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# Neurobiology: A case study of the imminent militarization of biology

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## Abstract

*The revolution in biology, including advances in genomics, will lead to rapid progress in the treatment of mental illness by advancing the discovery of highly specific ligands that affect specific neurological pathways. The status of brain science and its potential for military application to enhance soldier performance, to develop new weapons and to facilitate interrogation are discussed. If such applications are pursued, they will also expand the options available to torturers, dictators and terrorists. Several generic approaches to containing the malign applications of biology are shown, and it is concluded that success or failure in doing so will be significantly dependent on the active involvement of the scientific and medical communities.*

The ongoing revolution in biology, symbolized by the completion of the Human Genome Project, undoubtedly has enormous potential for benefit — for example, in the development of more effective, safer medicines. However, serious concerns have been raised about the consequences of the misapplication of the new capabilities for hostile purposes. As Professor Meselson, Thomas Dudley Cabot Professor of the Natural Sciences at Harvard University, has said: "[a] world in which these capabilities are widely employed for hostile purposes would be a world in which

* An early version of this analysis was presented at the 20th Workshop of the Chemical and Biological Weapons Study Group of the Pugwash Conferences on Society and World Affairs, Geneva, 8–9 November, 2003.

the very nature of conflict had radically changed. Therein could lie unprecedented opportunities for violence, coercion, repression or subjugation…"[1]

When renewed concerns about biological warfare arose in the mid-1990s, there were some open publications in which initial assessments were made of the way in which traditional microbiological agents might be modified by genetic engineering,[2] and of how new kinds of agents might be produced in the longer term.[3] Subsequently, consideration has been given to other kinds of agents, such as bioregulators, that might be misused.[4,5] Most recently, analysis has suggested how traditional agents, modified traditional agents, and then advanced biological agents — targeted at specific physiological processes — might successively become threats over the coming decades.[6,7]

In late 2003, the Office of Transnational Issues of the US Central Intelligence Agency issued as bleak a warning about the future of biological weapons as any academic or non-governmental organization has yet produced. The report, titled *The Darker Bioweapons Future*, argued that "[g]rowing understanding of the complex biochemical pathways that underlie life processes has the potential to enable a class of new, more virulent biological agents engineered to attack distinct biochemical pathways and elicit specific effects."[8] The report cited a number of specific examples of new biological weapons that might become possible, and noted that the panel of experts which had been convened to produce the report considered that "[t]he effects of some of these engineered biological agents could be worse than any disease known to man."[9]

However, to date no open analysis has taken Meselson's argument seriously and asked where we might end up later in the century if the militarization of biology is not prevented. Obviously it is not possible in a single paper to survey all of the areas of biology that might be subject to misuse, so here we focus on the potential for hostile manipulation of the human nervous system. We do this in part because the widespread public concerns over the misuse of microbiology have obscured other dangerous possibilities, but also because there are very clear reasons to have worries about the misuse of neuroscience by the military. No doubt, others could also have an interest in misusing the new knowledge, but

1 Matthew Meselson, "Averting the hostile exploitation of biotechnology," *Chemical and Biological Conventions Bulletin*, Vol. 48, June 2000, pp. 16–19.
2 William Cohen, *Proliferation: Threat and Response*, Department of Defense, Washington DC, 1997.
3 Steven M. Block, "Living Nightmares: Biological Threats Enabled by Molecular Biology," *The New Terror: Facing the Threat of Biological and Chemical Weapons*, Sidney D. Drell, Abraham D. Sofaer, George D. Wilson (eds.), Hoover Institution Press, Stanford, 1999, pp. 39–75.
4 George Poste, "Advances in biotechnology: Promise or peril," 2002, available at <www.upmc-biosecurity.org/pages/events/2nd_symposia/transcripts/trans_post.html> (visited 24 August 2005).
5 Claire Fraser and Malcolm Dando, "Genomics and future bioweapons: The need for preventive action by the biomedical community," *Nature Genetics*, Vol. 29, 2001, pp. 253–255.
6 James B. Petro, Theodore R. Plasse and Jack A. McNulty, "Biotechnology: Impact on biological warfare and biodefense," *Biosecurity and Bioterrorism*, Vol. 1, 2003, pp. 161–168.
7 Mark Wheelis, "Does the 'new biology' mean new weapons?", *Arms Control Today*, July/August 2004, p. 6.
8 Office of Transnational Issues, *The Darker Bioweapons Future*, Central Intelligence Agency, Washington, DC, 3 November 2003, p. 1.
9 *Ibid.*

it is unlikely that they will have the kind of resources available to the military and thus be able to lead the way to misuse. It is therefore the military that have to be the first concern and it is on the militarization of neuroscience (broadly conceived) that we concentrate here.

