L. (2004). Ask the Experts: Do we really use only 10% of our brains? *Scientific American* **290**(6):86.
- Calvert, G. A., Campbell, R. & Brammer, M. J. (2000). Evidence from functional magnetic resonance imaging of crossmodal binding in human heteromodal cortex. *Current Biology* **10**(11):649-657.
- Coffield, F., Moseley, D., Hall, E. & Ecclestone, K. (2004). Learning styles and pedagogy in post-16 learning: A systematic and critical review (Report No. 041543). London: Learning and Skills Research Centre.
- Dehaene, S. (1997). *The Number Sense: How the Mind Creates Mathematics*. (OUP).
- Fine, J. (2005). Reading deficits predicted by differences in structure of the corpus callosum. (Montreal: AERA).
- Kayser, C. (2007). Listening with your eyes, *Scientific American Mind* **4**(2):24-29.
- Kratzig, G.P. & Arbuthnott, K.D. (2006). Perceptual learning style and learning proficiency: A test of the hypothesis. *Journal of Educational Psychology* **98**(1):238-246.
- Mind Map. *Scientific American Mind*. June/July 2007;**18**(3):9.
- Sharp, J.G., Byrne, J. & Bowker, R. (2007). VAK or VAK-uous? Lessons in the trivialisation of learning and the death of scholarship. *Research Papers in Education* (in press).
- Thierry, Giraud & Price. (2003). Hemispheric dissociation in accessing the human semantic system. *Neuron* **38**:499-506.

www.brookes.ac.uk/schools/education/rescon/ocnef/ocnef.html
www.scienceoflearning.org/

Enhancing Memory in the Criminal Trial Process

by Willem A. Wagenaar

▸ Willem A. Wagenaar is Emeritus Professor of Experimental Psychology and Law, Leiden University and Emeritus Honorary Professor, Utrecht University, the Netherlands.

In many criminal trials the fact finding depends in a crucial manner on the memory of people, witnesses and defendants alike. But for various reasons these memories may be vague, incomplete or even entirely wrong. One reason is that the events that must be remembered took place a long while ago. Not infrequently criminal trials take place several years after the crime was committed. In the Yugoslavia Tribunal in The Hague it is not unusual for witnesses to be interrogated on events that happened 10 to 15 years ago.

My most extreme cases were the 1987 trial against John Demjanjuk in Jerusalem, who was suspected to have murdered 850.000 people in the extermination camp of Treblinka which was closed in the summer of 1943 – and the case against Marinus De Rijke in 1988, suspected of war crimes till 1944 (Wagenaar and Crombag 2005). Another impeding factor is that the finder of fact is often interested in details that were rather trivial at the time, such as licence plate numbers, what people looked like, how a certain person behaved in a crowd, what exactly was said, what the exact time was, or which day it was.

An example is the neighbour of the owner of an expensive Mercedes, who was asked to remember whether or not the owner had switched on the alarm on a specific Friday night, six years ago (Ibid. Ch. 8). Why would she ever have stored this information in her memory at all? Are there any substances or techniques that may help to improve vague, incomplete and false memories, or even to regain memories that seem entirely lost? Answers to these questions can only be understood after a more extensive explanation of how memory works.

Information storage and search processes

The successful usage of a database presupposes two clearly distinct processes: the storage of information in the data base, and an efficient search algorithm for retrieval of the information. To make this point clear, I will use the metaphor of a university library. The data base consists of a huge number of books, placed on shelves. The arrangement on the shelves may be according to subject, author, and year of publication. But it is also not unusual for university libraries to arrange books according to size and year of acquisition. No matter how the books are arranged, when the collection increases to many millions of books, it will be hardly possible to find any specific book, if there is no catalogue. Library catalogues are organised on the basis of search cues that are likely to be employed by the prospective users. Users are supposed to know combinations of book title, author, publisher, and year of publication. A sufficiently detailed query will result in a limited list of books, from which the user may select the desired book. This selection process may be further improved if the catalogue facility provides abstracts of the books that correspond to the initial query.

It is important to notice two aspects in this description of a storage and search facility. The first aspect is that the search cues must be selected and entered in the catalogue before the book is shelved. The selection of cues is based upon the anticipated knowledge of future users. The initial selection of search cues limits the future options. Users who only remember a 'big red book about fairy tales' will never find it through the catalogue, if these cues were not anticipated when the book was stored after acquisition. The second aspect is that a system with search cues is based upon one-directional associations. The book title can be used to retrieve the abstract, but information from the abstract will not necessarily lead to the identification of the book title. The title 'Tales of Mother Goose' may lead to a description of Bluebeard who killed his wives because they could not resist the temptation to use the golden key to the forbidden room. But the catalogue will not tell you the book title when you search for 'golden key, forbidden room, or killing wives.' (But note that Google will allow you this inverse type of search!).

I have studied the use of cues for retrieval of information from autobiographical memory during a period extending over six years. The study clearly demonstrated the two aspects described above: memories get lost when the effectiveness of search cues diminishes. Names of people and places are very effective cues when they are unique, i.e. when they lead to the memory of only one specific event.

But they become highly ineffective when more and more events are stored in which the same people or places play a role. The other finding of relevance here is that cue-memory relationships are asymmetrical. Dates do hardly ever lead to remembering what happened on that day, but a description of the event may lead to remembering the date. The traditional question "Where were you in the afternoon of 10 May 2007?" is less effective than "When did you last visit the British Ambassador's Residence in The Hague?" The typical requirements of a huge data base, from which information must be retrieved through specific search processes, leads to a number of 'memory rules' that will be explained in the next three sections.

Encoding

Memory can only work if three successive stages are successfully completed: the stages of encoding, storage, and retrieval. In the initial stage of *encoding*, information is perceived through one or more of the senses, transferred to a temporary memory store, and subsequently processed and prepared for storage in long term memory. Rule 1 is an obvious consequence of this simple logic: *Information that does not pass the encoding stage can never be remembered*. But even information that is successfully transferred into long term memory may have undergone considerable changes. Some aspects will be left out, due to a process of selection. Other aspects may be altered, for instance because the information is linked and adjusted to other information already present in earlier memories. And it is also possible that new information is added before transfer to long term memory, because the perceptions were interpreted in a certain manner.

A well-known example of the latter phenomenon is the perception and subsequent recall of a causal relationship, which is logically nothing else but a cognitive construct at hindsight (Ibid. Ch. 2). Encoding is not passive, as in a television recording. It is a complex and active process, in which the information is considerably transformed, and in some cases even distorted. Hence the important question is not so much whether information is encoded at all, but above all in which form it is encoded. The rather simple formulation of Rule 1, that information cannot be recalled if it does not pass the encoding stage, can therefore be refined to Rule 2: *Information can only be recalled in the transformation applied during the encoding stage.*

The most important operation during encoding, however, is the creation of access through search cues. Some of the information is stored in such a manner that it can be used as search cue; other information is given a more passive role, so that it can be retrieved only when the appropriate search cues are utilized. This then, leads to the additional Rule 3: *Information can be recalled only if in the encoding stage it is linked to search cues that will be employed in the retrieval stage.*

Storage

In the second stage, *storage*, information is kept in memory until it is needed for retrieval. This period between encoding and retrieval is called the *retention period*. In a naive conception of memory it is assumed that in the retention period information remains constant and unaffected. Psychological research since the 1970's has revealed that this assumption is unwarranted, which leads to the following simple Rule 4: *Information that is successfully encoded can not be recalled if it is lost in the retention period.* Especially research by Elizabeth Loftus has revealed that memories stored in long term memory are influenced by post-event information, i.e. by new information about the same event, or about similar events. In the stage of encoding links will be created between new information and older information to which it is related. The result can be more than just a new link; it can be a revision of the old memory trace, to the extent that a new trace is formed in which old and new information is blended. The search cues, formally linked to the old memory, are now linked to the blended memory, and during recall there is nothing to indicate that this recollection has been renewed. This leads to Rule 5: *New information has the power to alter old memories;* and Rule 6: *Search cues tend to be linked to the most recent revisions of memory traces.* The fact that at recall we are unable to detect that the retrieved memory trace is a composite based on a number of separate experiences is called in our jargon source amnesia. The effect of blending post-event information with the original memory, in combination with *source amnesia*, is that there is hardly any correspondence between the confidence of witnesses in their memories, and the demonstrable accuracy of these memories.

Forgetting during the storage stage is not so much caused by the decay of memory traces, but rather by the process of retrieval cues being linked to more recent inputs. Thus it is not the passage of time that causes forgetting, but the interference by similar memories. This leads to Rule 7: *Forgetting during storage is promoted by the occurrence of related events that are stored under the same retrieval cues.*

A highly relevant question is of course what happens to old memories that are not any longer linked to their cues. As far as we know their fate is not that they disappear, but only that they are rendered inaccessible. In an experimental study I have demonstrated that it is possible to regain access to memories that seemed to be lost through interference, by using alternative retrieval cues that were still linked to the old memory trace. The problem then is of course to find cues that are specifically linked to the older memories, and not to the updated versions. This will be more difficult when the original memory and the updated version look resembling. Rule 8: Older memories that are replaced through interference in the storage stage, can be retrieved only through the use of cues that are specific for the older version.

Retrieval

In the third stage recall is effectuated through the presentation of retrieval cues. Usually these cues may be in the shape of questions, but it is also possible to retrieve information through the presentation of a line up of faces, objects, voices, or even by means of smells. The success of retrieval is in the first place defined by cue effectiveness, which leads to a simple Rule 9: *Even if information is safely stored and preserved in memory, retrieval will only succeed if effective retrieval cues are presented.* There are two important aspects to this: the degree to which the desired information is still uniquely linked to the cues envisaged during encoding, and the ingenuity of the interrogator to find effective cues. The first aspect cannot be affected any more during retrieval, but the second aspect might be considered as the essence of professional interrogation. The retrieval of dates may serve as an example. The question "Where were you in the afternoon of 10 May 2007" does not promise much success. The inverse question: "When did you last visit the British Ambassador's Residence in The Hague?" is more likely to produce a correct answer.

It belongs to an interrogator's skill to know this. But it is well established that precise dates are hardly ever recorded in memory. Instead a list of 'landmark events' is stored of which the dates are known: a trip to the winter sports, a visit to Amsterdam on Queen's Day, a birthday party on May 20, or a short holiday during Pentecost. The event in the British Residence may be retrieved in relation to these landmarks. I myself remember that it was in the month of May before Ascension, and that it was on a Thursday, because of my regular class meeting in the morning. Hence it can be reconstructed that it must have been on the 10th or the 17th; since the 17th was Ascension, it must have been the 10th of May. The reconstruction process will be assisted considerably when the interrogator does not immediately ask about the date of the event, but instead enquires first after some landmark events in that period. This technique will be mentioned in a subsequent paragraph under the cognitive interview. Rule 10: *The selection of effective retrieval cues should be based on the understanding of memory representation processes.*

An often overlooked risk during retrieval is that the presentation of retrieval cues may not be neutral. Suppose the witness discovered the body of a murdered woman. The question: "And what did you do next?" does not contain itself any information about what the witness might have done. But this is entirely different in the question "Did you enter the kitchen afterwards?" The wanted information is now disguised as a search cue. It is possible that 'entering the kitchen' is used to retrieve an event in which the witness indeed entered the kitchen, even though that did not happen immediately after the discovery of the body. But a positive answer to the question may lead to an updating of the original memory. Now the representation includes entering the kitchen after the gruesome discovery, and cues leading to the original memory may now be uniquely linked to the updated version. Rule 11: *The presentation of retrieval cues may be the motor of memory distortion and forgetting. In everyday life this is not a problem that will concern us much.* But in the context of criminal investigation and the judicial finding of fact it may be requested that interrogation by professionals takes place in such a way that effects of memory distortion are evaded. Especially those who cherish the belief that memory can be enhanced by means of special interrogation techniques should take Rule 11 into account.

Memory enhancement?

The question whether the memory of witnesses and defendants can be enhanced by whatever means is very imprecise. Which stage of the memory process is intended? Should the encoding process be made more effective during the observation of a criminal act? Should the effects of interference during storage be reduced? Or should the relation between cues and original memories be restored in the retrieval stage?

A general consideration that must be taken into account is that everyone can be asked to testify about more or less any event that happened in the past. Enhancement can hardly be directed at specific groups, or in relation to specific events.

One might reason that police officers are the more promising targets for memory enhancement, because of their frequent encounter of crimes and criminals. On the basis of my analyses of some 1000 criminal files in the past 20 years, I have come to the conclusion that the witnesses most critical for the finding of fact are rarely police officers, but most frequently normal citizens who at the time did not expect to be confronted with any crime. Hence proposals for memory enhancement involve almost everybody, in all conditions of everyday life.

A second consideration is that the operation of memory processes, summarily described above, serves a clear purpose. Selection and reprocessing during the encoding stage are necessary steps for enabling effective search in a gigantic data base, and in real time. The updating of memory in the retention period maintains an accurate representation of the world around us, which in turn is needed for a rapid reaction to whatever is happening. The steering of search processes in the retrieval stage through continually redefined cue effectiveness is the best solution when exhaustive search of a data base is impossible. In as far as these mechanisms represent an optimal solution for our memory problems in everyday life it would be utterly undesirable to disrupt them, just because that might be advantageous in the unlikely case that we will be called upon to be legal witnesses.

But still, if any enhancement is possible at all, it should apply to one or more of the three main stages of the memory process. Therefore we may consider the options separately.

Enhancement of encoding

Encoding can be enhanced by improving the perception of witnesses, by increasing their attention, or by refining their encoding strategy. The most notorious obstacle for eyewitnesses is the perception of faces (see for instance the recent literature on DNA revisions, demonstrating that about 70% of judicial errors are caused by faulty recognitions). The most frequent problems are that the distance is too large, the illumination too dim, or the time too short. There is no promising way to enhance face perception under unfavourable conditions, not even in the limited target group of police officers. In situations in which face perception is relevant, such as in banks or in soccer stadiums, it is much better to install TV cameras, than to rely on eyewitness memory. Likewise there are many situations in which it will be useful to record voices, such as in telephone taps, or during interrogation of witnesses and suspects.

Especially in the latter situation the Dutch Police and Justice demonstrate an incomprehensible reluctance to do so; they rather rely on memory, even though it is absolutely certain that conversations are not literally encoded. Attention for details relevant to criminal investigation can be increased through instruction, but not without cost. Attention is a selective process; it is always a matter of focussing on specific details at the cost of ignoring other details. But whatever the cost, there will be no practical manner to instruct the rather ill-defined group of prospective witnesses, in situations in which we do not know on which details they should focus their attention. Encoding is most effectively enhanced by learning a more efficient code. Examples are mnemonists who have developed elaborate codes for the encoding of large numbers, and highly advanced chess players who have learned to encode entire chess positions in a glance. It may be possible to train police officers to become more efficient encoders of faces, but attempts of this kind have failed thus far.

There have been several research programmes on the improvement of memory through the intake of substances, like fragments of the hormones ACTH and vasopressin, caffeine, ginseng and all sorts of other herbs, etc. These attempts have typically been directed at the improvement of memory for learned material, as in the process of studying for an exam. This process is fundamentally different from the typical situation of an eyewitness. At the time of encoding the eyewitness does not consciously attempt to learn. But even without this obvious problem of generalization, there is no indication that reliable and robust effects of memory enhancement were found thus far.

Enhancement of storage

Protection of memory traces in the storage stage can in principle be achieved in a number of different manners. The most obvious solution would be to protect witnesses against interfering post-event information. That is most efficiently achieved by interrogating them very soon after the crime. Most often that is exactly what crime investigators do. The most frequent cause of delays is of course that it may take a considerable time to find the witnesses. But it must be admitted that the Anglo-Saxon system of adversarial law which implies the immediacy principle (i.e. the testimony of witnesses during their appearance in court) may cause extra delays as compared to the inquisitorial system mostly encountered on the European continent, in which witness statements may be recorded long before the actual trial takes place.

If extensive delays between encoding and retrieval do occur, the encounter of interfering post-event information can hardly be avoided. Enhancement should in that case be directed at maintaining access to the original memory traces, which is usually achieved through rehearsal. From the days of Ebbinghaus' memory studies in the late nineteenth century it has been established that frequent rehearsal makes memory traces immune to interference. The difficulty in the daily practice of criminal investigation is of course that witnesses often do not realise that their recollections will be needed, or that their memories are threatened by post-event information. On the contrary, rehearsal of memories together with other witnesses may have the opposite effect of creating new memories, based upon blends of the individual recollections. This process is also known as *collaborative storytelling* (Ibid. Ch. 10). If investigators can induce witnesses to rehearse their memories, it would be more practical to interrogate them and thus obtain perfectly stable memory records.

Enhancement of retrieval

Considerable effort has been devoted to the development of more effective retrieval techniques. Well-known is the claim that witnesses may remember more when under hypnosis. This is a myth, which is consistently refuted in empirical research. The only robust effect of hypnosis is that it makes people more sensitive to suggestion, and that is about the last thing one should do with witnesses in a legal trial. A more promising approach is the *cognitive interview* technique, which aims at providing a richer assortment of retrieval cues, not unlike the description of using landmark events for the recall of dates. Usually it is attempted to guide witnesses back to the time closely preceding the to-be-remembered event; this may be achieved by asking the witness to remember the course of that day, the weather, other events, the environment, other people, etc.

The cognitive interview technique has a small but significant effect on the enhancement of witness' memory. However, it must be added immediately that related techniques carry a substantial risk of creating false memories. These techniques are usually described under the name *memory work*. Examples are age regression, guided visualisation, hypothetical speak, trance writing, dream work, body work (Ibid. Ch. 9). Guided visualisation, for instance, is a technique used by therapists and aimed at the recovery of lost or repressed memories. The risk is that the visualisations are based on fantasy rather than memory, and subsequently combined with true memories to form a blend. Memory work techniques are by some researchers considered as the major source of the false memory syndrome. Again it needs little argumentation that witnesses in a legal trial should not be subjected to techniques in which old memories are blended with fantasies.

A number of techniques have been directed at discriminating between true and false memories. Examples are the various polygraph techniques, Statement Validity Analysis, and the Anatomically Correct Dolls Test. Naturally, such techniques do not enhance the quality of memories, but they may help to improve the quality of eyewitness testimony presented in court. The discriminatory power of such techniques ranges from nil to rather small. Moreover it must be stressed that they aim at discriminating between speaking truth and deliberately lying. There is no indication that such techniques may help to detect unintended memory mistakes.

Conclusion

The typical problems of eyewitness memory are caused, on the one hand, by the complex manner in which memories are encoded, maintained during storage and retrieved, on the other hand by the situation that most people are involved in criminal investigations as witnesses, long after the encoding took place and often even after a considerable retention period. Consequently, it is hardly possible to enhance eyewitness memory in these first two stages. Attempts to enhance recall in the retrieval stage by means of substances, training, or special interrogation methods have thus far not yielded significant or robust results, with possibly an exception for the *cognitive interview* technique. At the same time it must be realised that special retrieval techniques may make the problem worse, because they introduce the risk of altering the vague or weak memory traces still available. The best way to improve the quality of eyewitness testimony is to interrogate witnesses shortly after the crime, to record the interrogations on video in all cases, to prevent the confrontation with post-event information, especially post-event information produced by the process of investigation itself, and to use proper methods for interrogation and confrontation, so that all types of suggestion are avoided.

Reference

– Wagenaar, W.A., and Crombag, H.F.M. (2005). *The Popular Policeman and Other Cases.* Amsterdam: Amsterdam University Press.

Better Brains

by Gangani Niyadurupola

► Gangani Niyadurupola of the University of Bath is Fellow at the Parliamentary Office of Science and Technology, London, United Kingdom.

Introduction

As part of the Foresight Brain Science, Addiction and Drugs project a state of science review was carried out into current knowledge in the area of cognitive enhancers. These are factors that improve functions such as memory, learning and attention. The review concluded there would be significant improvements in our understanding of this area in the next twenty years, and that these would lead to an increase in the development of cognitive enhancers. It raised the possibility of otherwise healthy individuals using enhancers to boost their cognitive abilities. This article reviews existing methods of cognitive enhancement along with likely future developments, and considers the regulatory and ethical questions that they pose.

Background

Interest in the area of cognitive enhancement stems from an expected increase in our knowledge of the mechanisms involved in skills such as learning, memory and attention, together with a deeper understanding of the relationship between these functions and brain chemistry. The Foresight review indicated that in the first instance these enhancers might involve nutritional and pharmaceutical agents. (The Foresight state of science review on Cognition Enhancers is at *www.foresight.gov.uk/Previous_Projects/Brain_Science_Addiction_and_Drugs*). Some dietary factors associated with cognitive enhancement are summarised in Box 1.

These are generally considered less controversial than the use of novel drugs; for instance stimulants such as caffeine are widely accepted and used as a means of enhancing cognitive abilities. Many drugs have already been developed to treat specific cognitive impairment disorders and these could be used to treat less severely impaired, or even healthy individuals. This would raise ethical and regulatory issues which are discussed later. The area of pharmaceutical cognitive enhancement has already been the subject of a number of academic reviews (Rose 2002; Farah *et al.* 2004).

The Foresight report also considered the potential for cognitive enhancers to be developed using mechanisms as diverse as computer-brain interfacing and genetic manipulation, but such approaches are longer term and beyond the scope of this briefing.

Box 1. The role of nutrition in cognitive abilities

There is a general lack of large scale, robust trials investigating the role of diet in cognition. Furthermore, most current research is related to deficiencies of nutrients in particular disorders rather than enhancing cognitive function. However there is growing evidence from small scale studies that there may be a link between cognitive abilities and particular nutritional factors:

- Omega-3 essential fatty acids have specific roles in the brain and deficiencies have been linked to a risk of developing a variety of cognitive impairment disorders;
- Eating wholegrain foods that are slowly broken down and release a sustained supply of glucose into the bloodstream is thought to maintain optimum brain function;
- There is some evidence to suggest that dietary supplements of B vitamins, folic acid or foods rich in antioxidants such as blueberries improve cognitive function, and several larger trials are underway to investigate this.

Current pharmacological cognitive enhancers

A range of cognitive enhancing drugs are available which have been developed for therapeutic needs. The availability of these treatments has led to academic research trials which demonstrate cognitive improvements in healthy people. It is generally agreed that not enough is known about the long term effects of these drugs to advocate their use in healthy individuals at the present time.

Memory

Drugs to improve memory generally work by altering the balance of particular chemicals (neurotransmitters) in the brain that are involved in the initial learning of a memory or its subsequent reinforcement. The drug donepezil, which inhibits the cholinesterase neurotransmitter, is a common treatment for Alzheimer's disease but has also been shown to have an effect on otherwise healthy individuals. Studies carried out with healthy middle-aged airline pilots showed that donepezil enhanced their performance after flight simulator training (Yesevage *et al.* 2002).

Executive function

Executive function refers to a broad range of abilities that allow us to carry out tasks and to select and use the appropriate information from a range of competing stimuli. This is a difficulty for those diagnosed with Attention-deficit Hyperactivity Disorder (ADHD) and is often treated by stimulants such as methylphenidate which alter the balance of neurotransmitters in the brain (see Box 2). (Methylphenidate is marketed under a number of trade names, the most common of which are Ritalin™ and Concerta™).