In the next section ("The future threat") we assess the growing capabilities that could arise for misuse from the rapid advances in our understanding of the nervous system and the evidence that there might be those with the intention to make such use of the new knowledge. We conclude that there will be knowledge available for misuse and there will be some willing to misuse it. Then in the following section ("Implications") we sketch out the implications both in the medium term and, more tentatively, in the longer term if such misuse cannot be prevented. We conclude that there are terrible threats to human rights and dignity on the horizon. In a final section ("Responses") we review what responses are available to prevent neuroscience, and by implication much of the rest of biology, from becoming widely used for military purposes.

## The future threat

There is no doubt that the revolution in biology has greatly changed the situation from when the development of the first means of dealing with mental illnesses with effective drugs — in the 1950s — led in turn to the initial efforts by the main Cold War adversaries to develop incapacitating chemicals.[10] In particular, the elucidation of the structure of the diverse neuronal receptors for neurotransmitter chemicals[11] and the increasing discoveries of the functional circuits of the brain through neuroimaging techniques, promises much for good. As Andreasen has noted, we live in an age in which two huge knowledge bases will be increasingly interwoven: the map of the human genome and that of the human brain.[12]

In a report card for progress to date Andreasen shows plainly, however, that only in regard to the treatment of mood disorders can we say that we can now do a great deal better than in the 1950s. The near future will see diagnosis, understanding pathophysiology, treatment and prevention all be made more rational and effective in regard to the dementias, schizophrenia, mood, and anxiety disorders.

George Poste appears to have come to the same conclusion as Meselson. He has argued, for example, that "as we begin to understand the exquisite molecular mechanisms that regulate this remarkable structure called the human body (…) the ability to understand those circuits means simultaneously we gain the capacity to scramble them."[13] Pointing out the need for thinking "beyond bugs" he has referred to the "brain bomb" and noted that such capabilities imply "that you

10 Malcolm Dando, *The New Biological Weapons: Threat, Proliferation and Control*, Lynne Rienner, Boulder, 2001.
11 A form of what are generally termed ligands — small molecules that bind to proteins.
12 Nancy C. Andreasen, *Brave New Brain: Conquering Mental Illness in the Era of the Genome*, Oxford University Press, Oxford, 2001.
13 Poste, *op. cit.*, (note 4).

can engineer a series, a complete spectrum of activity from transient immobilization (…) to catastrophic effects which can be acute or chronic."[14]

It is certainly true that there have been enormous advances in our understanding of the human nervous system[15] since it was recognized in the seventeenth century that the brain controlled our behaviour. But there are, nevertheless, well-informed sceptics who still doubt that a mechanistic understanding of the brain is likely to come about soon — even if it is a formal possibility.[16]

In order to assess whether the new developments will allow the creation of advanced biological agents there are clearly two basic questions to be answered: does neuroscience seem likely to gain the necessary mechanistic understanding of the brain for malign manipulation to be, at least theoretically, possible, and who might wish to take advantage of that knowledge? Our two questions are therefore the familiar ones — about capabilities (that could arise from the increasing understanding of the nervous system) and intentions (to misuse this new understanding for hostile purposes).

## Capabilities

Mental illness causes an enormous worldwide burden of disease in terms of morbidity, mortality and social and economic costs.[17] Rightly, great efforts are being made in medicine and biology to understand the causes of diseases like depression and to find more effective means of helping afflicted people. One important development in this effort appears to be a coming together of previously disparate approaches to understanding human behaviour; one recent book, for example, was titled *Neuropsychiatry and Behavioural Neuroscience*. This text has a chapter on the principles of neuroscience that lists regularities — predictable brain-behaviour relationships — which can be used in understanding and helping to deal with mental illnesses.[18]

It is not difficult to accept such ideas, for example in regard to language production and comprehension. It has been known for many years that damage to specific areas of the brain produces specific deficiencies in language capability.[19]

14 *Ibid.*

15 Stanley Finger, *Minds behind the Brain: A History of the Pioneers and their Discoveries*, Oxford University Press, Oxford, 2000.