Studies on healthy volunteers show improved accuracy in completing a problem-solving task after receiving methylphenidate (Mehta *et al.* 2000).

Wakefulness

The most commonly used drug in this area is another stimulant called modafinil. This is licensed for the treatment of sleep disorders such as narcolepsy but also for the treatment of (healthy) workers who find their shift patterns difficult. Experiments with healthy volunteers have shown that modafinil can improve abilities in a range of cognitive tests (Sahakian *et al.* 2003) and allow subjects to function better after periods of sleep deprivation. It is thought to have potential as a cognitive enhancer as it appears to avoid some of the side-effects and dependence usually associated with stimulant use.

Expected developments in cognitive enhancers

Pharmaceutical companies are currently exploiting increased knowledge of how the brain works to target novel drugs for a range of cognitive impairment disorders, such as Alzheimer's disease and ADHD. Currently no new drugs are being

developed specifically for cognitive enhancement of healthy individuals but evidence for this may arise as a consequence of therapeutic developments.
Many cognitive impairments are spectrum disorders, in that they exist on a scale from very mild to severe.

While drugs are usually developed to treat patients at the severe end of the spectrum, once they are on the market, there may be a tendency to seek extensions to the licence which allow them to be prescribed to people with less severe disorders. Pressure for this to occur can come both from drug manufacturers and consumers. Companies would like their drugs to be available to a wider market and potential patients may also want to avoid 'missing out' on a perceived benefit. This could result in a shift in the boundary between what is considered normal and what is considered a medical condition. Some suggest that this can already be observed in the diagnosis of new disorders such as shift work sleep disorder and the rise in diagnoses of ADHD (see Box 2).

In the near future, the focus is likely to be on cognitive domains such as memory, alertness and planning, which involve specific neurochemicals and/or where there is already a large body of knowledge. Longer-term research may focus on pharmacological targeting of wider areas such as deleting unwanted memories and improving group bonding and cooperation. Looking even further ahead, 'electromagnetic' interventions, such as brain-computer interfaces and direct brain stimulation, could be developed that may have greater potential for affecting the higher cognitive abilities. Similar techniques have already been shown to improve complex abilities like creativity and 'savant-like' skills. These methods may be more routinely used by healthy individuals, especially if drugs continue to be developed solely to treat disease.

Box 2. Attention-deficit hyperactivity disorder

Disease and prevalence

ADHD is characterised by 'core' signs of inattention, hyperactivity and impulsiveness, although all three need not be present for a diagnosis to be made. Its biological basis is not fully understood. Estimates of prevalence vary within and between countries but it is estimated to effect between 3-9% of children and adolescents in the UK and about 2 – 4% of adults worldwide. In some US schools prevalence is thought to be as high as 17%. One of the reasons for this disparity is that different diagnostic criteria are used. Not all those diagnosed with ADHD should require drug treatment. It is thought that only 1-2% of young people in the UK have the severest form of the disorder.

Treatment

The National Institute for Health and Clinical Excellence (NICE) is currently reviewing guidelines for treating ADHD. At present NICE recommends use of one of three drugs. Methylphenidate and dextroamphetamine directly stimulate the central nervous system (CNS) to change the balance of neurotransmitters in the brain. The newer drug atomoxetine has a similar effect but works by blocking the reuptake and breakdown of a neurotransmitter (NIH 2006).
Use of CNS stimulants, particularly in children, has been controversial. Prescription rates have been steadily rising from 220,000 prescriptions of CNS stimulants in England in 1998, to 418,300 in 2004. There is also increasing concern that some prescriptions are being abused (methylphenidate is classified as a Class B controlled substance). However, there is conflicting information as to whether the disorder is underdiagnosed or whether more people receive drugs than necessary (see BMJ 329). It is generally agreed that more research is needed to determine the long term effects of taking these drugs over an extended period of time.

Issues

As a follow up to the state of science reviews in the Foresight *Drugs Futures 2025?* report, the Academy of Medical Sciences is conducting a consultation with experts and members of the public. This aims to canvass views on the societal, health, safety and environmental issues raised by advances in cognitive enhancers, in addition to drugs to treat addiction and for mental health. The final report is due to be published by the end of the year. Regulatory and ethical issues raised by the use of cognitive enhancers are discussed below.

Illegal drugs

Several medicines that are used to treat cognitive dysfunction, such as methylphenidate (see Box 2), have the potential to be abused and are therefore listed as controlled substances under the Misuse of Drugs Act 1971. There is concern about children taking drugs into school that may be traded for their recreational value. As a result, slow-release formulas, such as Concerta™, have been developed to allow children to take one morning dose under parental supervision.

Safety

The lack of clinical benefit inherent in cognitive enhancement of healthy individuals raises difficulties in licensing cognition enhancers as drugs under the current framework (see Box 3). Even where there is the potential for more substantial clinical benefit, assessing the safety of cognition enhancers is likely to be problematical. The precise mechanisms involved in currently available cognitive drugs are poorly understood and it may be difficult to examine different cognitive functions in isolation.

There may also be difficulty in determining the long term risks of using these drugs and the way they effect individuals in real life situations. However, some researchers suggest that it may be possible to reach a consensus among regulatory bodies to control the safety and allowed risks in cognitive enhancement in a way similar to other non-therapeutic interventions such as cosmetic surgery or Botox™. Others argue that it may be impossible to predict the many subtle effects of cognitive enhancement, particularly as these may differ from one person to the next, and that they should not thus be advocated as a lifestyle choice.

Access and information

In practice it might prove to be difficult to restrict access to cognition enhancers. For instance, drugs such as modafinil can already be bought on the Internet for as little as £35 for a month's supply. The MHRA enforcement team monitors internet sites based in the UK but cannot control the sale of prescription medicines from abroad. Hence the emphasis may be more on ensuring that individuals have access to good information on the likely risks and benefits so that they can make informed choices about whether to use cognitive enhancers on themselves or their children.

It has been suggested that in the first instance it may be desirable to enforce some form of gate-keeping, for example through doctors or pharmacists. This would also allow for monitoring to assess the longer term effects of enhancers. However, this could raise ethical and legal questions for doctors who would be asked to prescribe drugs to healthy individuals. In the case of drugs such as Viagra™, which may also be considered enhancing, it is considered preferable to allow access in a controlled and regulated environment through prescriptions so as not to encourage the use of drugs bought from illegal sources without any medical supervision or guarantee of quality.

Scientists suggest that cognitive enhancers available in the near future are unlikely to produce an overall improvement of brain function. It is possible to envisage a scenario where people can take a range of different enhancers depending on which improvements in cognitive function are desired. This may need specialists to advise on medication and to keep track of any negative drug interactions. It may also be necessary to determine a minimum age for the legal use of enhancers in the same way as alcohol or tobacco.

Coercion

Increased availability of cognitive enhancers could lead to greater pressure on individuals to use them. In the first instance, this could arise through pressure to compete with peers at school or in work. Indeed, legislation has already been introduced in the US to prevent school personnel promoting the use of cognitive enhancers (see Legislative Commissioners' Office, General Statutes of Connecticut, Title 10, Ch. 169, section 10-212b). There are also ethical questions as to whether employers would be within their rights to require employees in certain professions to use cognition enhancers in the workplace. For instance, QinetiQ are already investigating the use of enhancers such as modafinil for potential applications in the military (Science & Technology Committee 2006/2007).

Box 3. Current regulation

Medicines

The Medicines and Healthcare Products Regulatory Agency (MHRA) regulates medicinal products in the UK in line with EC regulations and the Medicines Act (see: Directive 2001/83/EC, amended by Directives 2002/98/EC, 2003/63/EC, 2004/24/EC and 2004/27/EC.). A medicinal product is generally defined as any substance presented as having roperties for treating, preventing or curing disease. In order to be granted a licence the manufacturing company must provide evidence that the drug is efficacious, of good quality and safe based on robust clinical trials, and that the intended benefit outweighs any documented risks.

Foods and nutritional supplements

The Food Standards Agency (FSA) is responsible for regulating the safety of food and nutritional supplements on sale in the UK. In July 2007, Regulation 1924/2006 of the European Parliament and of the Council will apply to control nutrition and health claims that can be made on foods. It will define positive lists of authorised claims and the criteria a product must meet to use them. Companies can currently submit eligible health claims to the FSA, which will be considered for the authorised list following assessment of the supporting scientific evidence by the European Food Safety Authority. It is thought that this legislation will allow people to become more informed about the foods they choose to eat and provide a greater level of consumer protection. However, companies will continue to be prohibited from making any claims explicitly regarding the treatment, prevention or cure of a particular disease as these are only permitted for licensed medicines, which are thus regulated by the MHRA.

Morals, diversity and personal identity

The Office of Science and Innovation conducted a public dialogue on cognition enhancers as part of the Foresight Brain Science, Addiction and Drugs project. This highlighted concerns regarding the 'unnatural' nature of pharmaceutical enhancers in comparison with food and herbal supplements which were regarded as natural and therefore harmless. Opinion among researchers remains divided as to whether allowing pharmacological enhancement of healthy individuals is a step too far or merely the latest in a continuum of technologies that do not necessarily require special consideration.

Widespread use of enhancers would raise interesting questions for society. Currently individuals with above average cognitive performance in areas such as memory, reasoning, etc., are valued and rewarded. Making such performance readily available to all individuals could reduce the diversity of cognitive abilities in the population, and change ideas of what is perceived as normal. However, researchers suggest that although currently envisaged cognitive enhancers may raise the baseline of cognitive abilities they will not effect talents such as creativity or the need to work hard to excel. Even a small upward shift in cognitive abilities may have a beneficial economic impact with more people able to work and fewer losses due to negligence. Many issues to do with morality and sense of self would depend on the culture that develops around the use of cognitive enhancers. It is unclear whether this would more closely resemble the widely accepted use of coffee in society or whether it would have more parallels with illegal recreational drug use.

Regulation

One of the main issues raised by cognitive enhancers is the question of how they might be regulated. The first wave of such products will have been developed as medicines to be given to patients with some form of severe cognitive impairment. As outlined in Box 3, companies wishing to market a medicine must provide evidence of its safety, efficacy and quality. Regulatory bodies such as the MHRA then weigh the clinical benefits against any potentially harmful effects in deciding whether to allow the drug to be marketed. The less severe the cognitive impairment, the smaller the clinical benefit and the more certain a regulator has to be regarding the drug's safety. It is by no means clear that regulators would be willing or able to license cognition enhancing medicines for use in people who are healthy.

If cognition enhancers are categorised as foods or nutritional supplements they would need to comply with the relevant legislation and, as outlined in Box 3, companies are then constrained about the claims they can make for such products. Some argue that wider claims on foods and supplements should be allowed to educate the public and encourage people to make healthy choices. For this reason the Food and Drug Administration in the US enacted the Dietary Supplement Health and Education Act in 1994. This allows manufacturers of food supplements to make claims of effect on the structure and function of the body, provided there is sufficient scientific evidence, and there are some calls that the UK should follow a similar line.

Another potential regulatory model is that used to regulate herbal remedies which make medicinal claims. Currently, these are not required to be regulated by the MHRA or the FSA, so their efficacy, quality or safety cannot be guaranteed. To rectify this the MHRA introduced the Traditional Herbal Medicines Registration Scheme in October 2005 which requires companies to register their products as meeting specific safety and quality standards. Manufacturers have until April 2011 to register their products.

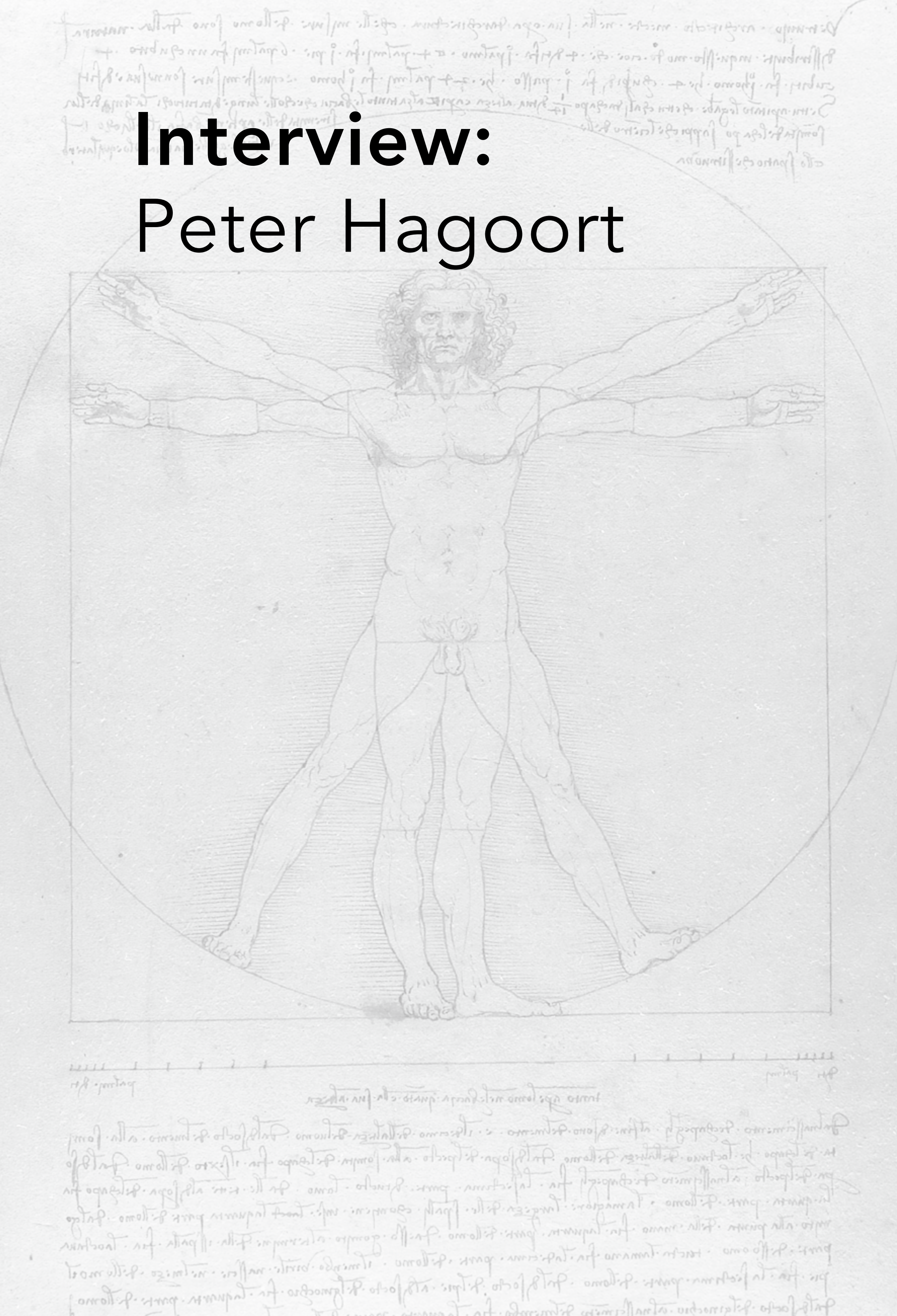
Summary

- There are a number of substances that have been shown to be effective in enhancing cognitive function, both in cognitively impaired patients and healthy individuals.
- It is generally considered that, although the role of nutrition in cognitive enhancement is not well understood, it is less risky and likely to be more widely accepted than pharmaceutical enhancement.
- Pharmaceutical enhancers developed for healthy individuals do not easily fit into the current regulations for foods, medicines or drugs of abuse. Specific regulations may be needed to govern areas such as safety, age and use in schools and workplaces.
- A range of issues may need to be considered by society before the use of cognitive enhancers became widespread. These include access, the potential for coercion, individual choice and questions surrounding identity and what is normal.

References

- BMJ (329) "Use of stimulants for attention deficit hyperactivity disorder: For and Against." *British Medical Journal* **329**:907-909.
- Farah M.J. *et al*. (2004). *Nature Reviews Neuroscience* **5**:421-425.
- Legislative Commissioners' Office, General Statutes of Connecticut, Title 10, Ch 169, section 10-212b.
- Mehta, M.A. *et al*. (2000). *The Journal of Neuroscience* **20**(6) RC65:61-66.
- National Institute for Health and Clinical Excellence Technology Appraisal 98, March 2006, *www.nice.org.uk/TA098*.
- Rose, S.P.R. (2002). *Nature Reviews Neuroscience* **3**:975-79.
- Sahakian, B.J. *et al*. (2003). *Psychopharmacology* **165**:260-269.
- Science & Technology Committee, Second Report of Session 2006-07, *Human Enhancement Technologies in Sport*, HC 67, Ev 17.
- Yesavage, J.A. *et al*. (2002). *Neurology* **59**(1):123-125.

Interview: Peter Hagoort



Cognitive Perfection is not the Optimal Condition

▸ Peter Hagoort is director of the F.C. Donders Centre for Cognitive Neuroimaging, director of the Max Planck institute for Psycholinguistics, and Professor of Cognitive Neuroscience at the Radboud University Nijmegen, The Netherlands.

Peter Hagoort in conversation with Leo Zonneveld and Marjan Slob

Utrecht, Friday 25 February 2008

"Do you know the fine opening sentence in a story by Marijke Höweler: 'Johnny had only been lying in his cradle for two days, and his parents already got going with his character.' One could have said that Johnny's parents had started enhancing him. Enhancement sounds perhaps scary, but is in fact nothing new. Within living memory we have been improving plants and we also try to raise people to a higher level through education and tuition. Nobody believes this to be a problem. Learning is nothing else than strengthening the synaptic connection between certain nerve cells. In his respect, I do not see a difference of principle between the slow, indirect way of learning and direct intervention. Such intervention should be safe of course when one touches on questions of equity, particularly when rich people could have themselves enhanced, it would expand societal segregation. Those questions are serious – but not new.

Do not forget that a large amount of science fiction is told about how easy the brain might be afflicted. Fantasy often runs away with fact. Realistic results of cognitive enhancement through technological intervention in the brain are still very modest. And even if there is a small result, there are plentiful examples of enormous amplification by the media."

LZ: *The establishment of the Centre for Cognitive Liberty and Ethics (CCLE) in the United States signifies that concerns about any future influence by the cognitive sciences upon elementary concepts of freedom and self-expression are not imaginary. How resistant are our brains against external influences which may threaten our cognitive liberty and personal identity?*

"I do recognise this concern; the citizens' panel that was looking for insights on new developments within the cognitive sciences on a European scale was equally concerned. But intrusion in the cognitive liberty of individuals is not a threat that comes to the fore as a result of developments in brain sciences; think about the locking up and drugging of Russian dissidents under the Soviet regime. Abuse of scientifically acquired knowledge is of all times, but is a problem that can not only or in the first place be attributed to science. As Jacob Bronowski said earlier: "That is not the tragedy of science, that is the tragedy of mankind."

Brain science is indispensable for the realisation of medical aspirations such as the treatment of Alzheimer's or Parkinson's disease. The more knowledge becomes available, the more its applicability accumulates. Evidently, increased knowledge also has its down side but that will not keep motivated and right-minded scientists from optimising their research work. I perceive scientists who use their work to plug into the thought of citizens with the aim to manipulate them, predominantly as a fear fantasy. Cognitive scientists will most certainly book small improvements, but these will not be dramatic. I do not see the majority of people soon walk about with all sorts of chips in their brains and I do not believe for a second that we could ever download a brain on a computer in the next hundred years, and perhaps even not thereafter."

MS: *Which future technological applications of cognitive enhancement do you believe to be realistic? In the light of the progressive integration of robotics, information technology and the neurosciences for instance?*

"All sorts of artificial intelligence-like systems will emerge, also considering research results from the cognitive sciences. Sophisticated android-like robots will more often fullfil a social function to people. The story goes that some American aged people, who participated in a test, were not willing to part with 'their' Aibo; Sony's robot dog that had been programmed to display social behaviour.

Deep Brain Stimulation via brain-implanted electrodes is already supporting patients suffering from Parkinson's and is rapidly finding new applications. A lot of activity takes place in the field of brain-computer interfaces. If one is able to hack the neuronal code of a specific action on-line, a computer can take that brain signal over, which enables one, so to speak, in steering an object in another continent purely by thinking about it. Dutch papers reported this week on a monkey in the United States which had been controlling a robot in Japan. This monkey's brain had been provided with electrode implants. There are, however, already non-invasive brain-computer interfaces which will improve.

Cognitive scientists are presently very much engaged in fathoming the plasticity of brain connectivity. We model the way the brain changes by learning and practicing. Knowledge acquired in doing this will certainly have significance for practical revalidation and for learning methodologies at school. But I estimate it will take another fifteen years before we can translate the principles of 'evidence-based learning' into concrete learning programmes."

LZ: *How is cognitive enhancement influencing evolutionary processes and will there be a moment at which the cognitive capacity of people fails to be improved, as a consequence of our having reached a biological limit?*

"Difficult to say, since we have no idea what its limits are. Such a limit presupposes proper understanding of the operation of the brain. At this moment we absolutely do not sufficiently understand the basic mechanisms of the brain to know what may mentally be achievable by people.

More important to me is the question: what is it that one really wants to achieve? A perfect memory? Forgetting has also a function. A perfect memory would enable one to store and reproduce all sorts of trivial data, but that might also burden other cognitive processes. Think about the *idiot savant*, who truly could memorise complete telephone books, but can not live a normal social life. A perfect memory is nice for a circus, but will predominantly stand in the way of a normal person. Filtering out things which are not relevant for a person, is beneficial.

I believe we can perfect ourselves within a certain bandwidth. Perfection of one function outside this bandwidth will be detrimental to other functions. Perfection has a cost. Should one observe cognitive abilities as individual units which allow separate enhancement, or are these abilities still interconnected? Presumably the latter; or at least inasmuch these abilities compete for neuronal space.

For the brain is subject to neuronal Darwinism. A sort of geographical piracy takes place in the brain; a competitive battle for available space. An example: blind people often have a better verbal memory than those who can see. When they remember words, researchers see brain activity in the visual cortex, an area that sighted people use for the assimilation of visual information. For the blind that area is fallow land; they recrute that part of the cortex for verbal memory. Which suggests that we remember words less well because we need a lot of brain capacity to be able to see. Apparently the crossing of a particular threshold signifies: improving one brain function is suppressing another."

MS: *Advice to future enhancers might well run: be aware of what one loses by enhancement?*

"Yes. For me it is not so interesting to perfect one function. Finding the optimum for a function is the important thing – such as, for instance, finding the ideal balance between forgetting and remembering. Often, we have no idea where this optimum lies. And if one enhances oneself, one could easily tumble across such an optimum."

LZ: *When individuals reach a position to manage their brain capacities at will, it is conceivable that societies will show up uniform cognitive characteristics. Could that result in cognitive diversity becoming indistinct in the long run?*

"Shopping streets worldwide become 'more of the same.' Over time, people worldwide may perhaps entertain the same beauty ideals, moreover, many of them may well have the financial means to convert themselves towards the desired direction. The result being that we may more and more look like eachother. Well...

I find it a precarious thought that some people may change themselves under social pressure. Freedom *not* to use a technology should be warranted. On the other hand, some people suffer lifelong from a personal shortcoming. Should one then say: "long live diversity!"? Honestly, the one-sided danger triangle that is placed alongside this sort of discussions sometimes tires me. More knowledge about the brain enables more possibilities for intervention in the brain. We will have to keep that in mind. That's it.

Why not turn your question round: would a nineteenth century labourer engaged in monotonous factory work have led such a cognitive diverse existence? The task reduction which technology brought us enabled our cognitive unfolding. It has led to a very complex society in which people execute very divergent tasks and hobbies. Such a complex society requires many different talents and idealises many divergent skills. One can excel in music, in sports, in languages or in leading a big enterprise. But can one do all these things simultaneously? I think that is doubtful. Excelling brains are specialised brains, and in view of neuronal Darwinism it seems doubtful that a human being can excel in many divergent tasks. Equally, one could defend the thesis that cognitive diversity has increased rather than decreased."

MS: *Which are in your opinion the issues and non-issues around cognitive enhancement?*

"A non-issue is the idea that enhancement through a pill would bring about fundamentally other ethical problems than drumming up the table of twelve in elementary school. In both cases one changes something in the composition of the brain. Another example: in brainscans we can visualise that conversational psychotherapy and a pill both affect the same mechanism in the brain. In other words, we have found intervention in the brain morally acceptable for a long time. That bare fact can not be an issue on itself – although one could argue whether the one route is better than the other.

Nick Bostrom says something in this volume which I do find an issue. In paraphrasing him: suppose a pill becomes available which improves memory. There is not one yet, but just imagine so. Some people are likely to want such a pill, but are not allowed to buy it as they are not ill – our society usually only dispenses pills as a 'medicant.' In order to still be considered for the desired pill, these people may be wriggling themselves to have that pill defined as a remedy for an illness from which they suffer. The perverse effect is that we will be ranking normal phenomena under a medical umbrella.

I found that remark by Bostrom an eye-opener. Indeed, one observes that parents sometimes walk half the world in order to get a medical label for their child, so that it can be treated. It is an interesting idea, I think, to break open the emerging discussions about enhancement. Why do we place discussion around enhancement within a sick-versus-healthy model? Why are not we talking about improvement of well-being? That would de-medicalise the debate and take it out of the moral domain."

LZ: *You are running the internationally renowned F.C. Donders Centre for Coginitive Neuroimaging at Radboud University. Could you give me an impression of your international network and your partners?*

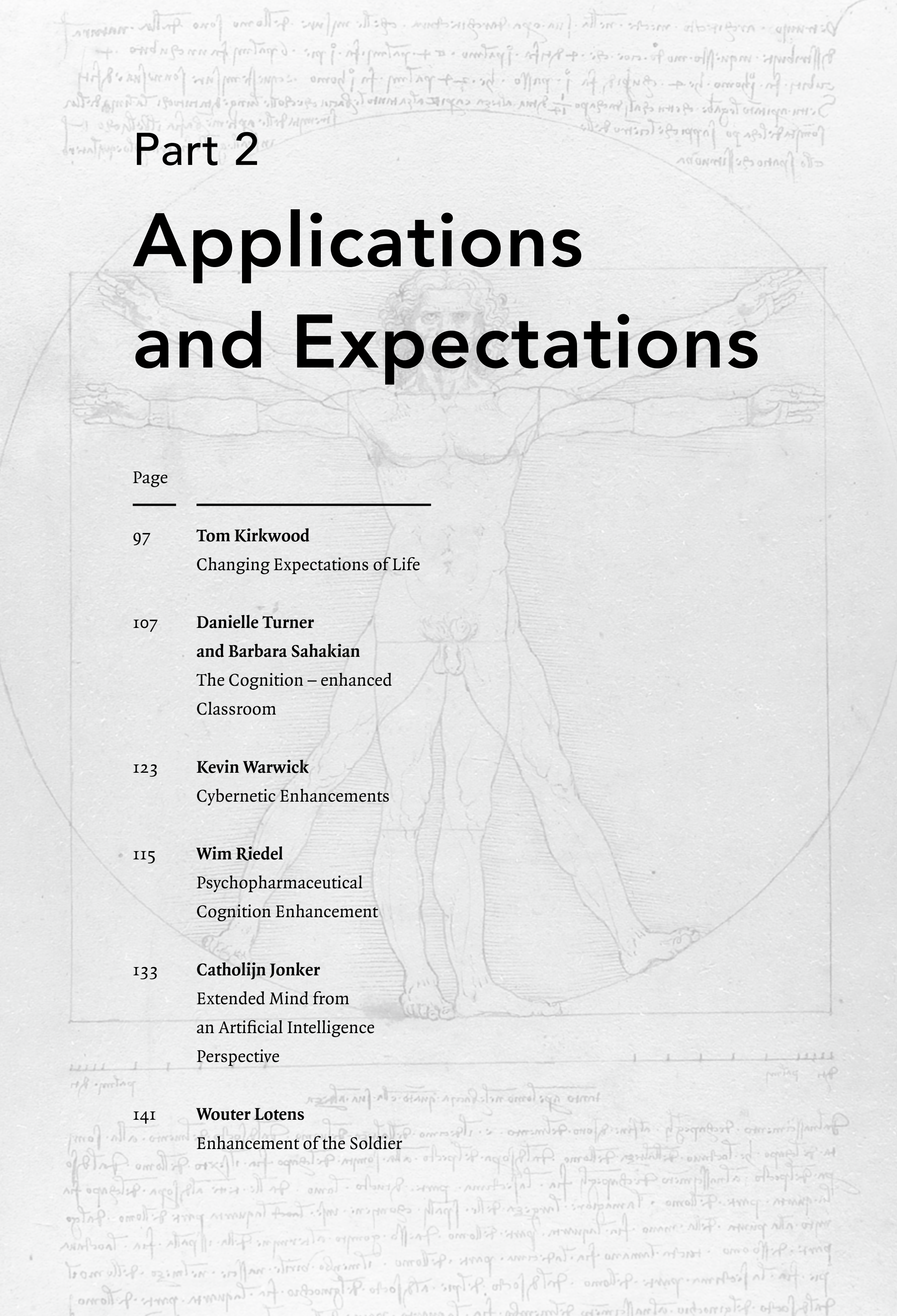
The F.C. Donders Institute does research in the field of plasticity and learning; memory; the interaction between emotion and memory; intention and action; language processing of course, my own area; and in ways to optimise existing methods of brain activity measurement. The latter is important as the brain is continuously active. In research, one tries to zoom in into one function but that function usually causes only a small wrinkling in an ocean of activity. It is a challenge to measure such a function well. We are now working on the integration of different measuring methodologies and hope, for instance, to raise funds to build a PET-scanner into an fMRI-scanner. In this way we could integrate metabolic and functional information.

We are wholly internationally oriented; some hundred-fifty people from twenty-five different countries work at the F.C. Donders Institute, and we have contacts with labs across the globe. Scientists really operate in a global village. We have good contacts with the United Kingdom, amongst others with Cambridge and Glasgow, where I have recently been awarded an honorary doctorate.

We do not limit our contacts to scientist-colleagues, but also work with commercial partners, including well-known multinationals in the food industry. Some of these are looking for a methodology to add tryptophane to foodstuffs. Tryptophane is an amino acid; shortage of it may augment the likelihood of getting a depression. Producers of foodstuffs wish to demonstrate via our scanners that their products show a direct effect on the segment for intervention, in this case on the amygdala. They are effectively looking for a biomarker. This works more efficient, and is often more convincing, than endless trials with volunteers."

LZ: *Have future expectations, which you had when you started your demanding work in fundamental brain research, come true?*

"People have always compared cognition and their own mind with the most complex technology thinkable. In antiquity it was the wax tablet, at the time of Freud it was the steam engine and presently it is the computer. In that sense there is nothing new under the sun. Yet with the arrival of fMRI in the early nineties, a technology that enables one, without any danger to the person, to image functional information about the brain, a unique development emerged: at present we can integrate knowledge about the brain with knowledge about cognition. That has really fundamentally changed my discipline. The bringing about of such a change was my ambition and that of my colleagues and we have succeeded in doing so beyond our expectation – this is particularly due to the rapid development of these technologies."



Part 2

Applications and Expectations

Page

Changing Expectations of Life

by Tom Kirkwood

▸ Tom Kirkwood is Professor of Medicine and director, Institute for Ageing and Health at Newcastle University, Newcastle upon Tyne, United Kingdom.

Introduction

The ongoing increase in human life expectancy is without doubt one of the greatest changes to affect humanity in the last two hundred years. It is a change which is long overdue for recognition, but it is only in the last two decades that some of its most startling aspects have become apparent. Even now they are not nearly as widely appreciated as they should be. To set this change in context, we can assert with considerable confidence that it is likely to be at least as sweeping in its impact on our lives as climate change, the emergence of global terrorism, and many of the other issues that command our daily attention. Yet unlike other challenges of our time, the increase in longevity is a change that, although dangerous if we ignore it, is the product of quite extraordinary success and has the potential to contribute to even greater successes in the future.

Policymakers, research scientists, industries and the public at large need to be helped to see this success for what it is and to realise the opportunities that it brings, as well as the challenges. To do this, it will be necessary to create and exploit much greater interaction between scientific research that is beginning to throw light on what actually drives the eventual ageing of our bodies and other areas of activity, in medicine, social science, technology, finance and industry. The case for investing in ageing can make itself without special pleading, once it is understood what is involved and what is at stake. Our lengthening lives have enormous societal and commercial potential. We need to make the transition from seeing population ageing as merely an inconvenient by-product of our success. We should be preventing people from dying before their time and focusing on how to make the most from our hard-won extra years of life.

Background

Life expectancy has increased steadily across most of Europe since around 1800, prior to which date the average length of life had probably changed rather little since the days of the Roman empire. From 1800 onwards, however, life expectancy has shown a remarkably uniform rise, at least in the countries that benefited from the technological advances that grew out of the industrial revolution. Although considerable poverty and squalor existed still, the gradual trend towards improved sanitation, cleaner drinking water and improved housing led to a steady decline in the rates of mortality due to infectious disease, which had previously caused particularly severe losses among infants but which also generated deaths across the life course.

In time, the control of infection was advanced through development of vaccines and, from the mid-20th century, by the discovery and general use of antibiotics. From the time that antibiotic use became widespread during the 1950s and 1960s, the death rates in the early and middle years of life dropped to be so low that although death from infection can still occur, there was no room for significant further increase in life expectancy as a result of further reducing mortality rates during the early and middle years of life. Since the prevailing view of the ageing process was then that the human life span had a fixed upper limit, imposed by an essentially immutable process of senescence, the demographic forecasts continued, up until the 1970s and 1980s, to project an imminent slowing and cessation of the trend towards increased longevity.

As the statistics show, however, populations failed to do as demographers expected. Life expectancy showed no sign of slowing its remarkably constant rate of increase, of around 2 years per decade. This continuing increase is no longer due to declining early mortality but, instead, results from dramatic declines in the death rates of those aged 75 years and above. Part of the cause for this improvement in late-life survival is undoubtedly due to improvements in medical care, but a large part also appears to be due to the fact that in today's developed countries, older citizens are reaching advanced old age in unprecedented bodily health. In effect, the nature of old age itself appears to be undergoing a quiet, yet profound transformation, despite the fact that the increased number of older people has led to much higher prevalence of age-associated conditions such as Alzheimer's disease, osteoporosis, macular degeneration, and so on.

Enter the new biology of ageing

At the same time that population ageing has been transforming the previous age-mix of societies, a series of important advances in our biological understanding of the ageing process has revealed that ageing is indeed more malleable than used to be thought. From the late 1970s onwards, the idea that ageing is due to some fixed biological programme for senescence and death has come to be seen as false. The current consensus is that ageing is driven by the lifelong, gradual accumulation of a broad variety of molecular faults in the cells and tissues that make up our bodies.

Further work has confirmed that, as has long been believed, there is a tendency for a genetic predisposition to above or below average longevity to run in families. Genes have been estimated to account for about a quarter of what determines length of life for the typical individual. However, the way in which genes exercise this influence on longevity comes not from controlling some kind of clock-like timing mechanism but rather from influencing the activity of the key cellular maintenance systems, such as DNA repair and antioxidant defence. Genes also appear to influence important features of our metabolism, such as how the body handles cholesterol, which in turn has an impact on the age-related accumulation of damage within the cardiovascular system.

Since genes do not programme the ageing process in a strict, clock-driven sense, there is plenty of scope for non-genetic factors to affect how fast or slowly the burden of molecular and cellular damage builds up during our lives. The first, very important implication of this new appreciation of ageing is that it underscores the life course nature of how our bodies age. The damage that will determine our health, vitality and level of independence in later life has been accumulating since we were in the womb. Indeed there is emerging evidence that some of the more important kinds of damage have their origins very early in our development. This means that research on the biology of ageing concerns not only those who are old already but is equally relevant to children of all ages.

Biological research on ageing is one of the newest branches of the life sciences yet already it is making a major impact in the best scientific journals and there are signs that the field is at last beginning to attract significant numbers of the brightest young researchers. This is a trend that needs to be actively encouraged and supported. As yet, the number of basic scientists working in the field of ageing research around the world is still tiny in comparison with longer established areas such as cancer research, immunology and human genetics. The urgency of building research capacity in ageing is so great that the process cannot simply be left to follow the slow trend whereby the handful of established research leaders train just a few new early-career researchers. The complexity of biological ageing is such that there is great scope for established specialists in other branches of the biological and biomedical sciences to be able to re-orient their research towards challenges of ageing, provided that adequate training and funding incentives are put in place.

An important catalyst of the recent advances in basic research on ageing has been the development of high resolution and high throughput analytic procedures, which have the power to analyse the fine scale and often heterogeneous molecular processes responsible for age-related cellular and functional decline. Because ageing is intrinsically multi-faceted, there is also particular opportunity for the recent advances in 'systems biology' research to make a crucial contribution. Whereas the last few decades of research have seen a trend that has been increasingly reductionist in nature – analysing individual components and pathways in ever narrower focus – the essence of the systems-biology approach is to generate a higher level understanding of how the components and pathways fit together and interact as a functional whole. This requires a new intensity of engagement between the biological sciences and other disciplines such as mathematics, statistics, bioinformatics, engineering and computing.

The medical challenge

Closely allied to the biological research agenda is the need to develop medicine for healthy ageing. Age brings increasing vulnerability to a wide range of medical conditions and indeed in today's hospitals, apart from the specific diseases of childhood and a relatively small range of other clinical conditions, the great majority of medical problems are ones for which age is a significant, and often the most important, risk factor.

Although there has been longstanding debate about the relationship between age-related diseases and what some call 'normal' ageing (i.e. ageing that is seen when individuals with specific diseases are excluded from consideration), it is becoming clearer all the time that the most likely avenue of progress toward understanding and intervening in age-related diseases will be to identify precisely why the aged cell or tissue is intrinsically more vulnerable to pathology.

The current understanding of intrinsic ageing is that it is due to the progressive accumulation of molecular and cellular defects. However, if we look at the equivalent understanding of neurodegenerative diseases, osteoarthritis, muscle wasting (sarcopenia), and even cancer, we find that an almost similar situation exists. The damage that leads to the accumulation in the aged brain of the amyloid plaques and neurofibrillary tangles, which are associated with Alzheimer's disease, appears to be so intimately associated with the intrinsic processes of brain ageing that we probably cannot understand the one without understanding the other.

The branch of medicine that has most directly addressed the challenge of ageing has been geriatrics. Geriatricians have long dealt with the distinctive spectrum of health problems affecting the very old. As we come, however, to a deeper understanding of the many links between intrinsic ageing and age-related frailty, disability and disease, it seems likely, indeed imperative, that a better integrated medicine of ageing will be developed that moves beyond simply seeing ageing as the ultimate cause of medical failure.

We have seen increasing recognition in recent years of the value of focusing greater attention to end-of-life issues such as improved palliative care and recognition of the importance of 'living wills' – advanced directives for those wishing to have some say over how they will be treated should ageing rob them of active autonomy over their affairs. For a long time, medicine has been concerned chiefly with stopping people from dying. Now that we are entering an era when most of us will survive to ages when we shall need to cope with a range of conditions requiring medical attention, it is high time to focus fresh attention on to how medicine can best address questions of maintenance of independence and quality of life in old age.

The social context

In many European countries, the realm of the social scientists has been quite far removed from that of the biologist and doctor. Social scientists, often with good cause, question the application of the 'medical model' to the range of issues encountered by older people. The points of interchange between social and biological scientists have been even more infrequent. However, when we confront the changing expectations of life in today's Europe it makes little sense for the biologist to ignore the social perspective, and vice versa. Human beings are social animals – our social interactions are influenced by the state of our bodies, and our bodies are subject to the effects of our social context.

One of the immediate challenges requiring engagement between social scientists and other disciplines is to understand how much of the 75% of that which determines length of life from a non-genetic standpoint can be modulated from a societal perspective. Part of this spectrum of factors will include nutrition, which is part biological but also, to a very significant extent, socially modulated. Part is related to lifestyle, including exercise, where the same inter-connection between biology and social science must be addressed. Part is also related to education, to housing, to employment status and the nature of work. The nexus of connections is extensive and urgently needs to be explored. It is a stark fact that length of life is positively correlated with socioeconomic status, with those at the bottom of the social scale suffering a disadvantage of 5-10 years less expectation of life.

The social sciences are also the locus for exploration of attitudes to ageing and the psychology surrounding our journey through the life course. The range of problem attitudes to ageing is legion. These include fatalism (the belief that ageing is fixed and cannot be altered), denial (the pretence, until it is too late, that one is immortal), negative stereotyping (the pervasive scourge of overt and covert ageism), tunnel vision (the inability to see alternative ways of addressing the challenges), and fantasy (the delusion, fuelled by popular imagination and an ever-eager media, that a 'cure for ageing' will soon be found). It is sometimes fondly believed that when it comes to matters concerning ageing, old people are the fount of all knowledge and wisdom.

The truth, of course, is very different. Older citizens have experience of what it means to be old and some of them can put this experience to outstanding use. For others, however, old age is, as Trotsky once remarked, "the most surprising thing that can happen." Many older people are confused by the experience of being old, have had little or no useful preparation for this state, and many have simply carried ageist prejudices formed in youth into their own old age. To find oneself the object of one's own negative prejudice is an unhappy state indeed, but one which appears far from uncommon.

The potential of technology

One of the greatest changes that has altered our lives over the last twenty five years has been the sequence of breakthroughs in technology, and particularly communications technology. It requires a conscious effort to remember a world without the mobile phone and the Internet. Yet both these innovations became widely available only ten years ago. Although very recent trends have seen significant growth in Internet use by older users (so-called silver surfers), Internet and mobile phone technology is largely driven by the imperatives of the youth market. This is a pity, because these technologies have so much to offer the older person whose life may be becoming gradually more restricted as a result of physical and cognitive impairments.

With ageing comes increased vulnerability to a range of disabilities and functional impairments. Yet disability is not an intrinsic state of incapacity but tends far more often to represent the failure of our environment to meet our needs adequately. Often a relatively simple modification of the environment can remove what was previously an insuperable obstacle, an obvious example being, for a wheelchair user, the provision of a ramp and a door wide enough to take a wheelchair. For a person with arthritis of the hand, use of a conventional mobile phone may be an impossibility, so such a person is disabled with respect to making telephone calls while on the move. However, simple technological solutions exist, at least in principle for this problem.

The development and widespread application of technologies to change the expectations and functional abilities of Europe's older citizens is such an obvious priority that it is truly remarkable that to date the advances have been so modest. There has certainly been some valuable development of alarm systems for frail or isolated older people, but to see these as any kind of flagship for the development of technology solutions to meet the challenge of population ageing is completely to miss the true nature of not only the need but also the opportunity.

Technology, properly developed and applied, will liberate large numbers of older people from entirely unnecessary social isolation and enforced dependency. The result, even if the technology solutions were funded entirely by the state resources, would be savings in the provision of high-dependency support services that would easily repay the necessary investments. However, there is no need to see the future provision of technology solutions as requiring state support. The market opportunities for companies are enormous already and growing every year. It is hard to escape the impression that what is holding these developments back is nothing less than a pervasive lack of imagination, propelled perhaps by equally pervasive ageism. It may well be that there is a role for enlightened policy makers to initiate programmes to kick-start a few positive exemplars.

Finance and industry

The problem of getting industry to engage proactively with the challenges of population ageing derives in part from the attitudinal problem just mentioned. However, there are signs that some of the more enlightened companies have recognised the market forces that will make it sensible to develop business ventures addressing the growing numbers of older people. Nevertheless, a recent report by the British House of Lords Science and Technology Select Committee on 'Ageing: Scientific Aspects' expressed surprise at the current failure of industry to see what is so clearly on the horizon.

There are obvious opportunities for the traditional health-related industries in addressing the challenges of ageing. The pharmaceutical industry, for example, is already investing heavily in new drugs aimed at treating neurodegenerative diseases, osteoporosis, and similar conditions. Nevertheless, it remains true that most of this effort is focused so far on treating end-stage pathology and there is little sign to date that research scientists in these industries have made serious connection with the emerging understanding of the underlying biological mechanisms of ageing. It is probably in the latter direction that the greatest promise is ultimately to be found, since early intervention against degenerative conditions is more likely to be successful than trying to intervene when the damage has already reached an advanced state. Such a realignment of targets for drug treatments may, however, require a concomitant adjustment in the regulatory procedures by which drugs are tested and approved. To license a drug that is to be given for early-stage presentation of an age-related condition raise issues around the ethics of medicating someone who is not yet seriously ill and around the duration of the necessary clinical trials.

Important progress may be made in the relatively near future with the development of improved biomarkers of ageing. Such biomarkers are needed not only to help understand the underlying pathobiology of intrinsic ageing and age-related disease but also to make it possible more quickly to determine whether or not a proposed intervention is having an effect.

In addition to the recognised biomedical industries, there are likely to be major opportunities for businesses offering nutritional, personal care and lifestyle products and services that will promote health and well being. These are likely to be developed not only through the existing manufacturers but also though novel offerings in the retail and service contexts. The provision of care is likely to become an increasingly important feature in tomorrow's Europe and we can anticipate major opportunities for novel businesses to emerge in this area, alongside the growth of existing components of the care-provision industries. The attraction of these developments is that there will be significant growth in business related to Europe's ageing population, while at the same time successful products and services will actually be extending the period of independent living and enhancing quality of life. It is thus quite easy to anticipate win-win outcomes for companies, individuals and states, but only if the right moves are made quickly. This may require strategic policy incentives and some pump-priming investment.