16 Dai Rees and Steven Rose, (eds.), *The New Brain Sciences: Perils and Prospects*, Cambridge University Press, Cambridge, 2004.

17 World Health Organization, *Mental Health: New Understanding, New Hope*, World Health Report 2001, WHO, Geneva.

18 Jeffrey L. Cummings and Michael S. Maga, *Neuropsychiatry and Behavioural Neuroscience*, Oxford University Press, Oxford, 2003. Some thirty such regularities are discussed, and it is clear that what is being described is a mechanistic science. For example, the first several principles state: "Brain-behaviour relationships underlying neuropsychiatric syndromes are rule-governed and reproducible across individuals (…) All mental processes derive from brain processes (...) Neuro-psychiatric symptoms are manifestations of brain dysfunction (…) [which] reflect abnormalities of underlying brain function, whether produced by genetic, structural or environmental influence…"

19 Working in the nineteenth century, Broca showed that damage to what is now called Broca's area of the cerebral cortex leads to loss of the ability to generate speech, and Wernicke demonstrated that damage to a neighbouring area, now named after him, leads to a loss of ability to understand language.

Similarly, it is clear that damage to the frontal lobes of the cerebral cortex can produce specific impairments of human behaviour.[20] Individuals with damage to the orbitofrontal cortex, for instance, lack social judgement, have limited insight into their own behaviour and are compromised in their ability to empathize with other people.

Yet not all human behaviour is so easily localized to specific regions of the brain. Indeed, there is every reason to believe that the biological basis of much human behaviour will be exceedingly difficult to understand even if this mechanistic paradigm is fundamentally correct. The question therefore is: what difference does the current revolution in biology make? Does it really open up radically new possibilities and capabilities for manipulation?

The principles listed in *Neuropsychiatry and Behavioural Neuroscience* include, in addition to the influence of both genetic and environmental factors, the idea that neuropsychiatric disorders typically reflect disruption of a system or circuit, and further that disturbances in transmitters or transmitter systems have specific associated neuropsychiatric symptoms. How well do such claims stand up to evidence from recent research?

Signals are conveyed within the cells of the nervous system — the neurons — by electrical means, but they are conveyed between neurons mostly by chemical means. During the last century a wide range of these so-called chemical neurotransmitters (ligands) were gradually discovered, along with the specialized receptors that they affect when released.[21] Neurons that produce different neurotransmitters are involved in different circuits within the brain, and for those who study mental illnesses like depression a particular group of "neuromodulatory" transmitters are of particular interest. Neurons with these transmitters — dopamine, noradrenaline, serotonin, for example — are located in lower, more ancient parts of the brain and, rather than having precise limited connections to other neurons, have very diffuse connections, which suggest they have widespread effects in the body.

In 2003 the journal *Science*, as its "Breakthrough of the year" featured a study of dark energy and dark matter that gave us a firm age for the universe and a precise speed of expansion. The runner-up was the study of mental illness,[22] and

20 The frontal lobes occupy about a third of the total cortical volume, are amongst the latest of our phylogenetic gains and are one of the last of the brain regions to develop in each individual. As with language, it is reasonable to suggest that they mediate characteristic human behaviours. Damage to this part of the cortex produces three behavioural syndromes. Which is manifest depends on the site of damage: an orbitofrontal syndrome, characterized by disinhibition and impulsiveness; a dorsolateral prefrontal syndrome, manifested primarily by executive dysfunction, and a medial frontal syndrome featuring apathy and akinesia.

21 When an electrical impulse reaches the end of the long projection, or axon, of a neuron, it causes the release of neurotransmitter molecules which then cross the small gap, or synaptic cleft, to the next cell and lock on to the relevant receptors on that cell. When they do this, changes take place within the affected second cell which can either enhance the likelihood of an electrical impulse being generated in that neuron (excitation) or make it less likely (inhibition). Various mechanisms clear the transmitter chemical from the synapse so that its effect is transient. Usually it is either destroyed by enzymes in the synaptic cleft, or taken back up into the secreting cell by membrane transporter proteins, and re-used.