In the area of finance, the overriding issue, to which much attention has already been given, is the provision of pensions. When pensions were first introduced across several European states, around a century ago, life expectancy was some 25 or more years less than it is today. The average period of time over which the average worker could expect to draw a pension was minus 10-15 years. Today the expectation is for plus 10-15 years, so it is small wonder that the systems are under strain. Indeed, it is a remarkable sign of the growth in the European economies that we have reached our current position without crisis occurring much sooner. We now see the beginnings of adjustment in pensionable age. It is obvious that with the combination of increasing life expectancy and static or declining birth rates that either retirement ages must be deferred or pensions become relatively less in monetary terms. However, there has been remarkably little attempt made so far to connect the planning of future pension and retirement policies with what we are learning about the science of human ageing. Making the appropriate adjustments will not be easy but it is likely to be more of a science and less a matter of guesswork if we can engineer better links between the financial planning sector, both public and private, and the other disciplines that are addressing the problem of our changing expectations of life.

Note: This essay first appeared in the proceedings of an EU-funded conference "AgeAction: Changing Expectations of Life" held at The Sage, Gateshead, UK, on 23 April 2007. Further information and other materials are freely available from the website http://ageaction.ncl.ac.uk.

The Cognition-enhanced Classroom

by Danielle C. Turner and Barbara J. Sahakian

► Danielle C. Turner is a postdoctoral research associate in the Department of Psychiatry, University of Cambridge and a Fellow of the Center for Cognitive Liberty (CCLE), USA. Barbara J. Sahakian is Professor of Clinical Neuropsychology at the University of Cambridge, United Kingdom.

Introduction

'Smart drugs' are used by all sectors of society to improve the functioning of the human mind. But there is now growing evidence, particularly from the United States, that pharmaceuticals are being both prescribed and illegally consumed by university students to maintain supernormal levels of concentration in the run-up to exams, with the suggestion that this trend will eventually encompass younger children. How should society react to this increasing desire by people to use smart drugs? What effects could their widespread use have on our educational systems? Could children in the future face blood or urine tests when sitting their A-level or GCSE exams?

Recent developments in drugs to improve memory and cognition certainly raise the prospect of drug-testing regimes in schools similar to those imposed on athletes. It is essential that educators in particular think hard about the implications of such developments. Are the smart drugs of the future more likely to be viewed as giving an unfair advantage to pupils, or will they be embraced by parents and teachers as a reasonable addition to the armament of self improvement techniques designed to give children the best possible start in life?

Until recently, psychotropic medications had significant risks that made them attractive only when the benefits to the patient were considered to outweigh the side effects. However, it is now becoming possible to enhance cognition pharmacologically with minimal side effects in healthy volunteers. For example, as part of a research programme to identify cognitive enhancers for patient use, we showed in our laboratory in Cambridge that a single dose of modafinil (Provigil™, a drug licensed for the treatment of narcolepsy) induced reliable improvements in short-term memory and planning abilities in healthy adult male volunteers (Turner and Robbins *et al.* 2003). Improvements in performance have also been shown in healthy young male students after a single dose of methylphenidate (Ritalin™) (Elliot and Sahakian *et al.* 1997).

Some research has indicated similar cognitive-enhancing potential with a group of memory-modulating drugs called ampakines (Lynch 2002). Such drugs are typically developed to treat a medical condition, but are proving to be safe enough for widespread use following healthy volunteer studies. The list of agents, including nutraceuticals and herbal enhancers, is also growing (Jones, Morris and Nutt 2005). More work is needed to determine if these drugs will maintain their beneficial effects when taken over a long period of time. Nevertheless, in the absence of contrary advice, increasingly they will be used for indications other than those they are licensed for.

The use and abuse of prescription drugs

Most of the evidence for off-label use of smart drugs by students and young adults currently comes from the United States. Researchers at the University of Michigan showed recently that just over 8 per cent of university undergraduates report having illegally used prescription stimulants (Teter and McCabe *et al.* 2005). The most common motives given by students for the use of such stimulants are to help with concentration and increase alertness, followed by a desire to get high.

These findings are backed by reports from the National Institute on Drug Abuse in the United States that, in 2004, 2.5 per cent of eighth graders (approximately 13–14-year-old children) abused methylphenidate, as did 3.4 per cent of tenth graders and 5.1 per cent of twelfth graders (NIDA 2005). A separate but equally burgeoning phenomenon is of students obtaining prescriptions for stimulants through diagnosis of conditions such as attention-deficit hyperactivity disorder (ADHD). In the United States it is estimated that almost 700,000 doses of methylphenidate were stolen between January 1996 and December 1997, with 15 per cent of students using illegal stimulants thought to be obtaining the drugs through theft (Kapner 2003). This is likely to stem from the difficulties that healthy individuals encounter in their attempts to obtain prescription drugs.

Currently in the UK (and the US) there is no regulatory framework in place to enable the licensing of drugs for use in healthy individuals. Drugs are either licensed for medicinal use in patients via the Medicines and Healthcare products Regulatory Agency or controlled under the Misuse of Drugs Act.

Smart drugs are most likely to be obtained illegally via the Internet or with a private prescription from a sympathetic prescriber. It is unlikely that there will be a regulatory change regarding drugs for people who have not been diagnosed with a psychiatric illness. Fear of litigation means that pharmaceutical companies developing smart drugs for use in clinical groups are not keen to seek a licence for these drugs to be used by healthy individuals. Nevertheless, some prescription drugs can be more readily obtained than others because they are licensed for more broadly defined illnesses. For example, the licence for modafinil was recently extended to include the condition of excessive daytime sleepiness, potentially opening an avenue for many more people to obtain this drug under broader diagnostic criteria.

What counts as enhancement?

There are many difficulties in defining what should be considered 'normal'. The subtleties of modern medicine, combined with the expectations of a well-educated public, mean that the distinction between treatment and enhancement is often blurred. In practice many conditions (including ADHD) present as spectrum disorders with a grey area in which diagnosis is largely subjective. It is impossible to determine categorically whether a child or student is functioning within the 'normal' range, or is suffering from a psychiatric condition requiring treatment. For example, despite attempts at standardising diagnostic criteria, cross-cultural studies of symptoms of ADHD show significant differences in the diagnosis of childhood ADHD across different countries, in that of children from different cultures within the same country, and even of children from within the same culture by different diagnosticians (Castellanos and Tannock 2002).

Furthermore, there are anecdotal reports of children younger than three years old (the current licensing limit) being prescribed stimulant medication for ADHD. Difficulty in diagnosis at such young ages increases the likelihood that children are receiving unnecessary drug exposure. Differing social and philosophical opinions make it difficult to determine what should be considered a sufficient impairment to warrant pharmacological intervention. However, scientific advances in objective biomedical markers, at least, are likely to improve diagnostic accuracy in the future to ensure that those children most in need of help will receive it (Academy of Medical Sciences 2005).

In addition to questions relating to the definition of 'normal', there are additional concerns about the safety of the use of smart drugs. This is particularly true if a pharmacological agent is to be used to enhance, rather than to treat. Is it ethical to make available drugs that potentially could cause harm to healthy individuals? It is always difficult to be certain about the potential for subtle, rare or long-term side effects, particularly in relatively new pharmaceuticals. Children, especially, are at risk from drugs that could adversely affect brain development. For example, researchers at Harvard Medical School showed recently that administration of methylphenidate to adolescent rats results in long-lasting behavioural changes and molecular alterations in the function of the brain's reward systems (Carlezon and Konradi 2004).

Weighing up benefits and risks

Despite the difficulties inherent in monitoring the effects of drug usage over several years, a full exploration of the long-term implications of new treatments is vital, especially those that might routinely be used by the healthy population. Pharmaceutical companies and drug regulators already invest considerable resources in ensuring the safety of drugs, although most of the safety studies are undertaken in adult groups and not child populations. Nevertheless, many believe that there is considerable underreporting of adverse drug reactions by healthcare professionals in the UK and that harmful drugs could be identified sooner (National Audit Office 2003).

Strategies are being put in place to increase early identification of harmful drugs, including encouraging patients – as well as healthcare professionals – to report adverse drug reactions, and providing a publicly available global clinical trials register aimed at ensuring that the results of all pharmaceutical research trials (including 'in-house' studies) are disclosed. No drugs are side-effect-free, which means there is a need for risk–benefit analyses that specifically consider the use of drugs for enhancement rather than treatment. This is especially true in paediatric care.

With the advent of pharmacogenomics – the discipline behind our increasing understanding of how genes influence the body's response to drugs – it is likely that the risk of side effects can be considerably reduced. It is also important to remember that the effects of smart drugs are not homogeneous, nor entirely predictable. For example, in healthy young university undergraduates, our laboratory showed that the cognitive-enhancing effects of methylphenidate were limited when the volunteers were in a novel situation, with no effects being seen when the psychological tasks were familiar to the volunteers (Elliot and Sahakian *et al.* 1997). It is also known that improvements in performance may depend on the individual's baseline level of performance.

In another study from our laboratory it was found that volunteers with the poorest memory capacity showed the greatest improvement on methylphenidate (Mehta and Owen *et al.* 2000b). Similarly, cognitive-enhancing drugs do not improve all aspects of cognition equally. A single dose of modafinil improves short-term memory and planning abilities, but has no effect on the ability to sustain attention in healthy individuals. Methylphenidate, in contrast, primarily affects attention. People might thus have to take several different cognitive enhancers to target all the functions they want to improve, with a risk of drug interactions and increased side effects.

Drugs in the classroom

If educators are to make decisions about the use of smart drugs by students and school children it is important to examine the reasons behind their use. If students feel compelled to take cognitive enhancers in order to improve their abilities to concentrate, are they simply succumbing to the intensifying demands of a 24/7 society? Are unrealistic feats of memory and attention being expected of today's students? Are parents demanding drugs for their children in order to help them succeed against increasing numbers of medicated contemporaries (Singh 2005)? Or are the main pressures from schools and teachers desiring better-behaved classrooms? Should education systems be restructured towards guiding students to lead fulfilling, responsible lives as adults, instead of being driven primarily by exam results? And if this were the case, would we see the same phenomenon of children and students resorting to pharmacological solutions to their difficulties?

There are also questions about the more intangible effects smart drugs could have on children and students. Is it possible that these drugs could be used to reduce social inequality and injustice in society? Or it is more likely that their use will fuel further disparity based on a lack of affordability? Could cognitive enhancers have unexpected social ramifications, as people are deprived of a sense of satisfaction at their own achievements? How likely is it that human diversity could be limited through the widespread use of these drugs? As our scientific understanding advances, there is a need for educators, the government, academics and the public to start an open debate about these issues.

One recent proposal is for the creation of professional 'neuroeducators', who could guide the introduction of neurocognitive advances into education in a sensible and ethical manner (Sheridan and Zinchenko *et al. forthcoming*). Already a number of UK universities, including Cambridge, are offering courses that consider neuroscience in education. However, a new cadre of neuroeducators should not be expected to provide answers to all of the ethical dilemmas posed by smart drugs and other advances. Children have the right to an open future, and a delicate balance must be struck between an individual's right to use psychoactive substances, their responsibilities to society, and indeed society's responsibility to the individual.

References

- Academy of Medical Sciences. (November 2005). *Safer Medicines: A report from the Academy'sFORUM with industry* Available at: *www.acmedsci.ac.uk/images/page/1132655880.pdf* (accessed 4 Jan 2006).
- Carlezon, W.A. Jnr & Konradi, C. (2004). Understanding the neurobiological consequences of early exposure to psychotropic drugs: Linking behavior with molecules. *Neuropharmacology* **47**S1:47-60.
- Castellanos, F.X., & Tannock, R. (2002). Neuroscience of attention-deficit / hyperactivity disorder: The search for endophenotypes. *Nature Reviews Neuroscience* **3**(8):617-628.
- Elliott, R., Sahakian, B.J., Matthews, K., Bannerjea, A., Rimmer, J., & Robbins, T. W. (1997). Effects of methylphenidate on spatial working memory and planning in healthy young adults. *Psychopharmacology (Berl)* **131**(2):196-206.
- Elliott *et al*. Effects of methylphenidate.
- Jones, R., Morris, K. and Nutt, D. (2005). Cognition Enhancers. Available at: *www.foresight.gov.uk/Brain_Science_Addiction_and_Drugs/Reports_and_Publications/ScienceReviews/Cognition%20Enhancers.pdf (accessed 4 Jan 2006).*
- Kapner, E. (2003). Recreational use of Ritalin on college campuses. *InfoFactsResources – The Higher Education Center for Alcohol and Other Drug Prevention.* Available at: *www.edc.org/hec/pubs/factsheets/ritalin.pdf* (accessed 4 Jan 2006).
- Lynch, G. (2002). Memory enhancement: The search for mechanism-based drugs. *Nature Neuroscience* **5** Suppl:1035-1038.
- Mehta, M.A., Owen, A.M., Sahakian, B.J., Mavadatt, N., Pickard, J.D., & Robbins, T.W. (2000b). Methylphenidate enhances working memory by modulating discrete frontal and parietal lobe regions in the human brain. *Journal of Neuroscience* **20**(6) RC65:61-66.
- National Audit Office. (2003). *Safety, Quality and Efficacy: Regulating medicines in the UK.* Report by the Comptroller and Auditor General HC 255 (London: Stationery Office).
- NIDA. (2005). InfoFacts.Methylphenidate (Ritalin). *National Institute on Drug Abuse*. Available at: *www.drugabuse.gov/pdf/infofacts/Ritalin05.pdf* (accessed 4 Jan 2006).
- Sheridan, K., Zinchenko, E., & Gardner, H. 'Neuroethics in education' in Illes, Judy (ed.) *Neuroethics: Defining the Issues in Research* (New York: Oxford University Press, forthcoming).
- Singh, I. (2005). Will the "real boy" please behave: Dosing dilemmas for parents of boys with ADHD. *American Journal of Bioethics* **5**(3):34-67.
- Teter, Christian J., McCabe, Sean Esteban, Cranford, James A., Boyd, Carol J & Saliy, K. (2005). Prevalence and motives for illicit use of prescription stimulants in an undergraduate student sample. *Journal of American College Health* **53**(6):253-262.
- Turner, D.C., Robbins, T.W., Clark, L., Aron, A.R., Dows0n, J., & Sahakian, B.J. (2003). Cognitive enhancing effects of modafinil in healthy volunteers. *Psychopharmacology (Berl)* **165**(3):260-269.

Psychopharmaceutical Cognition Enhancement

by Wim J. Riedel

▸ Wim J. Riedel is Professor of Experimental Psychopharmacology, Faculty of Psychology, University of Maastricht, The Netherlands.

Introduction

In 2000, the Dutch Ministry of Health, Welfare, and Sport asked the Netherlands Centre for Doping Affairs (NeCeDo) to create an advisory board to consider the possibility of compiling a doping list for the so-called 'Mind Sports' Chess, Draughts, Go and Bridge. Such a list needed to materialise as a consequence of signing the International Anti-Doping Arrangement (IADA). In signing, the Dutch government confirmed its agreement to implement an anti-doping policy for all sports. An ensuing question was whether or not Dutch Mind Sport Federations should enforce anti-doping regulations (de Hon and Hartgens 2000).
In essence, the problem that the advisory board needed to address was twofold:

- Should substances on the existing doping-list, because of their physical performance enhancing potential, also be considered beneficial to those performing mind sports?
- Could substances, on the basis of their specific beneficial effects in mind sports but not known for physical performance enhancing effects be identified?

We consider this example an excellent real-world formulation of the question whether human cognition enhancement is effectively possible with psychoactive substances, and if so, what the consequences of their uses are. In psychopharmacology, these substances are described as cognition enhancing substances or nootropic drugs. The development of such compounds by the pharmaceutical industry is driven by medical needs in disease areas such as dementia; age-related cognitive decline (or forgetfulness); cognitive impairments in schizophrenia; depression; attention-deficit hyperactivity disorder (ADHD); Parkinson's disease; stroke, and head injury.

A somewhat neglected area is the potential abuse of these substances as 'smart drugs' by healthy individuals aspiring to boost momentary cognitive performance and general intellectual capacity. A brief overview is presented on the issues around potential cognition enhancing substances in medicinal and non-medicinal drugs known or expected to achieve cognitive enhancement, highlighting caffeine as an example.

Psychoactive substances

In describing the effectiveness of reaching human enhancement by means of psychoactive substances, a wide variety of drug labels are used in scientific literature. Their descriptions include tags such as *psychostimulants*, *nootropics*, *cognition enhancers* and *smart drugs*. These are specific subsets of all psychoactive drugs. Psychoactive drugs are categorised in classes aimed at: Mood (antidepressants, mood stabilizers); Anxiety (tranquilizers); Sleep (hypnotics); Psychosis, agitation (neuroleptics); Pain (analgetics); Epilepsy, Narcolepsy (anticonvulsants, psychostimulants); Attention-deficit hyperactivity disorder (psychostimulants); Dementia, cognitive impairment (cognition enhancers).

In this paper we do not necessarily limit ourselves to medicinal drugs, but also consider nutrients (eg. glucose, caffeine, etc.) as well as licit or illicit recreational drugs (eg. efedrine, cocaine and others). The primary characteristic of *psychostimulants* is the stimulation of the sympathetic nervous system. Psychostimulants facilitate effect on many cognitive processes indirectly by increased arousal and lead to heightened sensory acuity and response readiness. They usually do not affect memory and executive functions such as error monitoring and the process of decision making.

Nootropic properties of drugs were first defined in 1972 for effecting enhancement of learning and memory, facilitation of intercallosal transfer and neuroprotection. They appeared to show a lack of adverse effects (Giurgea 1972). Given this profile, the primary target groups for nootropic treatment consisted of the elderly and dementia patients. Since then, many substances have been developed with the same aim, but they do not all fulfil the above definition of nootropic drugs.

These newer substances are called *cognition enhancers*, and they are primarily defined in terms of their effect. Nowadays, the term nootropic drugs is hardly used anymore and now only refers to piracetam-like compounds containing a 2-oxopyrrolidineatic acid derivative (-racetam) structure (Gouliaev and Senning 1994). Cognition enhancement can, in principle, also be achieved by psychostimulants and antidepressant drugs, but we do not refer to these as cognition enhancers as this is not their most characteristic feature (Riedel and Jolles 1996). Another 'definition' that is frequently encountered is the term '*smart drugs*' (Dean *et al*. 1993).The thesis behind this term is that it refers to substances that make humans essentially smarter, i.e. its use would lead to increased intellectual capacity.

The context of drug-induced cognition enhancement

At large, one would have to consider two different concepts as frames of reference for cognition enhancement with psychoactive substances.

- The Medical Model
- Intellectual Doping

The medical model refers to the use of cognition enhancing substances for patients in whom a diagnosis of cognitive impairment has been worked up. These could be a variety of patients diagnosed with cognitive impairment including dementia, schizophrenia, depression, attention-deficit-hyperactivity disorder (ADHD), stroke, closed head injury and narcolepsy. For all these indications, cognition enhancing medicine either exists (e.g. cholinesterase inhibitors in Alzheimer's disease; methylphenidate in adult ADHD), or is under development. But it is fair to say that cognition enhancing medicinal drugs only have a short history. Cognitive enhancement is relatively new in medicine and there is a large amount of mostly justified scepticism as to whether this concept will ever be much more than at present.

Intellectual doping in essence tries to address the question whether drug-induced cognition enhancement is possible in 'normal' healthy adults. The effect on cognition would largely depend on the use of the same substances. Apart from these there are nutritional supplements being offered by industry. There is a tendency among the general public to be more and more sensitive to (mostly unjustified) claims from manufacturers of nutritional supplements that these are able to 'boost' mental power.

Properties of caffeine as cognition enhancing substance

To illustrate the state-of-the-art, we consider the properties of caffeine, the most active of the 150 or so ingredients present in coffee. Caffeine is also present in (black) tea and is often added to sweet drinks. According to the standard recipe for coffee, one cup contains 85 mg of caffeine (Schaafsma 1989). A cup of espresso should contain 180 mg. A can of sweet drink contains 80 mg and a cup of black tea contains 40 mg.

Caffeine rapidly enters the brain after consumption of any of the above caffeine containing drinks. Within 20 minutes, 40-80 mg already has a mood enhancing effect (Lieberman *et al.* 1987) while a quantity of 80-150 mg has a beneficial effect on memory consolidation of newly learned items (Hogervorst *et al.* 1999). However, these positive effects may disappear when the intake is increased. After the intake of 3-4 consumptions (250-320 mg) positive effects on cognition alter into increased wakefulness and alertness. Under normal circumstances such effects are only manifest in situations characterised by a low level of physical activity in combination with prolonged monotonic vigilance (Vermeeren *et al.* 2006). Examples are activities such as (radar-) watch keeping, particularly in situations with a low probability of significant events occurring. But also long monotonous car driving and remaining alert during a lecture are well-known examples. The effects of caffeine on alertness are beneficial in situations where normal wakefulness is challenged, such as remaining vigilant at night, or after sleep-loss. In these situations caffeine, but also amphetamine and modafinil, have demonstrated beneficial effects on a variety of cognitive functions (Wesensten *et al.* 2005). Furthermore, 50% of ingested caffeine is eliminated from the circulation within approximately 5 hours, so a relatively modest amount of coffee will help subjects overcome – at least partly – the detrimental effects of sleep deprivation while performing at night. It is not clear whether the effect of coffee could be truly considered cognition enhancement or psycho stimulation; it may also be a combination of both.

Certainly intellectual activity can often be challenged in both cases. Caffeine keeps the performance of the individual closer to its optimum under difficult circumstances. Despite caffeine's 'cognition-enhancing fingerprint' at low doses, it has not been considered intellectual doping by the advisory committee involved in the creation of a doping list for Mind Sports. The reason was that it was not considered feasible to detect a very low level of caffeine and also, since caffeine is such an accepted compound, at low doses it is considered a nutrient.

In comparing mind sports to physical sports, a positive test for caffeine in urine can be achieved after an intake of approx. 6 mg/kg, which would occur in a 75 kg normal male adult after the intake of approx. 6 cups of coffee. Significant improvement of endurance in exercise was observed during controlled experiments after the consumption of doses of 225-320 mg, equivalent to 3-4 cups of coffee (Kovacs *et al.* 1998).

Which drugs are cognition enhancers or intellectual doping?
The advisory committee that considered substances for intellectual doping looked at three questions:

1 Do substances enhance cognitive processes?
2 Do substances enhance performance in mind sports?
3 Do substances harm health?

In brief, the assessment considered valid for 1) was that there are several substances, such as caffeine, that have this effect. Effectiveness in healthy individuals is small and mainly prominent during challenging situations. There was also agreement that if 1) was achieved, it is very likely that 2) would also be achieved. The question whether substances exist that have a direct and specific effect on mind sports, such as chess playing, was also discussed. However, it was generally felt that at the present state of neuroscience it was not possible to a) identify specific neural structures or functional circuits that can be identified to exist in chess players only, although such entities may be observable in the future; and b) it was also not possible to specifically target those neural substrates with drugs.
The third question has a 'sports hygiene' history. Substances that have no proven record of having a beneficial effect on either people performing physical – or mind sports, but are known to be harmful, shall be banned. Finally there exists also a legal clause concerning the sports hygiene concept: sportsmen shall not have detectable concentrations of illegal substances in their system, irrespective of whether their effects are enhancing or impairing, or non-existent.

In addition, there is a potential indirect beneficial intellectual effect from substances or medicines that are taken to promote relaxation, relieve stress, or enhance sleep. A well-known effect is that of beta-blockers on stage-fright. Although it is proven to have a relieving effect on tremor only, which is evidently beneficial for musicians and shooters, or help in masking hand-tremor visibility from using a laser pointer during an oral public slide presentation, there is actually only faint evidence that centrally active beta-blockers such as propranolol have a direct cognition-enhancing effect (Beversdorf *et al.* 1999).

Beta-blockers can be slightly sedative and impair part of memory function known as emotional memory (Van Stegeren *et al.* 1998). Nevertheless, when properly timed, such drugs may have an indirect beneficial effect on intellectual performance in an unusually challenging situation. For a more indepth overview of which substances were considered potentially cognition enhancing, the reader is best referred to the topical report by the doping authority which can be downloaded from their website.

Concluding Remarks and Future Perspective

The advisory committee that considered the problem of intellectual doping was of opinion that there is a principal difference between doping in physical vs. mental sports, i.e. that in mental sport it is, at least at present, impossible to push maximum intellectual capacity using drugs. Doping for mental processes may be most important to maintain optimal state and prevent loss of focus and concentration by enhancing 'cognitive endurance'.

Another important contribution to success lies in the prevention of stress and anxiety that impairs optimal cognitive performance. Moreover, there was no consensus opinion on contention that cognitive enhancement in laboratory tests would be a valid index for effect during a real-life situation such as a chess-match. This also implies a similar view on the prediction of drug effects in real life on the basis of laboratory observation using abstract tests of cognitive function. A similar problem, but also documented views on how to tackle it, exists in the development of new compounds targeting cognition (Riedel *et al.* 2006).

In conclusion, apart from identifying truly effective cognition enhancing substances, there is a need for translational research: the validation of laboratory observations in real-life, to ensure measuring valid outcomes. This could be achieved by comparing the effects of substances used during cognitive tests in the laboratory with a diversity of real-life behaviours such as performing effectively during exams, learning a course, performing effectively during meetings, remaining alert during prolonged military and safety rescue operations, and safe operating performance of dangerous equipment including motor vehicles.

References

- Beversdorf, D.Q., *et al*. (1999). Noradrenergic modulation of cognitive flexibility in problem solving. *Neuroreport* **10**(13): 2763-7.
- Dean, W., Morgenthaler, J., & Fowkes, S. (1993). *Smart Drugs II: The next generation. New drugs and nutrients to improve your memory and increase your intelligence.* Vol.2, 288 (Menlo Park, CA: Health Freedom Publications).
- de Hon, O., & Hartgens, F. (2000). *Mind sports and doping – An investigation of pharmacological substances that may enhance performance in mind sports.* See: *http://www.dopingautoriteit.nl/campagnes/publicaties/documenten/mindsportsanddoping*.
- Giurgea, C.E. (1972). Vers une pharmacologie de l'activit©* integrative du cerveau. *Actual Pharmacologie* **25**:115-157.
- Gouliaev, A.H., & Senning A. (1994). Piracetam and other structurally related nootropics. *Brain Res Brain Res Rev* **19**(2):180-222.
- Hogervorst, E., *et al*. (1999). Caffeine improves cognitive performance after strenuous physical exercise. *International Journal of Sports Medicine* **120**(6):354-361.
- Kovacs, E.M., Stegen, J., & Brouns, F. (1998). Effect of caffeinated drinks on substrate metabolism, caffeine excretion, and performance. *Journal of Applied Physiology* **85**(2): 709-15.
- Lieberman, H.R., *et al*. (1987). The effects of low doses of caffeine on human performance and mood. *Psychopharmacology* **92**(3):308-312.
- Riedel, W.J., & Jolles J. (1996). Cognition Enhancers in Age-Related Cognitive Decline. *Drugs & Aging* **8**(4):245-274.
- Riedel, W.J., Mehta, M.A., & Brown, J. (2006). Cognition Assessment in Drug Development. *Current Pharmaceutical Design* **12**(20):2525-2539.
- Schaafsma, G. (1989). De samenstelling van koffie in Nederland: cafeine, mineralen, spoorelementen en vitamines. *Voeding* **50**:223.
- Van Stegeren, A.H., *et al*. (1998). Memory for emotional events: Differential effects of centrally versus peripherally acting <beta>-blocking agents. *Psychopharmacology* **138**(3/4): 305-310.
- Vermeeren, A., *et al*. (2006). Effects of histamine-3 receptor antagonism on electrocortical arousal during vigilance performance in man. *Journal of Psychopharmacology* **20**(Suppl. 5):A31.
- Wesensten, N.J., Killgore, W.D., & Balkin, T.J. (2005). Performance and alertness effects of caffeine, dextroamphetamine, and modafinil during sleep deprivation. *Journal of Sleep Research* **14**(3):255-66.

Cybernetic Enhancements

by Kevin Warwick

► Kevin Warwick is Professor of Cybernetics at the University of Reading, United Kingdom.

Introduction

Research is carried out in which biological signals are measured, are acted upon by some appropriate signal processing technique and are employed to control a device or as an input to some mechanism (Finn and LoPresti 2003; Penny *et al.* 2000; Roitberg 2005). In many cases Electroencephalogram (EEG) signals are measured externally to the body, using externally adhered electrodes on the scalp (Wolpaw *et al.* 1990) and are employed as a control input. However, interpretation of EEG data is extremely complex – due to both the compound nature of the multi-neuronal signals being measured and the difficulties in recording such signals. Recently interest has grown in the use of functional Magnetic Resonance Imaging for applications such as computer cursor control. This involves an individual activating the brain in different areas by reproducible thoughts (Yoo *et al.* 2004) or by recreating events (Xie *et al.* 2004). Alternatively, these technologies can be combined so that individuals can learn how to activate external devices (Hinterberger *et al.* 2005).

The definition of what constitutes a Brain-Computer Interface (BCI) can be extremely broad. A standard keyboard could be so regarded. It is clear however, that virtual reality systems, e.g. glasses containing a miniature computer screen for a remote visual experience (Mann 1997), are felt by some researchers to fit this category. Certain body conditions, such as stress or alertness, can be indeed be monitored in this way.

***In vivo* Studies**

Animal studies are often considered to be a pointer for what is achievable with humans. In one study the extracted brain of a lamprey was used to control the movement of a small wheeled robot to which it was attached (Reger *et al.* 2000).

The lamprey exhibits a response to light reflections on the surface of water by aligning its body appropriately. When connected into the robot body, this response was utilised by surrounding the robot with a ring of lights. As different lights were switched on and off, the robot moved around.

In studies involving rats, a group were taught to pull a lever in order to receive a reward. Electrodes were implanted into the rats' brains such that the reward was proffered when each rat thought about pulling the lever, but before any physical movement occurred. Over a period of days, the rats learned that they did not need to initiate any action; merely thinking about it was sufficient (Chapin 2004). Implants consisting of microelectrode arrays were positioned into the brains of two monkeys. Each monkey learned how to control a robot arm through arm movements coupled with visual feedback. Ultimately one of the monkeys was able to control the arm using only brain derived neural signals with no physical movement (Carmena *et al.* 2003; Nicolelis *et al.* 2003).

Human Application

The largest driving force for this research to date has been the requirement for new therapeutic devices such as neural prostheses. The most ubiquitous of which is the cochlea implant (Finn and LoPresti 2003). Here the destruction of inner ear hair cells and the related degeneration of auditory nerve fibres results in sensorineural hearing loss. The prosthesis is designed to elicit patterns of neural activity via an array of electrodes implanted into the patient's cochlea, the result being to mimic the workings of a normal ear over a range of frequencies. It is claimed that some current devices restore up to approximately 80% of normal hearing. There are now over 10,000 of these prostheses in regular operation.

Studies investigating the integration of technology with the human central nervous system have varied from diagnostic to the amelioration of symptoms (Yu *et al* 2001). In the last few years some of the most widely reported research involving human subjects is that based on the development of an artificial retina (Rizzo *et al.* 2001). Here, small electrode arrays have been successfully implanted into a functioning optic nerve. With direct stimulation of the nerve it has been possible for the blind recipient to perceive simple shapes. The difficulties with restoring sight are though far greater than those of the cochlea implant because the retina contains millions of photodetectors that need to be artificially replicated. An alternative is to bypass the optic nerve altogether using intracortical stimulation to generate phosphenes (Dobelle 2000).

Neural stimulation has proved to be extremely successful in other areas, including the treatment of Parkinson's disease. With Parkinson's disease diminished levels of the neurotransmitter dopamine cause over-activation in the ventral posterior nucleus and the subthalamic nucleus, resulting in slowness, stiffness, gait difficulties and hand tremors. By implanting electrodes into the subthalamic nucleus to provide a constant stimulation pulse, the over activity can be inhibited allowing the patient, to all external intents and purposes, to function normally (Pinter *et al.* 1999). Ongoing research is investigating how the onset of tremors can be detected in the initial stages such that a stimulation current burst is required rather than a constant pulsing (Gasson *et al.* 2005).

Some research has centred around patients who have suffered a stroke. One brain implant enables a physically incapable brainstem stroke victim to control the movement of a cursor on a computer screen (Kennedy *et al.* 2000; 2004). Functional Magnetic Resonance Imaging of the subject's brain was carried out to localise where activity was most pronounced whilst the subject was thinking about movements. A glass electrode containing two gold wires was then implanted into the motor cortex, in the area of maximum activity. When the patient thought about moving his hand, activity was detected by the electrode, amplified and transmitted by a radio link to a computer where the signals were translated to bring about movement of the cursor. The subject learnt to move the cursor by thinking about different movements. Eventually the patient simply thought about moving the cursor. No rejection of the implant was observed, neurons growing into the electrode.

Some of the most impressive human research to date has been carried out using the microelectrode array (see figure, p. 128). The individual electrodes are 1.5mm long and taper to a tip diameter of less than 90 microns. Although a number of non-human trials have occurred (Branner and Norman 2000), human tests are at present limited to two studies. In the second of these the array has been employed in a recording only role (Donoghue 2002; Donoghue et al. 2004; Friehs et al. 2004), as part of the 'Braingate' system. Activity from a few neurons monitored by the array electrodes was decoded into a signal to direct cursor movement. This enabled an individual to position a cursor on a computer screen, using neural signals for control combined with visual feedback. The first use of the array will be discussed in the following section as this has considerably broader implications which relate directly to human enhancement.

One final therapeutic procedure is Functional Electrical Stimulation (FES), which has been shown to be successful for artificial hand grasping and release and for standing and walking in quadriplegic and paraplegic individuals as well as restoring some basic body functions such as bladder and bowel control (Grill and Kirsch 2000).

In the cases described the aim is to either restore functions, since the individual has a physical problem of some kind, or to give a new ability to an individual who has very limited motor abilities. In this latter case, whilst the procedure can be regarded as having a therapeutic purpose, clearly it is quite possible to provide an individual with an ability that s(he) has in fact never experienced before. It may be that whilst the individual in question has never previously experienced such an ability, some or most other humans have – and in this case it could be considered that the therapy is bringing the individual more in line with the 'norm' of human abilities.

It is thought also possible to give extra capabilities to a human, to enable a person to achieve a broader range of skills – to go beyond the 'norm'. Apart from the, potentially insurmountable, problem of universally deciding on what constitutes the 'norm', extending the concept of therapy to include endowing individuals with abilities that allow them to do things that a perfectly able human cannot do raises enormous ethical issues. Indeed it could be considered that a cochlea implant with a wider frequency response range does just that for an individual. An individual who can control the curser on a computer screen directly from neural signals, falls also into this category. But the possibilities of extended therapy, something that can be considered as enhancement, are enormous. In the next section we consider how far things could be taken, by referring to relevant experimental results.

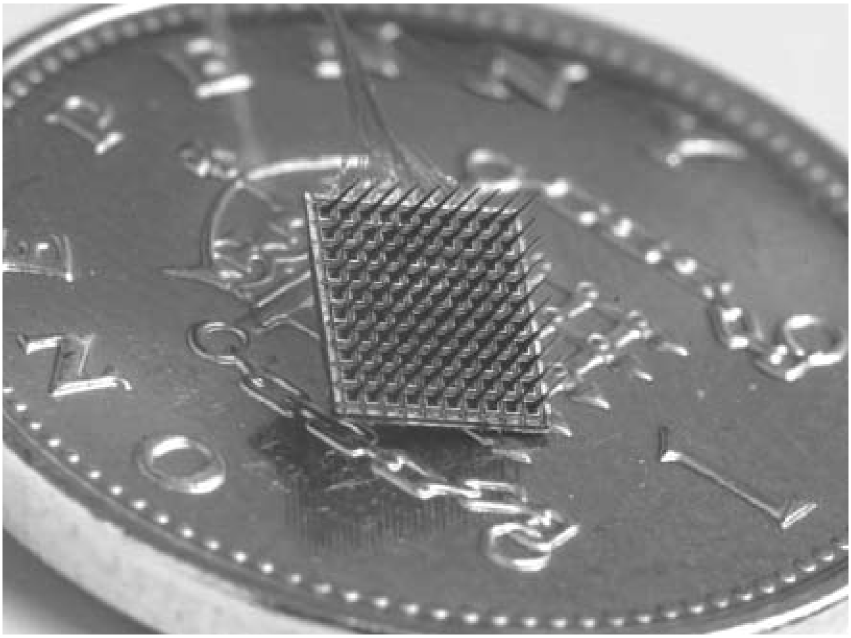
Enhancement

The interface through which a user interacts with technology provides a distinct layer of separation between what the user wants the machine to do, and what it actually does. This separation imposes a considerable cognitive load upon the user that is directly proportional to the level of difficulty experienced. The main issue is interfacing the human motor and sensory channels with the technology. One solution is to avoid this sensorimotor bottleneck altogether by interfacing directly with the human nervous system. It is certainly worthwhile considering what may potentially be gained from such an invasive undertaking.

Advantages of machine intelligence are rapid and highly accurate mathematical abilities in terms of 'number crunching', a high speed, almost infinite, Internet knowledge base, and accurate long term memory. Additionally, it is widely acknowledged that humans have only five senses that we know of, whereas machines offer a view of the world which includes infra-red, ultraviolet and ultrasonic. Humans are also limited in that they can only visualise and understand the world around them in terms of a limited dimensional perception, whereas computers are quite capable of dealing with hundreds of dimensions. Also, the human means of communication, essentially transferring an electro-chemical signal from one brain to another via an intermediate, often mechanical medium, is extremely poor, particularly in terms of speed, power and precision. It is clear that connecting a human brain, by means of an implant, with a computer network could in the long term open up the distinct advantages of machine intelligence, communication and sensing abilities to the implanted individual.

As a step towards this concept of human-machine symbiosis, in the first study of its kind, the microelectrode array (see figure, p. 128) was implanted into the median nerve fibres of a healthy human individual (myself) in order to test bidirectional functionality in a series of experiments. A stimulation current applied direct onto the nervous system allowed information to be sent to the user, while control signals were decoded from neural activity in the region of the electrodes (Gasson *et al.* 2005; Warwick *et al.* 2003). In this way a number of experimental trials were successfully concluded (Warwick 2004; Warwick *et al.* 2004; 2005).
In particular:

- Extra-sensory (ultrasonic) input was successfully implemented and made use of.
- Extended control of a robotic hand across the Internet was achieved, with feedback from the robotic fingertips being sent back as neural stimulation to give a sense of force being applied to an object. [This was achieved between New York (USA) and Reading(UK)].
- A primitive form of direct telegraphic communication between the nervous systems of two humans was performed.
- A wheelchair was successfully driven around by means of neural signals.
- The colour of jewellery was changed as a result of neural signals – as indeed was the behaviour of a collection of small robots.



A 100 electrode, 4x4mm Microelectrode Array, shown on a UK 1 pence piece for scale.

In each of the above cases it could be regarded that the trial proved useful for purely therapeutic reasons, e.g. the ultrasonic sense could be useful for an individual who is blind while the telegraphic communication could be very useful for those with certain forms of Motor Neurone Disease. However, each experiment can also be seen as a potential form of enhancement for any individual. The question then arises as to how far should things be taken? Clearly such enhancements open up all sorts of new technological and intellectual opportunities but they also throw up a raft of different ethical considerations that need to be addressed directly.

Conclusions

External input-output interfaces with human and animal brains have been studied for many years. In this article an attempt has been made to put such systems in perspective. Emphasis has been placed on enhancements that can be obtained by means of implanted devices through invasive surgery. In particular a number of recent trials in this area have clearly shown the possibilities of monitoring and stimulating brain functioning.

It is clear that the interaction of electronic signals with the human brain can cause the brain to operate in a distinctly different manner. Such is the situation with the stimulator implants that are successfully used to counteract, purely electronically, the tremor effects associated with Parkinson's disease. This technology can though potentially be employed to modify the normal functioning of the human brain and nervous system in a number of different ways.

Usually, where invasive interfaces are employed in human trails, a purely therapeutic scenario exists such as detailed in section 3. In a small number of instances, such as the use of a microelectrode array as an interface, an individual has been given different abilities, something which opens up the possibilities of enhancements. These latter cases however raise topical ethical questions. What might be seen as a new means of communication for an individual with an extreme form of paralysis or a new sensory input for someone who is blind, thus opening up new worlds for both of them, can also be seen as an unnecessary extra for another individual, even though it may provide novel commercial opportunities. Indeed, what is therapy for one person may be regarded as an upgrading for another.

Whilst there are still many technical problems to be overcome, significant recent experimental results have indicated that a sufficient technological infrastructure now exists for further major advances to be made. Although a more detailed understanding of the underlying neural processes will be needed in the years ahead, it is not felt that this will present a major hold up, rather it will provide an avenue of research in which many new results will appear through trials and experimentation, possibly initially through animal studies although it must be recognised that it is only through human studies that a full analysis can be made.

References

- Branner, A. & Normann, R. (2000). A multielectrode array for intrafascicular recording and stimulation in the sciatic nerve of a cat. *Brain Research Bulletin* **51**:293-306.
- Chapin, J.K. (2004). Using multi-neuron population recordings for neural prosthetics. *Nature Neuroscience* **7**: 452-454.
- Carmena, J., Lebedev, M., Crist, R., O'Doherty, J., Santucci, D., Dimitrov, D. Patil, P., Henriquez, C., & Nicolelis, M. (2003). Learning to control a brain–machine interface for reaching and grasping by primates *Plos Biology* **1**(2):e2.
- Dobelle, W. (2000). Artificial vision for the blind by connecting a television camera to the visual cortex. ASAIO J **46**:3-9.
- Donoghue, J. (2002). Connecting cortex to machines: recent advances in brain interfaces. *Nature Neuroscience Supplement* **5**:1085-1088.
- Donoghue, J., Nurmikko, A., Friehs, G., & Black, M. (2004). Development of a neuromotor prosthesis for humans. Chapter 63 in *Advances in Clinical Neurophysiology, Supplements to Clinical Neurophysiology* **57**:588-602.
- Finn, W., & LoPresti, P. (eds.) (2003). *Handbook of Neuroprosthetic methods.* (CRC Press).
- Friehs, G., Zerris, V., Ojakangas, C., Fellows, M., & Donoghue, J. (2004). Brain–machine and brain–computer interfaces *Stroke* **35**(11):2702-2705.
- Gasson, M., Hutt, B., Goodhew, I., Kyberd, P., & Warwick, K. (2005). Invasive neural prosthesis for neural signal detection and nerve stimulation. *Proc. International Journal of Adaptive Control and Signal Processing* **19**(5):365-375.
- Gasson, M., Yung, S., Aziz, T., Stein, J., & Warwick, K. (2005). Towards a demand driven deep brain stimulator for the treatment of movement disorders. Proc. 3rd IEE International Seminar on Medical Applications of Signal Processing, pp.16/1-16/4.
- Grill, W., & Kirsch, R. (2000). Neuroprosthetic applications of electrical stimulation. *Assistive Technology* **12**(1):6-16.
- Hinterberger, T., Veit, R., Wilhelm, B., Weiscopf, N., Vatine, J., & Birbaumer, N. (2005). Neuronal mechanisms underlying control of a brain-computer interface. *European Journal of Neuroscience* **21**(11):3169-3181.
- Kennedy, P., Bakay, R., Moore, M., Adams, K., & Goldwaith, J. (2000). Direct control of a computer from the human central nervous system. *IEEE Transactions on Rehabilitation Engineering* **8**:198-202.
- Kennedy, P., Andreasen, D., Ehirim, P., King, B., Kirby, T., Mao, H., & Moore, M. (2004). Using human extra-cortical local field potentials to control a switch. *Journal of Neural Engineering* **1**(2):72-77.
- Mann, S. (1997). Wearable Computing: A first step towards personal imaging. *Computer* **30**(2):25-32.
- Nicolelis, M., Dimitrov, D., Carmena, J., Crist, R., Lehew, G., Kralik, J., & Wise, S. (2003). Chronic, multisite, multielectrode recordings in macaque monkeys *Proc. National Academy of the USA* **100**(19):11041-11046.
- Penny, W., Roberts, S., Curran, E., & Stokes, M. (2000). EEG-based communication: A pattern recognition approach, *IEEE Transactions on Rehabilitation Engineering* **8** (2):214-215.

- Pinter, M., Murg, M., Alesch, F., Freundl, B., Helscher, R., & Binder, H. (1999). Does deep brain stimulation of the nucleus ventralis intermedius affect postural control and locomotion in Parkinson's disease? *Movement Disorders* **14**(6):958-963.
- Reger, B., Fleming, K., Sanguineti, V., Simon Alford, S., & Mussa-Ivaldi, F. (2000). Connecting Brains to Robots: an artificial body for studying computational properties of neural tissues. *Artificial life* **6**(4):307-324.
- Rizzo, J., Wyatt, J., Humayun, M., DeJuan, E., Liu, W., Chow, A., Eckmiller, R., Zrenner, E., Yagi, T., & Abrams, G. (2001). Retinal Prosthesis: An encouraging first decade with major challenges ahead. *Opthalmology* **108**(1).
- Roitberg, B. (2005). Noninvasive brain–computer interface. *Surgical Neurology* **63**(3):195.
- Warwick, K. (2004). *I Cyborg*. (University of Illinois Press).
- Warwick, K., Gasson, M., Hutt, B., Goodhew, I., Kyberd, P., Andrews, B., Teddy, P., & Shad, A. (2003). The application of implant technology for cybernetic systems. *Archives of Neurology* **60**(10):1369-1373.
- Warwick, K., Gasson, M., Hutt, B., Goodhew, I., Kyberd, P., Schulzrinne, H., & Wu, X. (2004). Thought Communication and Control: A First Step Using Radiotelegraphy. *IEE Proceedings on Communications* **151**(3):185-189.
- Warwick, K., Gasson, M., Hutt, B., & Goodhew, I. (2005). An Attempt to Extend Human Sensory Capabilities by means of Implant Technology. Proc. IEEE Int. Conference on Systems, Man and Cybernetics, Hawaii, pp.1663-1668.
- Wolpaw, J., McFarland, D., Neat, G., & Forheris, C. (1990). An EEG based brain-computer interface for cursor control, *Electroencephalogr. Clin. Neurophysiol.* **78**:252-259.
- Xie, S., Yang, Z., & Yang, Y. (2004). Brain-computer interface based on event-related potentials during imitated natural reading. International *Journal of Psychology* **39**(5-6) Supplement S.:138.
- Yoo, S., Fairneny, T., Chen, N., Choo, S., Panych, L., Park, H., Lee, S., & Jolesz, F. (2004). Brain-computer interface using fMRI: spatial navigation by thoughts. *Neuroreport* **15** (10):1591-1595.
- Yu, N., Chen, J., & Ju, M. (2001). Closed-Loop Control of Quadriceps/Hamstring activation for FES-Induced Standing-Up Movement of Paraplegics. *Journal of Musculoskeletal Research* **5**(3):173-184.