22 Anon, "Breakthrough of the year: The runners-up," *Science*, No. 302, 2003, pp. 2039–2040.

specifically mentioned was an article in *Science* in July of that year.[23] The article was entitled "Influence of life stress on depression: Moderation by a polymorphism on the 5-HTT gene." A polymorphism is a slight natural variation in a particular gene, and the 5-HTT gene is the gene which encodes the transporter protein that removes serotonin (5-HT) from the synapse. In the past, many people believed that whilst a few devastating mental illnesses such as Huntingdon's disease were caused by malfunctions in single genes, the vast majority were caused by the combined actions of many genes with small effects — thus making causal elucidations very difficult. However, the study on depression concluded by stating: "We speculate that some multifactorial disorders, instead of resulting from variations in many genes of small effect, may result from variations in fewer genes whose effects are conditional on exposure to environmental risks."[24] In short, if one considers both the genetics and the environmental experience, some mental illnesses may soon be clearly understood with our new knowledge of the genome.

The polymorphism in the 5HTT gene concerned the structure of the promoter. This region determines how efficiently the gene is expressed, and therefore the amount of protein produced. There are two different forms ("alleles") of the promoter — the "long" form allows more expression of the gene than the "short" form. Thus the long form would mean that there was more transporter protein, and presumably more precise synaptic action (as the serotonin would be more rapidly removed back into the pre-synaptic neuron). We each carry two copies of the gene, so it is possible to separate people into three groups on this basis. We each have either two long forms of the promoter, two short forms, or one of each. Of course, the researchers had good reasons for suspecting that this gene might be involved in depression, because one class of drugs used effectively in treating depression act by inhibiting serotonin reuptake.

The researchers conducted a study of a cohort of 1,037 children in New Zealand who had been regularly studied since birth, ninety-six per cent of whom were still being studied at age 26. Many aspects of their lives could be studied, for example stressful life events occurring between their twenty-first and twenty-sixth birthdays could be carefully catalogued for each individual. These events included employment, finance, housing, health and relationships as types of stressor. Members of the group were also assessed for the occurrence of depression over the year from their twenty-fifth birthday. The results from assessing the interaction of the different alleles of the 5-HTT gene and life stressors were very clear-cut. As the authors reported, "[i]ndividuals with one or two copies of the short allele of the 5-HTT promoter polymorphism exhibited more depressive symptoms, diagnosable depression, and suicidality in relation to stressful life events than individuals homozygous for the long allele [i.e. with

23 Avshalom Caspi *et al*., "Influence of life stress on depression: Moderation by a polymorphism in the 5-HTT gene," *Science*, No. 301, 2003, pp. 386-389.

24 *Ibid.*

two long forms]." The impact of life events was conclusively shown here to be moderated by the individual's genetic constitution — a quite remarkable discovery only made possible by modern biotechnology capabilities.[25]

It may be argued, of course, that whilst it is a breakthrough to show how such gene and environment interactions can affect behaviour, there is still a long way to go to the kind of detailed mechanistic understanding that would really allow malign manipulation of the brain and of people's behaviour. It must be remembered, however, that the genomics revolution has not taken place in isolation. There have been associated major developments in bioinformatics, combinatorial chemistry, neuroimaging and other technologies.

This is evident from a paper published in *Science* in 2002. Again it was on the subject of the serotonin transporter gene and was titled "Serotonin transporter genetic variation and the response of the human amygdala". The amygdala is known to be centrally involved in the processing of threatening inputs and fearful and anxious states.[26] If we encounter a potentially threatening situation, a rapid signalling pathway through the amygdala triggers the body's set of reactions that ready it for action — the so-called "fight or flight" response. The 2002 study was published before the work on gene and environment interactions discussed earlier. However, a later, much larger, study involving some ninety people confirmed the 2002 results.[27] This study concluded in part that "heritable variation in 5-HT signalling associated with the 5-HTT (…) results in relatively heightened amygdala responsivity to salient environmental cues." In short, if you have the short version of the promoter you are likely to have a stronger amygdala response to threatening situations. Furthermore, the authors went on to argue that if such threats occur early in life, before the full development of the higher centres' control of the over-response of the amygdala, this could bias the system towards over-response. In line with this view, a study