Extended Mind from an Artificial Intelligence Perspective

by Catholijn M. Jonker

► Catholijn M. Jonker is Professor of Mediamatics, Human-Machine Interaction, Delft University of Technology, Delft, The Netherlands.

As humans we are accustomed to the use of the environment to enhance our cognitive abilities. Computer science and artificial intelligence contribute to this idea of the extended mind by developing software that supports humans in decision making. Intelligent agents are forms of artificial intelligence that are autonomous to a high degree, can interact and cooperate with other agents and/or humans, and can act reactively and pro-actively in their environment. Assuming, for the sake of argument, that intelligent agents have a mind of their own, this article argues that intelligent agents cannot only be used to extend the minds of humans, but alternatively, the mind of such intelligent agents can similarly be extended by means thus far only used to extend the human mind. The benefits are the same and more: additional capabilities, improved efficiency in terms of computation, memory, representation, and sometimes even a reduced need for perceptional power. The paycheck for these benefits is a necessary increase in interaction.

The mind is generally believed to set humans apart from other animals on this planet. When looking for definitions of what the mind actually is, one can find for example: mind refers to the collective aspects of intellect and consciousness which are manifest in some combination of thought, perception, emotion, will and imagination. Human consciousness that originates in the brain is manifested especially in thought, perception, emotion, will, memory, and imagination. Others refer to the faculty of thinking, reasoning, and applying knowledge. The latter basically considers faculties that, to some extent, can be found in intelligent agents.

An agent is an entity that exhibits at least the following: autonomous, responsive, pro-active, and social behaviour. Autonomy relates to control; although an agent may interact with its environment, the processes performed by an agent are in full control of the agent itself. An agent exhibits responsive (or reactive) behaviour if it reacts or responds to new information from its environment. Pro-activity refers to the capability to take the initiative, i.e., not only acting in response to the environmental signals. Typically, the initiatives taken by an agent are in correspondence with their goals.

An agent exhibits social behaviour if it communicates and co-operates with other agents. Intelligent agents are used to support humans in various demanding tasks such as negotiation, diagnosis, planning, strategic reasoning and social or economic simulations, by which agents simulate human behaviour. Although agent technology is still far removed from creating agents with intelligence comparable to that of humans, agents do show sophisticated reasoning and knowledge application for specific tasks.

Depending on the definition of the mind one adheres to, it is not so far-fetched to claim that an agent can have a mind. For most applications of intelligent agents, the agents need to have a good idea of the preferences of the humans they are supposed to assist in order to efficiently set up collaborations, as well as understand the preferences and capabilities of other agents in their environment. In fact one of the goals in research is to create agents that have a Theory of Mind of both agents and humans within their environment. The assistance that agents provide to humans would comply with the latest form in which humans enhance their cognitive abilities, or in other words, extend their minds.

In literature two positions can be found on the idea of extended mind: the active externalist, and the individualist position. As far as the active externalists are concerned, mind and cognition are not only in the brain but extend to the body and the environment. See, for example, (Clark 1997), (Chalmers 1998), (Haugeland 1995), (Maturana and Varela 1987), (Chiel and Beer 1997).

The individualist position is that mind is only in the brain, though strongly related with the body and environment. See, for example, (Butler 1998), (Adams and Aizawa 2001). Accepting the concept of the extended mind requires an active externalist position. Consider, for example, the relatively hard cognitive task of multiplication. It is much harder (if not impossible) to do large multiplications without the aid of pencil and paper. The individualists emphasise that the paper and pencil, the writing hand and the perceiving eye, are tools of the mind but not part of a cognitive process. The active externalists, on the other hand, claim that the processes are so coupled, that they are part of the mind. The debate between these positions is ongoing.

For the sake of this article the active externalist position is taken, and the extended cognitive theory (Holland 2006) adhered to, stating that human cognition is not limited to the biological brain, and that humans employ external aspects of the environment to aid and/or enhance cognition in a way that moves cognition outside the human body. When considering the extended mind from an Artificial Intelligence perspective, an important goal of AI is to create ways towards extending the mind, namely, to improve the quality of life; to extend human capabilities; to reduce complexity on part of the task to be fulfilled by a human, and to add to the environment (e.g., a computer with intelligent programs) in a way to achieve the above. To accomplish those goals, Artificial Intelligence often finds inspiration in nature, and folklore.

Consider, for example, the famous story of Little Thumb by Charles Perrault. It is the story of people so poor that, rather than watching their children starve to death, they decided to lead their children deep into a dense forest and then leave them behind. The youngest child was when born no bigger than a thumb, which made him be called Little Thumb. Little Thumb, having overheard his parents, made sure he had his pockets full of white pebbles. On the way into the woods, Little Thumb regularly dropped a pebble, which enabled him to lead all children safely back home. Of course, this did not solve the problem of his parents, so out they went again, making sure that Little Thumb had no pebbles in his pockets. This time Little Thumb dropped bread crumbs. Birds eating the bread crumbs ensured a rather bizarre adventure before the happy end. From the active externalist position, Little Thumb extended his mind by using the environment.

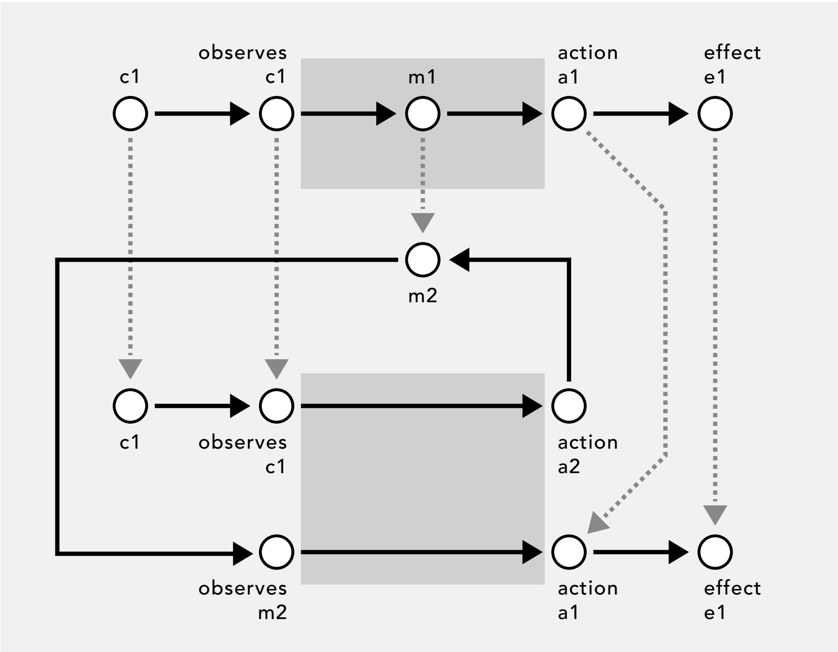
The brilliance of Little Thumb's use of pebbles from an artificial intelligence perspective is that his solution requires less computational power, less memory, and less powers of perception than any solution that does not use the environment. Consider not using the pebbles. While being led into the woods, you would have to pay the utmost attention to your environment and make a mental map of the woods and the route taken into the woods. The map would have to be detailed enough to identify enough individual trees (both looking forward and backward) to ensure that you can find your way back. The parents knew full well, that this task was impossible for their children. Learning to find your way in the woods takes years. Learning what features of trees, shrubs and such, to remember takes experience, and a lot of perceptional power. Following a line of pebbles is easy, the only thing you need to remember is that indeed following the pebbles will lead you home. Therefore, from an AI perspective extending the mind obviously brings important advantages:

- Reducing computational complexity: you don't need to learn a map, you only need to drop pebbles at a visual distance from each other, and you don't have to know exactly where you are to find your way back.
- Reducing the required memory: no map needs to be stored, only that following the pebbles will lead you home.
- Reducing the required perceptional power: you only need to be able to recognise pebbles, not enough features to recognise individual trees.

Since there is no such thing as a free lunch, the costs of extending the mind should also be considered. You need enough resources (the pebbles) to mark the environment, your marks can be manipulated by others or natural events (as happened with the bread crumbs) and when you are lost, you need to interact with your environment more often (collecting and then dropping the pebbles). Finally, your location awareness is different (but not necessarily worse): you know approximately where you are relative to a sequence of pebbles, in stead of a remembered sequence of memorable trees. To decide whether or not an extended mind should be used, the advantages should be weighed against the costs and risks.
Both solutions have been formally modelled and compared (see figure, p. 137). The isomorphic mapping between them shows that the solutions with and without an extension of the mind actually lead to the same behaviour, assuming that the environment does not disturb the pebbles (modelled by *m2*), and the memory (modelled by *m1*). For more details, see (Bosse *et al.* 2005).

In Artificial Intelligence the above advantages are typically very important: no matter how much faster computer chips become, computational costs are a serious problem for executing interesting tasks. This is also true for memory. Perception of environment, especially natural environment, is difficult.

Models and isomorphisms



Consider a modern equivalent of Little Thumbs problem. Humans are frequently plagued by questions such as "Where am I?" and "How do I get from here to …?" The already old-fashioned way (which already is a fantastic extension of the mind) is to use paper maps, and looking a lot around you to find street names, and then locating those street names on your paper map. The modern way is to use a navigation system that through interaction with satellites solves these questions more efficiently.

Let us consider an alternative way in designing a navigational system. The system would not get access to satellites to determine its location. It follows that the agent would either need sophisticated computer vision techniques to read road signs to determine its current location, or alternatively it would need sophisticated motion sensors to determine the direction and speed of movement. The last option, certainly is not robust, and once something has gone wrong, it cannot recover its position by itself.

However smart we think we are, nature always seems to be ahead of us. Whereas we need stories like Little Thumb to teach us how use the environment to extend our minds, nature has a much more refined example in every ant heap you see. When studying ants, one comes to the conclusion that the ant is the intelligent version of Little Thumb. Instead of using pebbles (having a permanent character) or bread crumbs (having an unreliable character), they use pheromones (odorous chemicals). By having different pheromones for different purposes, several recognisably different paths can exist to different locations. For example, different pheromones are used for marking paths to locations with food, or building materials.

The interesting property of pheromones is that they dissipate over time and space. This has fantastic additional advantages. You don't have to clean them up behind you, the smell is gone by the time you don't need them anymore. Well-traveled routes (highways) are marked with lots of pheromones and are therefore easy to locate. Other routes that are no longer interesting will lose their markings. For example, if a food source is depleted ants will no longer mark that route as one that leads to food. After a while that route can no longer be smelled and therefore, that route is erased naturally from their shared map.

The system works very well, because of the huge number of ants. All ants contribute to marking the interesting trails. The map created in that way is shared. As is argued in (Bosse *et al.* 2005), the ant's mind is not only extended by the use of pheromones, but also by similar and cooperative behaviour of other ants. This phenomenon was coined a *shared extended mind*, comparable to the hive mind of the Borg of the popular Star Trek television series.

The shared extended mind has capabilities that are more than the sum of the capabilities of the individual. It shows even more clearly the intelligence gained as a result of the interaction with others and with the environment. On the down side, from the individual perspective, individual interests might be sacrificed to the advantage of the majority. Furthermore, the examples show that consciousness is not necessary for a shared extended mind. Necessary conditions are (Clark and Chalmers 1998): trust, reliability and accessibility.

To come back to the Artificial Intelligence perspective, there are a few side remarks to be made before we can summarise. Extending the human mind by artificial means enabling humans to delegate some tasks which therefore allows them to shift their attention to other tasks. Regarding tasks that cannot be delegated (yet) completely to artificial means, artificial intelligence can provide support for hard mental labour. The earliest trend in human enhancement was the use of tools to support humans in hard physical labour. Tools can therefore be seen as ways to extend the human body. Nowadays, combinations of machines and machine intelligence provide an even stronger support and enhancement of human both in body and in mind.

If consciousness is not necessary for a (shared) extended mind, then one wonders if everybody needs to know how things are done? Or is it enough that some people know, as is currently the case with cars, calculators and computers?
What would the long term effect be? More specifically, will human enhancement have an evolutionary effect? Or will it only have an effect on humans that are thus extended, in that those humans will become worse/bad in executing tasks otherwise carried out by technical means? Such effects are already known for our powers of computation and memory. And then again, would that be a negative effect?

To conclude, in this article we showed how to progress from a mind to an extended mind, and even a shared extended mind. The phenomenon of an extended mind clearly can be seen as a human enhancement in terms of additional capabilities and improved efficiency with respect to computation, memory and representation. Furthermore, it changes the perceptional powers needed and it leads to an increase in interaction. Within artificial intelligence these insights are used to create more efficient intelligent agents. By applying the concepts of the (shared) extended mind to intelligent agents, their behaviour becomes more effective. Furthermore, requirements for their perceptional power could become simpler.

References

- Adams, F., & Aizawa K. (2001). The Bounds of Cognition. *Philosophical Psychology* **14**(1):43-64.
- Answers.com: a web dictionary.
- Bosse, T., Jonker, C.M., Schut, M.C., & Treur, J. (2005). Simulation and Analysis of Shared Extended Mind. *Simulation Journal (Transactions of the Society for Modelling and Simulation)* **81**:719 – 732.
- Butler, K. L. (1998). Cognitive Explanations. In Butler, K., *Internal Affairs: Making Room for Psychosemantic Internalism.* (Kluwer).
- Chiel, H. J., & Beer, R. D. (1997). The brain has a body: adaptive behavior emerges from interactions of nervous system, body, and environment. *Trends in Neuroscience* **20**: 553-557.
- Clark, A. (1997). *Being There: Putting Brain, Body, and World Together Again.* (Cambridge, Massachusetts: MIT Press).
- Clark, A., & Chalmers D. (1998). The Extended Mind. *Analysis* **58**(1): 7-19.
- Gershenson, C. (2001). Comments to Neutrosophy. In Smarandache, F. (Ed.) *Proceedings of the First International Conference on Neutrosophy, Neutrosophic Logic, Set, Probability and Statistics.* University of New Mexico. (Gallup, NM).
- Gershenson, C. (2002). Complex Philosophy. In: *Proceedings of the 1st Biennial Seminar on Philosophical, Methodological & Epistemological Implications of Complexity Theory.* (La Habana, Cuba).
- Haugeland, J. (1995). Mind Embodied and Embedded. *Acta Philosophica Fennica* **58**:233-267.
- Holland, G.A. (2006). Extended Cognition and Social Constructionism as Underpinnings for Knowledge Management Practice. *Journal of Knowledge Management Practice* **7**(1).
- Hutchins, E. (1995). *Cognition in the Wild.* (Cambridge: MIT Press).
- Menary, R. (ed.) (2004). The Extended Mind, Papers presented at the Conference The Extended Mind – The Very Idea: Philosophical Perspectives on Situated and Embodied Cognition, University of Hertfordshire, 2001.
- Maturana, H. R., & Varela F. J. (1987). *The Tree of Knowledge: The Biological Roots of Human Understanding.* (Shambhala).
- Wooldridge, M., & Jennings, N.R. (1995). Intelligent Agents: Theory and Practice. In: *Knowledge Engineering Review* **10**(2): 115 – 152.

http://www.mmi.tudelft.nl

Enhancement of the Soldier

by Wouter Lotens

▸ Wouter Lotens is project manager Soldier Efficiency, TNO Defense, Safety and Security, Human Factors Branch, Soesterberg, The Netherlands.

Introduction

The employment of military power for political purposes, rather than for the defence of territory, requires a different perspective on roles, responsibilities, risk, control and damage of all sorts. Much more is asked from individual soldiers and, in fact, they are not the soldiers we used to know. Soldier systems are replacing the classical soldier, providing enhanced capabilities. The future is in networked soldier operations, but education of the soldier, in particular in the cognitive and emotional area, needs to keep up with technological advance.

The core of modern operations

Unlike the classical defence of national territory and assistance of allies in defending allied territory (the first two main tasks of NATO), the third main task 'peace operations' is highly politically driven, depending on public support for the objective set. As we learned from the Vietnam conflict and again from Iraq and Afghanistan, the public support suffers from casualties, uncontrolled soldier behaviour, the occurrence of Post Traumatic Stress Syndrome with veterans and the confrontation with the misery of the people involved. While the anger at the start of the mission fades, resistance grows. When peace is restored quickly enough, the military-political position may be maintained but when a conflict lasts, growing resistance exceeds the anger and withdrawal is inevitable. Insurgents know that and their policy is smart and focussed: extend the peace keeping phase and keep abreast of public support. In the peace enforcing phase they lack military power, but disrupting security and causing random casualties do not take a lot of resources. It also slows down every move of the civilians and military involved, hampering reconstruction.

Peace operations are thus not very peaceful. Expeditionary states have fierce debates in parliament on the conditions under which they will join the coalition. During the Balkan conflict terrible misjudgements have been made of the promises that can be kept. In the Netherlands, the aftermath of the Sbrenica massacre forced the government to step down and left a scar on our soul. Not surprisingly, participation in the Iraq and Afghanistan missions has been negotiated carefully between political parties and coalitions. The underlying agreements to the purpose of reconstruction were firmly laid down. The conditions in Afghanistan currently prevent much progress towards this end, putting a question mark at the further possible extension of the mission.

If the Balkans proved anything, it must be that ground presence can not be replaced with air attacks. Air attacks are safe for one's own forces, but the success rate of missions is invariably lower than planned and the main deficiency is that control over the area is lost as soon as the air force returns to its base. Ground troops are the only asset that can establish the transition from peace enforcing to peace keeping, staying in close contact with the actors in the theatre. Unfortunately, close contact is dangerous. Safe areas are being created and from these safe areas patrols and raids are started, with varying tactical purposes. Upon leaving the safe area, soldiers are potential targets in a world that they only half understand. Obviously, being well informed is of key importance to safety.

The ethical dilemma of peace operations

Pertinent to the mission is that soldiers run a risk of being hurt, killed or disabled. They are tasked by their governments to do this job and the state acts like taking the responsibility, but in reality the state can not. The advantages are harvested by the state, but the risks are personal. The state can only suffer material losses, which are a negligible burden compared to an individual losing his life or a family losing its father. In contrast, when humans are used in medical experiments, the state demands from the experimenter that the risk for the individual is in balance with the interest of the subject in the outcome (maybe a potential cure for one's disease) while the interest that science has in the result may be unique additional knowledge on possible treatments. I have never seen a protocol approved in which there was a serious risk that a healthy subject would die of treatment, regardless of the potential of the experiment. In fact, experiments of this kind were performed in WWII and have been disapproved ever since in the strongest possible way.

Apparently, the state does not think that a politically founded expeditionary mission is comparable to a medical experiment, whereas on objective grounds it would be difficult to tell the two apart.

Both in the US and the UK the families of soldiers who were killed in action have filed claims with the state that the victims were not receiving the best possible personal protection. This must have been worrying, because for money more protection can be offered, putting the state up with unaffordable bills. Or at least that is what the general perception is, but unaffordable is a relative concept and that is exactly the core of the matter. Providing financial and material resources is all the state can do and it is insufficient. That individuals think that they are not being compensated fairly for their personal risk may be concluded from the dropping interest in joining the services, running into another ethical dilemma: that only those persons sign up who have no other options. In the US illegal immigrants are recruited and promised a legal status after service. Returning to medical ethics, subjects, persuaded to participate by disinformation, irresistible reward or incapability to consider the odds, are considered involuntary and using involuntary subjects can cost an experimenter imprisonment.

Can the state take responsibility for what happens on its behalf during a mission? It is doubtful. The state has no control over what happens in the field. That is up to the local commanders, sometimes leading to what is perceived later as excessive violence, cruelty, torture, homicide and other horrors. Being a soldier is very difficult and decisions have to be made in seconds, while the decision maker is under stress and fears for his life. Typically, if he decides to apply power, he is personally safer, yet overall violence increases. His other option, to wait and see if the situation can be resolved without violence, demands enormous self control. This demonstrates better than anything else that a battle between insurgents who take honour in killing and being killed and Westerners who want to return unhurt, must end up in excess violence and killing by mistake.

Transition of forces

In the days that soldiers, in particular infantry, were exchangeable, warfare was largely dominated by attrition. Death and destruction were the measure of success and soldiers were consumed at a high rate; thousands on a single day was no exception in 1850 till 1918. Also, a large toll was paid among survivors by shell shock. It is impossible to train new soldiers and refill the ranks at that scale and the victory was at the side of the party with the longest sustainability. This was basically the model that prevailed among superpowers until the wall fell. The conflict in Bosnia, Croatia and Macedonia changed the rules. The local population became a party, the conflict got asymmetric, involving unidentified parties operating at a small scale, along with formation based troops.

The first Gulf War was an anachronous event in this sense, Saddam bragging about 'The mother of all battles.' Indeed there was concern with the allied troops that this could become a messy war, but one thing had changed: the US troops had moved into the information age. Lab equipment was rolled out in the field, providing night vision, satellite imagery and common operational pictures. When General Schwartzkopf looked through the equipment, he was said to cry out that he had always been blind. Saddam's elite troops were defeated rapidly, but the march on Baghdad was stopped at the outskirts in fear of this other type of battle, in the urban area, with close combat and a hostile population.

Iraq was then controlled from the sky, effectively maintaining the embargo, but no control over the political system was obtained. In the second Iraq war and in Afghanistan soldier operations were changed forever. Attrition is too rough for high precision wars. Apaches took over, guided by forward air controllers or nearby special forces. Other weapons, other tactics and other protection are needed in urban areas, and the lack of formal opponent forces makes formation battles obscure. Search for weapons, arrests, road blocks, crowd and riot control, information and social patrols, house clearing and other routines took their place.

Soldier modernisation

After the first Iraqi war NATO started an innovation process of the soldier, which turned the position of the soldier around. No longer was he the cheapest weapon system of all; it was recognised that soldiers would be the prime asset for future operations and that the typical recline in readiness after a won conflict should be counteracted by outstanding clothing and equipment and new capabilities. The number of soldiers would drop and the capability needed to increase. By now, there are typically ten soldiers, support staff and technicians behind every soldier in the field, enabling him to do his work. The soldier has become the spearhead of a team, not unlike a fighter pilot.

The outstanding vision of NATO was to provide the soldier with new technology for communication, identification, night vision, situation awareness, new weapon effects, protection and other assets, upgrading his capabilities. This process started in 1992, with a NIAG study, and results are becoming visible after a long learning process, in the application of soldier systems in the field. Germany was first in this. A soldier system is a soldier together with his equipment (everything he is wearing, carrying or consuming) working synergistically towards defined competencies. A group of soldiers is connected through a network and trained to co-operate in various compositions. It is the power behind the concept which adapts the group according to the situation. Groups are interconnected via a commander's network and connected to the Battlefield Management System.

Soldier systems have been designed to do current tasks better. Operations that used to be possible during daytime only became feasible in the night, thus extending the operation to 24 hrs a day. Operations that were possible in open terrain could only be done in urban environment. Presently, precision operations can be done by carefully identifying targets and sharing that information, avoiding fratricide and collateral killing. But there is a profound and unforeseen effect of the technology on behaviour as well. Soldiers can reliably perform without supervision and their commander can focus on his planning and information task, rather than on control. Trust in leadership is enhanced. Soldiers now have the information to take their own decisions, relaxing the command and control task, workload and communications. This empowerment is known as power to the edge of the organisation.

Doctrine changes and new skills

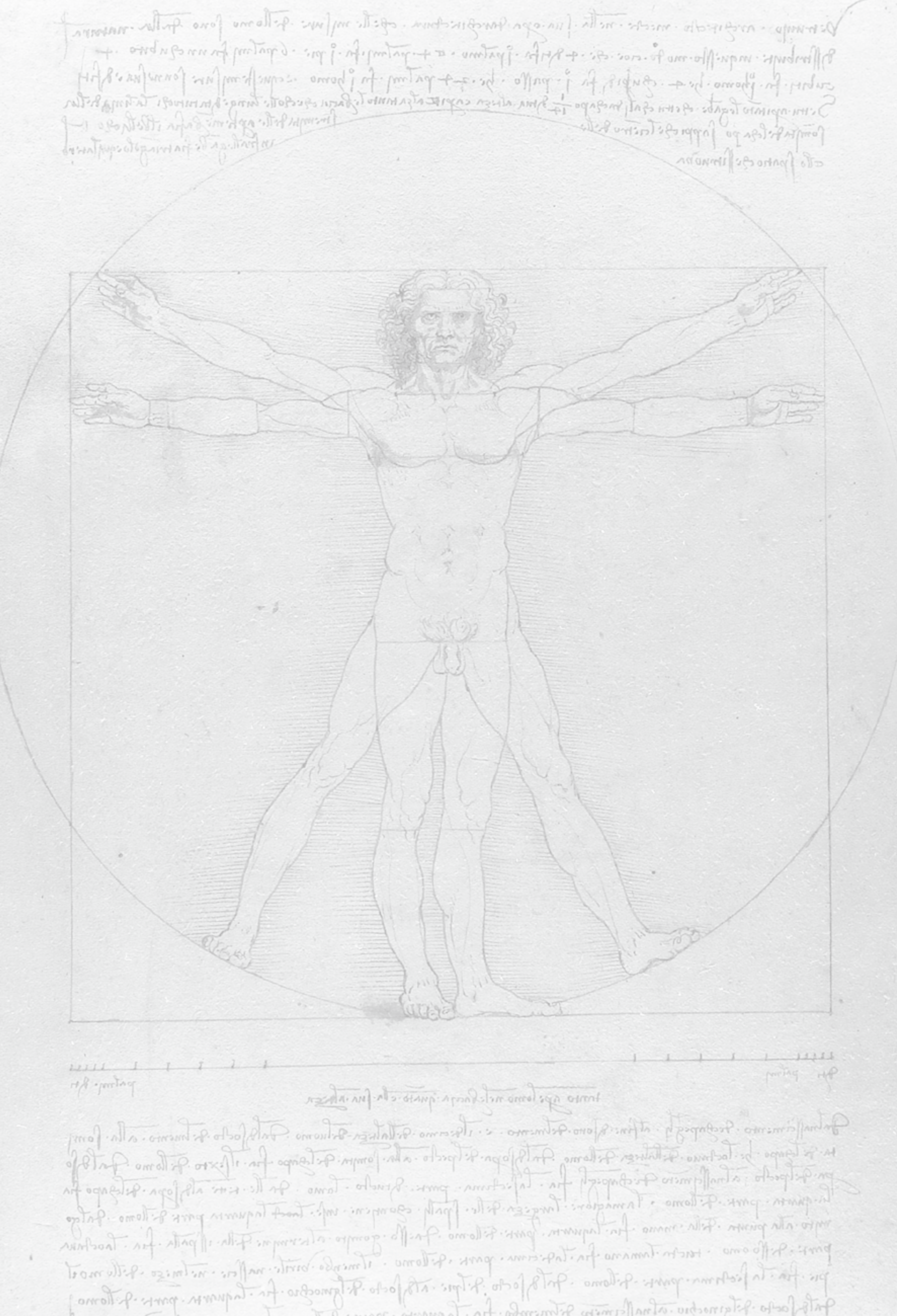
The next step in soldier enhancement is the exploitation of doctrinal changes. Doctrines are shifting towards specifying the desired end state, leaving the manner to the operational units. This is known as Effects Based Operations. The Netherlands doctrine is advanced in this respect, taking advantage of the traditional resourcefulness of the Dutch soldier. Experience in Iraq and Afghanistan shows that units that leave the compound have to rely on their own judgements, turning the doctrine into a necessity rather than a philosophy. Soldiers are in contact with the local population, try to obtain information and need social skills and cultural training to succeed. Another required skill is risk assessment and decision making. These skills are now developed along with another important skill: to give emotional support to others, in counteracting effects of stress. Although stress reactions are personality-dependent, (thrill seekers and the self confident being less stressed), observation of stress symptoms in others can be helpful to provide support in time, reducing extreme reactions.

Research in this field has shown that emotional support is a key parameter in team performance, fed by confidence, trust, leadership, cohesion and other team characteristics. Nevertheless, Post Traumatic Stress Syndrome is common amongst just retired soldiers. The incidence rate is estimated at 10-25%, 5-10% in need of treatment. The neglect of treatment may cause deviating behaviour even decades later and is often destructive for the individual and his social environment.

Further soldier enhancement

The next step in operations is the Network Enabled Capability. Nobody knows yet what the potential of NEC is in the soldier realm. Current studies look into the co-operation of soldiers and robots, information collection systems in the first place. A host of new technologies is becoming available in portable form, including unmanned aerial vehicles, dispersed self-organising sensors, 3D situational displays, bio-monitoring sensors, remotely controlled weapons, relay stations and more.

The expectation is that soldiers will be capable of forming *ad hoc* distributed teams, receive their briefings on the move, act with increased momentum and then be dismantled to form other teams. However, the information capability is just one of the five capabilities generally discerned. The others are sustainability, lethality, mobility and survivability. We will not go in details here, but all capabilities need to be developed in concert and supported by the education and training required. It is unlikely that the stress will ever be relieved. Exhaustion, heat and cold, sleep deprivation, fear, disorientation, pain, dehydration and other stressors belong to the profession. What can be done is to reduce uncertainty, harden soldiers, give them accurate and graded weapons and train their interaction with the operational environment. Carrying the equipment becomes a major problem. Weight, mobility and power supply are called the bottlenecks in any soldier conference. The selection of the equipment needed from all the available equipment will become a key factor in future operations. Attempts have been made to enhance the soldier physically with an exoskeleton. DARPA, the US-based advanced research centre, believes this is possible, but military feasibility is another challenge.



Afterword

by Jan Staman, Huub Dijstelbloem and Martijntje Smits

► Jan Staman, Huub Dijstelbloem and Martijntje Smits work at the Rathenau Institute, the Netherlands' national organisation for Technology – and Science System Assessment, based in The Hague, The Netherlands.

Introduction

Is it an individual affair or a collective task to answer the question what it means to be human? That question comes to mind after reading the contributions to this book. Throughout history, ideological, philosophical and religious scholars have been trying to determine the meaning of 'humanity'. Nowadays, the growing availability of so-called human enhancement technologies for the public at large, puts this question more and more on the desk of the individual citizen.

The developments in the broad field of human enhancement bring the question of the meaning of being human back to the forefront of attention again. This time, the new scientific and technological possibilities raise that question. However premature the current momentum may be, these possibilities promise us all the Olympic dream of living: *citius*, *altius*, *fortius* – swifter, higher, and stronger. Inevitably, such dreams will also lead to questions about our limitations and to reflections on a human condition which does not solely consist of a godlike life on Olympus but has its tragic sides as well.

Answering the question what it means to be human is difficult, yet the issue whose task it would be to provide an answer is not easy either. Are we as individuals in a position to decide what it means to be human? Is that something one could decide upon individually? Or is the question much too big and in need of collective deliberation? And do we have the collective tools to answer it?

A collective conversation

Contemporary liberal societies have an ambivalent relationship with this notion of 'collectiveness'. On the one hand, we are equal citizens in respect to democracy.

The principle of 'one man one vote' gives every citizen an equal say. In that way sovereign citizens form a democratic 'collective'. On the other hand, when it comes to liberal society, we are free citizens that make their own choices which can vary widely. On the market, in our social and in our private lives, we follow our own intimations. Here, not equality but differentiation seems to be the motto. Under these circumstances it is doubtful whether answering the question 'what does it mean to be human' would be seen nowadays as some collective endeavour. More likely it would be considered as something we may decide upon our own.

An important acceleration to this modern way of thinking about individuality was given by the ongoing development of science and technology. New technological developments widen, whether one likes it or not, the limits of the traditional concept of a human being as a natural or cultural phenomenon. Nowadays, the human person is also a scientifically assessed phenomenon. Developments in medical technology, like ambient intelligence and man-machine interactions, shape new socio-technological environments. The biotech revolution makes it possible to read, to modify, to change and to exchange our body materials. Neurophysiological and pharmacological innovations lead to the production of drugs that influence the functioning of our brain and nervous system. All these developments offer new insights that change our self-perception. Moreover, they also create possibilities to change ourselves.

In this book, a variety of authors have sketched, whether in an optimistic or sceptical fashion, new possibilities to widen the capabilities of human beings. With a slightly provocative move we have gathered together the chapters under the label of 'human enhancement'. A common way to circumscribe human enhancement is to say that it is the sum of the scientific and technological developments that cross the division between prevention and cure by medical necessity, by moving towards the enhancement of people who do not have any strict medical reason for it. A well-known example is the use of doping in sports. But also in the military domain, in the field of life expectancy research, in pharmacological areas and in cognitive fields we could observe certain trends to cross this bridge.

The inevitable question is of course whether these developments offer really something new. Is not this so called process of enhancement nothing more than a new variant of wearing glasses, of living safe, sound and hygienic, of making use of new artefacts and medicines that help us but also transform us a little bit?

It is impossible to give a final answer to this question. But what we can see is that technological developments go faster than ever, and that their results do reach the consumer market sooner than ever. Modern laboratories are no longer ivory towers but part of society that severely influence the way we lead our lives. Science and industrial research develop new products and consumers use these products and ask for them. As a consequence, modern societies are being transformed to a large extent by scientific and technological developments. The direction societies take is based on individual choice.

The question we would like to pose after reading the contributions in this book is: would one be content to leave the further implementation of human enhancement technologies to such a great extent to individual choice by individual consumers? The idea that precedes this question is whether human enhancement is an individual prerogative, fit enough to evoke answers towards determining what it means to be human.

Nowadays it is hard to see what alternative there could be. State-promulgated policies and religious movements that have been claiming a monopoly in defining 'humanity' have a rather dubious track-record. Still, new technological developments can have collective effects. To discuss and to re-think the consequences of enhancement in terms of their meaning for our self-perception is a necessary condition for a well-functioning democracy. But what space is there left to start such a collective conversation?

The social contract

The basic design of modern liberal societies was delivered with the introduction of the social contract. Though this was a philosophical construct that was not shared by many at the time, its central elements have succeeded to become a political reality in liberal democracies. The social contract intended to be an instrument to optimise the human condition, saving humans from a life that was 'poor, nasty, brutish and short.' It did so by settling several other components that are still basic traits of contemporary society (and that moreover condition the technological control over nature). It enabled the rise of free, autonomous individuals that could determine their fate on the one hand and that of the state on the other. It ruled mutual relations between individuals and their relationship to the state, ensuring the general conditions that allow for peaceful cohabitation and profitable cooperation in a pluralist society.

Basically, the state protected the personal sphere of the individual, as long as it respected the personal sphere of others. In that way, the social contract implied a new relation between the domains of the *public* and the *private*. The private domain marked the place where individuals could cherish their own habits, morals and worldviews, without bothering others and without being bothered by others. The core of the public domain was arranged as a market place where individuals could choose according to their private preferences. Thus politics by the state, guaranteeing the personal sphere of the individual, were essentially about the safety and security of the citizens and ruling the market place. It cared after the conditions for the free distribution of goods and it prevented the individual from risks and harm.

As a consequence, the moral discourse of the public domain is limited: it is about guaranteeing safety and freedom of the citizens, preventing risks, harm and violence, warranting justice and rights and asserting duties of individuals. It is not about the good life, about how to become a good person, about the meaning of love, loss and suffering, how to restrict insatiable wishes for joy, health, richness and honour, or how one should live and behave. These questions were banned from the public to the private domain and they still are. Public discourse is available to articulate these dimensions of existence.

This situation has had its repercussions on political debates of new, complex technological developments. Usually public involvement starts with divergent and often inarticulate moral concerns about unintended possible consequences for the collective, such as a fear for loss of control, or a fear for transgressing fundamental borders. However, in the process of articulation in the political realm these moral concerns are often transformed into the regulatory discourse. Whether it is about cloning, IVF, genetically modified animals and crops, or nuclear energy and nanotechnology, ethical concerns on new developments are discussed in terms of the public repertoire at hand: in terms of the economic benefits, the risks for health and environment, and freedom of choice for the individuals.

Western societies have developed several institutional bodies to deal with social and ethical concerns on new developments, including Health Councils and Ethical Committees. Their debates show a specific format and procedure. Risks and benefits are balanced. Clearly detected risks, either to humans or to the environment, will deliver important arguments for political redirection or even prohibition of a technology. But other moral concerns appear to be much harder to articulate. Often, the direct interests and preferences of those who desire the new technology to be established, take precedence over the perhaps lesser articulated, vague concerns uttered by those who are feeling threatened. These vague concerns might touch the collective but they are often 'privatised'.

The basic scheme for decision-making on such a dazzling topic as human enhancement in a liberal society seems therefore to consist of two components. It is the responsibility of the state to prevent negative external effects of new technologies that reach the market. The regulatory process therefore aims at risk control, and to prevent harm to public health, to the environment, etc. Once there are no longer barriers on that side, it is up to individual consumer responsibility to decide whether it wishes to make use of new products or techniques.

Of course, this picture is a bit of a caricature. Nevertheless, it serves to make our main point, namely that notwithstanding the great benefits of having a liberal society, in its basic structure it might have insufficient space for public discourse to address questions on collective issues that can not be dealt with on a satisfactory level by either state regulation or individual choice.

But what if the various developments that were presented in these chapters do indeed lead to a more structured and uniform conglomerate of developments that enable individuals in the nearby future to massively raise their cognitive and physiological capabilities in such a way that we can really speak about sustained human enhancement? What if neuro-enhancers, memory-enhancers, cognitive enhancers, 'smart-drugs' of all kinds, come on the market and become available to everyone? What if these technologies do indeed change the standards of how we look at ourselves, at what is considered natural and what is artificial, at what is bad luck and what is one's own fault, at what is to be taken for granted and what is to be corrected or improved? Big questions, indeed, but not science-fiction.

A new bio-politics

The lack of public discourse to address collective questions of how we perceive ourselves, what kind of humanity we are and what limits we agree on to live with, bears a risk in it. Terrifying examples from the past that were aiming to introduce some kind of bio-politics; initiatives to determine the life and the biology of citizens such as the eugenics programmes before World War II. These were attempts, top-down, to define what it is to be human and to exclude or to transform the ones that did not fit within that definition. Our time is risking a new form of bio-politics. This time it is not the state, but we ourselves that transform the norms we want to live by. Through imitation, cultural acceptation, socialisation and group force we are setting new societal standards. The new bio-politics work bottom-up.

The bio-political disasters from the past are not to be denied and the current situation, although it's hard to tell how it will develop exactly in the near future, should not be underestimated. Still, given the political and regulatory standard procedures of liberal democracies, human enhancement should be an issue that can be dealt with. Unpredictable as it may be, with its possible benefits and negative side-effects, human enhancement still fits in the category of complex policy problems in the field of science and technology that modern societies are frequently confronted with.

Having said this, one has to underline that, as the cliché will, past performance is not always a good predictor of future results. Complex issues in the field of science and technology hardly lead to robust policy-routines because they fail to become business-as-usual. They always lead to unexpected surprises.

From our political context and from past developments we should be able to make an educated guess on how human enhancement may become embedded in our society. There is not much to be predicted yet about the content of new preferences, rights and identities that will emerge. These are shaped alongside and in interaction with scientific and technological developments. But it is not reckless to speculate on the possible course of political debate, that will quite probably resemble that of former ones: we are likely to follow the discourse of detectable risks and benefits and we will have trouble to prevent other moral concerns from being privatised, thus being unable to articulate them as new moral concerns for the collective. See for instance the concern uttered with regard to genetic screening: the fear for loss by the collective of solidarity with the weak and handicapped that might become regarded as the result of individual choice.

Preferences, rights and identities in human enhancement options have not yet found stability, therefore it is necessary to take a lead on actively deliberating them. In contrast to what current discourse on the autonomous individual suggests, these preferences are not expressions of authentic selves, but they are shaped in the process of development and thus they are open to be discussed. New technologies create new wants. There are no such things as authentic wants, untouched by society. There might be even more collectiveness here than we may assume: despite apparent individualism and its inherent freedom of choice, in practice people massively make the same choices. So in no time IVF had become a wide-spread option, and not the preference of just a small group. Similar effects hold for the impact of the PC, the Internet and the mobile phone. These preferences are negotiable, the more so if we start at an early stage to reflect upon them.

Engaging with new collectives

Already these discussions are taking place. The effects of human enhancement express themselves in specific practices and lifestyles, in relatively distinctive social domains. But not only there: when we follow the applications of human enhancement technologies, they will lead us to new social domains as well. One of the important consequences of the further development of human enhancement is that it will lead to the coming-into-being of 'new-collectives', new groups of people that share a common goal, a common want, a common task or a common disability that will bring them to use one form or another of human enhancement technologies, varying from smart-drugs to man-machine interactions. These groups discuss the various possibilities of human enhancement technologies, the possibilities and the impossibilities. In their exchange of knowledge, experiences, hopes and desires, the reality of human enhancement gets shape. These groups form a middle-layer between the level of the state and the level of the individual. They form the stuff society is made up of. By identifying them and closely look at them we can see what new practices come up and what specific questions they pose so that they might give us a clue not only about what the future discussion of human enhancement will be, but also where that discussion will take place.

In the contributions to this book we could already identify the contours of some of these new collectives. We heard about the very outspoken movement of transhumanists, a group of people connected by a shared desire to become 'human beyond the humans' and to cross the limitations of what they perceive as our out-dated natural and cultural state of being. Having the possibility to use various cultural, financial and scientific sources and being well-organised through the Internet, they are capable to develop a sophisticated image of a possible future where it is up to individuals themselves to create their own physical, psychological and cultural identities.

But there were more stories. We read about the various groups of disabled people that use human enhancement technologies to reach a 'normal' standard of living, a standard that under their current condition they would be unable to reach by themselves. We heard about the group of people using doping in sports. Although forbidden, the use of doping is widespread, and the discussion about which means are tolerable to reach the sportive goals they have set themselves is an ongoing affair. We were offered an insight in the military domain. Traditionally, with an exception perhaps for the game of love, the only domain where goals justify the means is the state of war. The traditional soldier was, roughly spoken, not an end in itself but a pawn on the battlefield directed by higher forces. Nowadays, distinctions between classical warfare, guerrilla-wars, peace-keeping operations and other military interventions become blurred, requiring more intelligent ways to conduct military operations where the role of the individual soldier becomes crucial in making a difference. Human enhancement technologies, we read, fit in that development.

Other collectives we saw pass by were the witnesses in the courtroom, the groups of people undergoing education in a variety of ways and people making use of cosmetic surgery. Surely we could make this list even longer and without any doubt we may have even missed some crucial groups. The point, however, we are trying to address is that the consequences of human enhancement will become manifest in specific social domains and sometimes emerge within new social domains, where they will express themselves under specific conditions in a specific form. These domains are positioned between the individual and the state. They will create an environment where new practices, new norms, new social rules and new identities are to be developed. They are of importance to us in a twofold way, both as matters of concern to be taken care of, and as teaching material, to learn from.

It is doubtful whether the two main levels for public and private decision-making, the state and the individual, offer us the right forum to give these developments collective treatment. Developments in several fields of human enhancement, however, pose questions that demand such a wider, collective approach. They force us to reflect on who we are, how we think about new scientific, medical and cultural norms, identities and practices. Human enhancement requires a more moral debate than regulation and risk-control by the state can offer. And it demands more public consideration than is possibly available by reflection from individual consumers.

The future of human enhancement will evolve alongside a wide variety of discourse. Such discourse will be evaluating technological advance concurrent with continuing scientific effort. Different groups of people, all having their own objectives, will contribute and develop domains of expertise and experiential reflection within specific contexts. Only by engaging in communication with these new collectives will we learn how developments are shaping up, what new practices may emerge and where discussions may lead to.

Appendix 1
Glossary of Terminology

ACTH	Andrenocorticotropic hormone, secreted from the anterior pituitary gland in the brain, released in response to many types of stress. Fragments of the synthesized derivative have been used in several research programmes on the improvement of memory.
Ampakines	Drugs thought to be potentially useful in improving memory and concentration in people who have attention-deficit hyperactivity disorder (ADHD) and Alzheimer's disease. Research has indicated cognitive–enhancing potential in healthy volunteer studies.
Amphetamine	Alpha-methylphenethylamine, prescription stimulant of the central nervous system, commonly used to treat attention-deficit hyperactivity disorder (ADHD) in adults and children. Amphetamine increases energy levels, concentration and motivation for an extended period of time.
Amygdala	Almond-shaped group of neurons, deeply located in the brain, performing a primary role in the memory and processing of emotional reactions.
Beta-blockers	Medicines used to treat high blood pressure, congestive heart failure, abnormal heart rhythms, and chest pain. Beta-blockers diminish the effect of excess stimulation of the sympathetic nervous system e.g. extreme nervousness in performing.
Biomarker	Substance, validated by genetic and molecular biology methods as an indicator of a biological state.
Brain-Computer Interface (BCI)	Direct communication pathway between a brain and an external computational device used for restoring or augmenting human functions.
Brainstem	Lower part of the brain, structurally continuous with the spinal cord, consisting of medulla, pons and midbrain.
Carbohydrates	Sugars and starches in food, broken down in the liver into glucose and used in the body to energise cells, tissues and organs.

Central Nervous System (CNS) Largest part of the nervous system, including the brain and the spinal cord.

Cerebellum 'Little brain', integrating sensory perception and motor control, situated in the hindbrain. The cerebellum also plays a role in some of the cognitive functions.

Cochlea implant Surgically implanted electronic device stimulating auditory nerves inside the cochlea by electrical impulses and providing a sense of hearing.

Cognitive enhancement Cognitive enhancement may be defined as the amplification or extension of core capacities of the mind through improvement or augmentation of internal or external information processing systems.

Cognition Cognition refers to the processes an organism uses to organise information. These include acquiring information (perception), selecting (attention), representing (understanding) and retaining (memory) information, and using it to guide behaviour (reasoning and coordination of motor outputs). Interventions to improve cognitive function may be directed at any of these core faculties. (Nick Bostrom, 2006).

Cognitive liberty Term coined by the Centre for Cognitive Liberty & Ethics (CCLE) depicting the freedom of absolute sovereignty of one's own consciousness, extending earlier concepts of freedom of thought, individual sovereignty and self-ownership.

Cognitive neuroscience A branch of both biology and neuroscience that studies the biological basis of neural phenomena and the behavioural manifestations of mental processes.

Concerta™ Prescription stimulant offering sustained release of methylphenidate for the treatment of ADHD.

Corpus callosum A white, flat bundle of axons, beneath the cortex that connects the left and right hemispheres in the mammalian brain.

Cortex cerebri The outer layer of the vertebrate cerebrum, part of which is the forebrain.

Cingulate gyrus The cingulate gyrus 'fold' or 'belt' in the brain partially wraps around the corpus callosum. It coordinates sensory input with emotions and regulates emotional responses to pain.

Deep brain stimulation	A neurosurgical option by which a brain 'pacemaker' is implanted that sends electrical pulses to specific parts of the brain. Used experimentally for people suffering from Parkinson's disease, depression or intractable pain. According to a recent press report, deep brain stimulation boosted memory function in a patient undergoing brain surgery to treat morbid obesity.
Dextro-amphetamine	Psycho-stimulant which produces increased wakefulness, energy and self-confidence in association with decreased fatigue and appetite.
DHA	Docosahexaenoic acid (DHA) is an omega-3 fatty acid. It is found in cold water fatty fish and in fish oil supplements. Low levels of DHA result in reduction of brain serotonin levels. DHA is essential for the development of the brain of an unborn child.
DNA Damage	Damage to the DNA is mainly due to environmental factors and normal metabolic processes in the cell which alter the spatial configuration of the helix. Such alterations can be detected by the cell and once damage is localised, specific DNA repair molecules bind and form a complex that enables the actual repair.
Dopamine	Hormone and neurotransmitter linked to sexual desire, pleasure and movement. It occurs in a wide variety of animals and is produced in several areas of the brain including the hypothalamus.
Electro-encephalogram (EEG)	Neurological test used to measure the electrical activity of the brain, via electrodes applied to the scalp. EEG can help diagnose a number of medical conditions including epilepsy, sleep disorders and brain tumours.
Epigenetics	The study of heritable changes in gene function that occur without a change in the DNA sequence.
Exoskeleton	A skeleton or supporting structure, on the outside of the body.
fMRI	Functional Magnetic Resonance Imaging is used to map regions of the brain. It employs radio frequency (RF) pulses to manipulate the magnetisation of nuclei in tissue. The form of contrast that is used in fMRI is provided by dynamically measuring the blood oxygenation level dependent (BOLD) contrast.

Folic acid	Water-soluble Vitamin B9 which occurs naturally in food and can also be taken as supplements. Folic acid is not made by the human body. It sustains crucial events in the development of the neural tube during pregnancy.
Functional Electrical Stimulation (FES)	Therapeutic procedure that uses electrical currents for the regulation of organs and the restoration of limb functions. Applications include helping awaken injured human brains. FES is an important tool in biomedical engineering research projects.
Fusiform gyrus	Part of the temporal lobe of the brain, amongst others involved in processing of colour information and face and body recognition.
Hemispheres	Cerebral hemispheres are the symmetrical right and left halves of the brain each controlling the opposite side of the body. The central sulcus and the lateral sulcus divide each celebral hemisphere into four sections, called lobes.
Hippocampus	Part of the forebrain and located in the medial temporal lobe. It forms a part of the limbic system and plays a role in spatial navigation and in the transfer of information to long term memory.
Histones	Histone proteins act as a spool around which DNA winds. Histones are essential for the packaging of DNA into chromosomes within the nucleus of a cell. They also control, to some degree, the expression of proteins from DNA.
Intelligent agent	In artificial intelligence, an intelligent agent is a robot or embedded software system that interacts with its environment in a manner that would normally be regarded as intelligent if that interaction was carried out by a human being. An intelligent agent might be wholly autonomous, carrying out its own agenda, and acting as an agent for no one.
Limbic system	The limbic system is a complex set of structures that lies on both sides and underneath the thalamus, just under the cerebrum. It includes the hypothalamus, the hippocampus, the amygdala, and several other nearby areas. It appears to be primarily responsible for our emotional life.

Lock-step education	Conventional format of class room education.
Memory encoding	The processing of visual, semantic, acoustic and tactile input into one's memory. It is the first of three steps in memory information processing; the remaining two steps are memory storage and memory retrieval.
Memory retrieval cue	Any stimulus that helps recalling information in long-term memory, such as pictures, words, sounds or smells.
Methylphenidate	A prescription stimulant of the CNS commonly used to treat ADHD which presumably activates the brain stem arousal system and cortex to produce its stimulant effect.
MicroRNAs (mi-RNAs)	Single stranded RNA molecules which regulate gene expression. Several mi-RNA's have been found to have links with some types of cancer.
Mnemonist	Individual who has developed elaborate codes for the encoding, and ability to remember and recall unusually large lists of data.
Modafinil	Pharmaceutical substance widely used off-label to suppress the need for sleep. It is also used off-label in combating general fatigue unrelated to lack of sleep, in treating attention-deficit hyperactivity disorder (ADHD) and as an adjunct to antidepressants. Recent research underlines cognitive enhancing effects enabling high-performance functionality in healthy individuals.
Morphogenesis	Fundamental aspect in developmental biology controlling the organised spatial distribution of cells and concerned with the shapes of tissues, organs and entire organisms.
Motor Neurone Disease	Motor Neurone Disease (MND) is a progressive neurodegenerative disease that attacks the upper and lower motor neurones. MND leads to wasting of muscles, loss of mobility of the limbs and difficulties with speech, swallowing and breathing.
Neural prosthesis	Neural prosthetic devices are artificial extensions to the body that restore or supplement functions of the nervous system lost during disease or injury.

Neuroimaging technology	The use of various techniques including Positron Emmission Tomography (PET), Computed Axial Tomography (CAT) and Magnetic Resonance Imaging (MRI) to image the structure and/or function of the brain. Functional imaging (fMRI) is used in neurological and cognitive psychology research. It enables the processing of information by centres in the brain to be visualised directly.
Neuronal pathway	Neural tract, usually named by its origin and termination, connecting one part of the nervous system with another and consisting of bundles of elongated, myelin – insulated neurons. Neuronal pathways serve to connect relatively distant areas of the brain or nervous system.
Neurotransmitter	Neurotransmitters are chemicals such as dopamine (DA), serotonin, (5-HT) and melatonin (Mel) that are used in the brain to relay, amplify and modulate signals between a neuron and another cell. It should be present in sufficient quantity in the presynaptic neuron to affect the postsynaptic neuron.
Noradrenaline	Norandrenaline (BAN) is a neurotransmitter originating from the central and sympathetic nervous system where it is released from noradrenergic neurons. BAN is a stress hormone which affect parts of the brain where attention and responding actions are controlled.
Omega 3	There are three major types of Omega 3 fatty acids that are ingested in foods and used by the body: alpha-linolenic acid (ALA), eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA). Once eaten, the body converts ALA to EPA and DHA, the two types of Omega 3 fatty acids more readily used by the body. These essential fatty acids are highly concentrated in the brain and appear to be particularly important for cognitive (brain memory and performance) and behavioural functioning.
Palliative care	Palliative care is an approach that improves the quality of life of patients and their families facing the problems associated with a life-threatening illness.
Pharmaco-genomics	The study of how an individual's genetic inheritance affects the body's response to drugs. Pharmacogenomics holds the promise that one day individuals will be treated with tailor-made and genetically adapted medicine.

Phonemes	A phoneme is the smallest contrastive unit in the sound system of a language. Phonemes are not the physical segments themselves, but in theoretical terms, cognitive abstractions of them.
Phosphenes	Luminous, ephemeral bright lines and dots produced by mechanical or electrical stimulation of the retina, as by pressure on the eyeball through the closed eyelid.
Plasticity of the brain	Neuroplasticity is the lifelong ability of the brain to reorganize neural pathways based on new experiences.
Pre-implantation diagnosis	A procedure used to decrease the chance of a particular genetic condition for which the foetus is specifically at risk by testing one cell removed from early embryos conceived by in vitro fertilisation (IVF).
Propranolol	Non-selective beta-blocker mainly used in the treatment of hypertensia and preventing migraine in children. It may be used incidentally in stressful situations and has a stress-reducing effect during intellectual functioning and in social situations.
Psycholinguistics	Interdisciplinary field of research involving cognitive science, linguistics and psychology, to acquire scientific data about the psychological and neuro-biological factors which enable humans to acquire, use and understand language.
Psycho-pharmacological research	The scientific study of the interactive effect of drugs on mood, sensation, consciousness or other psychological state and behavioural activity. The central theme running through psychopharmacological research is that principles of behaviour can be used to understand and predict drug effects.
Psychostimulants	Amphetamine-like drugs that enhance, amongst others, locomotor behaviour and are used in the treatment of ADHD. They include methamphetamine, methylphenidate and arecoline, a natural organic compound which is an alkaloid found in betel nuts.
Psychotropic medications	Any medication capable of affecting the mind, emotions and behaviour.

Shared extended mind	Principle of collective intelligence found in social species. Some types of species exploit the external environment in support of their cognitive processes, by patterns which they create in the environment that function as external mental states and serve as an extension to their mind. In the case of social species the creation and exploitation of such patterns can be shared, thus obtaining a form of shared mind or collective intelligence.
Smart drugs	Pharmaceutical substances that may theoretically be used for human enhancement, boosting mental function in otherwise normal healthy people.
SNAP25	SNAP25 (synaptosomal-associated protein of molecular mass 25 kDa) is a highly conserved and membrane bound protein associated with cognitive ability.
Spermatogonia	Non-differentiated germinal stem cells located within the seminiferous tubules of the male reproductive system where sperm is produced.
Spiral curriculum	Educational methodology where certain themes run through the years of learning, spiral upwards, getting broader, with more knowledge, skills and appropriate attitudes being established as the learner develops.
Subthalamic nucleus	Small lens-shaped nucleus in the brain where it is a part of the basal ganglia system. Subthalamic neurons can generate spontaneous action potentials at rates of 80 to 90Hz in primates.
Synapse	In archetypal chemical synapses, such as those found at dendritic spines, mushroom-shaped buds project from each of two cells toward each other. At this interface, the membranes of the two cells flank each other across a slender gap, which enables signalling molecules (known as neurotransmitters) to pass rapidly from one cell to the other by means of diffusion.
Synthetic Aperture Magnetometry (SAM)	SAM is a spatial filtering technique that enables demonstration of the spatiotemporal distribution of oscillatory changes (synchronisation and desynchronisation) in magnetoencephalography (MEG) signals elicited by specific brain activation.

Theory of Mind (ToM)	Theory of mind is the ability to attribute mental states (beliefs, intents, desires, pretending, knowledge, et cetera) to oneself and others. As originally defined, it enables one to understand that mental states can be the cause of (and thus be used to explain and predict) others' behaviour. In neuroimaging, particular brain regions that seem to be important for theory of mind have been identified. These studies identify the medial frontal cortex, temporal poles and temporoparietal junction as the brain regions which are most active when people perform theory of mind tasks.
Transcranial magnetic stimulation	Non-invasive method to trigger brain activity by exciting neurons through the application of weak and rapidly changing magnetic fields in brain tissue.
Translational research	Procedure in applied medical research that attempts to develop and apply new technologies which more directly connect basic research to patient care, emphasising early testing and evaluation.
Tryptophan	Essential amino acid, not produced by the body, necessary for normal growth in infants and for the nitrogen balance in adults. The body uses tryptophan to help produce the B vitamin niacin and serotonin. In several human clinical studies tryptophan is used to treat depression.
Ventral posterior nucleus	Somato-sensory cluster of nerve cell bodies behind the ventral lateral nucleus of each thalamus, containing an inverted topographic map of the body. The ventral posterior nucleus relays somatic sensory information to the cerebral cortex.

Appendix 2
List of Contributors

Dr. Nick Bostrom
Director, Future of Humanity Institute and Faculty of Philosophy & James Martin 21st Century School, Oxford University, United Kingdom.

Dr. Huub Dijstelbloem
Program Coordinator Technology Assessment, the Rathenau Institute, The Hague, The Netherlands.

Professor Dr. John Geake
Professor of Education, Westminster Institute of Education, Oxford Brookes University, Oxford, United Kingdom.

Professor Dr. Peter Hagoort
Professor of Cognitive Psychology, Radboud University, Nijmegen, The Netherlands. Director, F.C. Donders Centre for Cognitive Neuroimaging and director, Max Planck Institute for Psycholinguistics, The Netherlands.

Professor Dr. Catholijn M. Jonker
Professor of Mediamatics, Man-Machine Interaction, University of Technology Delft, The Netherlands.

Professor Dr. Thomas Kirkwood
Professor of Evolution and Ageing, Newcastle University. Director, Institute of Ageing and Health, Newcastle-upon-Tyne, United Kingdom.

Dr. Wouter Lotens
Project Manager, Soldier Efficacy, TNO Laboratories for Defence, Security and Safety, Soesterberg, The Netherlands.

Dr. Gangani Niyadurupola
Royal Society of Chemistry Research Fellow at the Parliamentary Office of Science & Technology (POST), London and University of Bath, United Kingdom.

Lyn Parker
British Ambassador to the Netherlands.

Professor Dr. Wim J Riedel
Professor of Experimental Psychopharmacology, Faculty of Psychology, Dept. of Neuropsychology & Psychopharmacology, University of Maastricht, The Netherlands.

Dr. Danielle Ringoir
Science & Innovation Officer, British Embassy, The Hague, The Netherlands.

Professor Dr. Barbara J. Sahakian
Professor of Clinical Neuropsychology at the Department of Psychiatry, Cambridge School of Clinical Medicine, Cambridge University, United Kingdom.

Dr. Martijntje Smits
Senior Researcher Technology Assessment, the Rathenau Institute, The Hague, The Netherlands.

Jan Staman
Director, the Rathenau Institute, The Hague, The Netherlands.

Dr. Danielle C. Turner
Post-doctoral Research Associate, Department of Psychiatry, Cambridge University, United Kingdom.

Professor Dr. Willem A. Wagenaar
Erstwhile Vice-Chancellor, University of Leiden, Emeritus-Professor of Experimental Psychology and Law, Leiden University and Emeritus Honorary Professor, Utrecht University, The Netherlands

Professor Dr. Kevin Warwick
Professor of Cybernetics, University of Reading, United Kingdom.

Leo Zonneveld
Erstwhile Science Attaché, British Embassy, The Hague, The Netherlands.

Appendix 3
Bilateral Conference

The Human Enhancement Colloquium

An Exploration into the Challenge, Essence and Human Boundaries of Future Science

- Location: British Ambassador's Residence, Plein 1813 No.1 The Hague
- Date: Thursday, 10 May 2007
- Participants: Scientists and delegates from Centres of Excellence in Britain and the Netherlands
- Organisation: The British Embassy, The Hague and Rathenau Institute, The Hague

Objectives

The objectives of the Colloquium are:

1. To stimulate the formation of bilateral networks and the exchange of expert knowledge in Human Enhancement.
2. To explore the potential for bilateral collaborative agreements.
3. To discuss national policies and exchange experience on the formation of centres of excellence.
4. To discuss the psychosocial and ethical aspects.
5. Formulation of issues for public debate.

Host event: Lyn Parker, H.M. British Ambassador
Host conference: Jan Staman, Director, Rathenau Institute

Thursday, May 10

8:30 – 9:00 **Registration and coffee/tea**

9:00 **Opening**
Lyn Parker, British Ambassador

9:05 **Introduction morning programme**
Prof. Dr. Barbara Sahakian, University of Cambridge,
Chair Morning Programme

Scientific Developments

9:20 **Life Span Enhancement**
Prof. Dr. Thomas Kirkwood, University of Newcastle,
(Institute for Ageing and Health)
Prof. Dr. Jan Hoeijmakers, Erasmus University Rotterdam,
(Department of Molecular Genetics)

10:00 **Psychopharmaceutical Enhancement**
Dr. Danielle Turner, University of Cambridge
(Department of Psychiatry)
Prof. Dr. Willem Riedel, University of Maastricht

10:40 **Coffee/tea**

11:00 **Military Enhancement**
Major Ollly Brown, MOD UK
Dr. Wouter Lotens, TNO Defence, Safety and Security

11:40 **Education and Human Enhancement**
Prof. Dr. John Geake, Oxford Brookes University
(Professor of Education)

12:00 **Evaluation Morning Presentations with Delegates**
Prof. Dr. Barbara Sahakian, University of Cambridge
(Chairing Discussion)

Observations on the Discussion and Notes to be taken to the Forum:
Prof. Dr. David Cope, Director Parliamentary Office of Science & Technology and Jan Staman, Director Rathenau Institute, The Hague

12:30 **Lunch**

Context of applications

13:25 **Introduction afternoon programme**
Jan Staman, Chair Afternoon Programme

13:40 **Cognitive Enhancement**
Prof. Dr. Barbara Sahakian, University of Cambridge
(Department of Clinical Psychiatry)
Dr. Chris Dijkerman, University of Utrecht
(Neuropsychology)

14:20 **Memory, Recollections, Jurisdiction and Human Enhancement**
Prof. Dr. Willem Wagenaar, University of Leiden
(Cognitive Psychology)

14:40 **Cybernetic Enhancement**
Prof. Dr. Kevin Warwick, University of Reading
(Cybernetics)
Prof. Dr. Catholijn Jonker, Delft University of Technology
(Man Machine Interfaces)

15:20 **POST work on Human Enhancement in the UK**
Gangani Niyadurupola, University of Bath
(Royal Society of Chemistry Research Fellow)

15:40 **Forum and Summary**
Professor Dr. David Cope (Chair)
Director, Parliamentary Office of Science and Technology
Dr. Nick Bostrom, University of Oxford,
Faculty of Philosophy

Human Enhancement: Summary
(Future Perspectives of the Discipline)
Jan Staman, Director, Rathenau Institute

Human Enhancement: Summary (Reflection of the Colloquium)

16:10 **Closing**
Lyn Parker, British Ambassador
Drinks

Contributing organisations

The Rathenau Institute

The Rathenau Institute is an independent organisation in The Netherlands that concerns itself with issues on the interface between science, technology and society, and provides politicians with timely and well-considered information. The Institute was founded in 1986, is based in The Hague, and currently has some 45 staff.

The Rathenau Institute has two core tasks. Traditionally, it studies the impacts of science and technology on society from the public's point of view. This is known in professional circles as Technology Assessment, or TA.

Since 2004 the Institute has also been investigating how the science system performs and how it responds to scientific and social developments. This task is called Science System Assessment, or SciSA.

British Embassy, Science & Innovation Network, The Netherlands

The Science & Innovation Section of the British Embassy in The Hague has mapped out areas of scientific excellence in both UK and The Netherlands and has worked in partnership with the Netherlands' scientific community in building bilateral science programmes across wide areas in breakthrough disciplines. In building bridges between both countries' governments and academic communities on science policy and strategy, the Science & Innovation Section provides official linkage for academics, science policy makers, businesses, and the media. As a European Science & Innovation network we foster collaborative links, which directly contribute to the generation of prospective partnerships involving universities, governments and the business communities. We play a key role in knowledge transfer and information exchange through Europe, while putting scientists in touch with contacts to develop their science and technology projects.

Parliamentary Office of Science and Technology

POST is the UK Parliament's in-house source of independent, balanced and accessible analysis of public policy issues related to science and technology. Our aim is to inform parliamentary debate. We do this in several ways, by:

- Publishing POSTnotes (short briefing notes) and longer reports. Both focus on current science and technology issues and aim to anticipate policy implications for parliamentarians;
- Supporting Select Committees, with informal advice, oral briefings, data analyses, background papers or follow-up research. Committees may approach POST for such advice at any stage in an inquiry;
- Informing both Houses on public dialogue activities in science and technology;
- Organising discussions to stimulate debate on a wide range of topical issues, from small working groups to large lectures;
- Horizon-scanning to anticipate issues of science and technology that are likely to impact on policy.

Reshaping the Human Condition
Exploring Human Enhancement

Executive Editor: Leo Zonneveld
Co-Editors: Huub Dijstelbloem and Danielle Ringoir

Human Enhancement is generally considered as the discipline to improve the physiological and cognitive functions of human beings without a strict medical need. Well-known examples are the use of doping in sports and the use of Ritalin™ or other enhancers by students. But there is more. Anti-aging technologies, military tools, memory enhancers: innovations and applications from the broad field of Human Enhancement are rapidly getting a societal foot on the ground and are reaching the consumer market. Various technologies to improve our bodies and our life emerging from the fields of biotechnology, the neurosciences and pharmacology, and cybernetic advance to facilitate direct man-machine interaction are no longer laboratory experiments but are becoming social tools. A dream for some but a nightmare for others, the possibilities of Human Enhancement force us to think about the ethics and impact of these developments and their possible applications. They raise new questions about possible risks but also about the way people give shape to their hopes, fears and identities. Human Enhancement Technologies are reshaping the human condition. They ask us again to reflect on what it means to be human.

In order to identify and assess the scientific possibilities, their impact and applications, the Rathenau Institute, the British Embassy in The Netherlands and the UK Parliamentary Office of Science and Technology organised a colloquium to start a bilateral dialogue on these themes. This book is the result of that colloquium and contains contributions by such eminent scientists as Nick Bostrom, John Geake, Catholijn M. Jonker, Thomas Kirkwood, Wouter Lotens, Gangani Niyadurupola, Wim J. Riedel, Barbara Sahakian, Danielle Turner, Willem A. Wagenaar and Kevin Warwick. Their contributions are accompanied by interviews conducted with Peter Hagoort and Lord Robert M. Winston.

About the Editors

Leo Zonneveld is erstwhile Science Attaché, British Embassy, The Hague, The Netherlands.

Huub Dijstelbloem is Program Coordinator Technology Assessment, the Rathenau Institute, The Hague, The Netherlands.

Danielle Ringoir is Science and Innovation Officer, British Embassy, The Hague, The Netherlands.

Rathenau Instituut

British Embassy The Hague
Science & Innovation Network

Houses of Parliament
Parliamentary Office of Science and Technology