25 The researchers also demonstrated a similar impact of childhood maltreatment on those carrying one or two short alleles. An analogous association has been shown in monkeys (see Christina S. Barr *et al*. "Sexual dichotomy of an interaction between early adversity and the serotonin transporter gene promoter variant in rhesus monkeys," *Proc. Nat. Acad. Sci*., Vol. 101, 2004, pp. 12358–12363) and in other children (see Joan Kaufman *et al*., "Social supports and serotonin transporter gene moderate depression in maltreated children," *Proc. Nat. Acad. Sci*., Vol. 101, 2004, pp. 17316–17321). However, the latter report showed, too, that adequate social support could greatly reduce the risk to such maltreated children. This happy result also tends to confirm another principle that "[t]he beneficial effects of psychotherapy are mediated through changes in brain function" (see Cummings and Maga, *op. cit.*, note 18). Unfortunately, more recent work has again demonstrated the link between the serotonin transporter promoter polymorphism and suicide (see Pao-Yen Lin and Gaochuan Tsai, "Association between serotonin transporter gene promoter polymorphism and suicide: Results of a meta-analysis," *Bio. Psychiatry*, Vol. 55, pp. 1023–1030).

26 Ahmad R. Hariri *et al.*, "Serotonin transporter genetic variation and the response of the human amygdala," *Science*, Vol. 297, 2002, pp. 400–403. These researchers used a form of functional magnetic resonance imaging to assess subjects' responses to frightening facial images. They divided people into two groups: those with two long alleles of the 5HTT gene and those with one or two copies of the short form of the gene. The subjects were all healthy but nevertheless there was a clear difference in the responses of the two groups. People with the short form showed greater activity in the amygdala in response to frightening stimuli than those with only the long form. The difference was located in the right amygdala, consistent with the right hemisphere's known role in processing facial images.

27 Ahmad R. Hariri *et al*., "A susceptibility gene for affective disorders and the response of the human amygdala," *Arch. Gen. Psychiatry*, Vol. 62, 2005, pp. 146–152.

of people with social phobia showed that when put under stress, those with the short allele had a stronger response in the right amygdala.[28] It concluded: "the present results support a genetically determined link between serotonergic functions, anxiety proneness and a brain region central for emotional experience and processing." The mechanistic details of how the system dysfunction arises are being worked out in animal models.[29]

As this example clearly demonstrates, our understanding of the brain and human behaviour is reaching the level at which precise manipulation for beneficial reasons is becoming increasingly feasible. Yet such information might also potentially be used for malign purposes, for example to induce anxiety disorders.

## Intentions

The question that remains is whether anyone would wish to misuse such information to create new biochemical weapons. As the genomics revolution proceeds, we can obviously no longer maintain a differentiation between chemical and biological weapons and have to view these as a continuous biochemical threat spectrum, with the Chemical Weapons Convention and Biological and Toxin Weapons Convention (CWC and BTWC) overlapping in their coverage of mid-spectrum agents such as toxins and bioregulators. Lethal chemical weapons such as the nerve gases which attack the acetylcholine neurotransmitter system are completely prohibited by the Chemical Weapons Convention, but it is far from clear whether all countries would agree that so-called "non-lethal" chemical weapons are outlawed as well. As was pointed out at the time the Convention was negotiated, there is an ambiguity at the heart of the text caused by the peaceful purposes exemption for so-called law enforcement chemical agents: "[i]s the Convention really to be read as allowing any non-Schedule 1 toxic chemical or precursor to be developed, produced, weaponised, stockpiled or traded, so long as it is said to be for 'law enforcement' purposes?"[30] One would hope not, because such a loophole would allow the development of new, undisclosed, chemical agents. Furthermore, whilst no such loophole exists in the Biological and Toxin Weapons Convention, it is reasonable to ask how well this weak convention — lacking both an organization and any effective verification system — will stand up to the current wave of scientific and technological change and the "opportunities" offered thereby to military and police forces around the world.

Much of the recent military interest in chemical agents that affect the brain has focused on incapacitating chemicals. An incapacitating chemical may

28 Tomas Furmark *et al.*, "Serotonin transporter polymorphism related to amygdala excitability and symptom severity in patients with social phobia," *Neuroscience Letters*, Vol. 362, 2004, pp. 189-192.

29 See Christina S. Barr *et al.*, "Rearing conditions and rh5-HTTLPR interact to influence limbic-hypothalamic-pituitary-adrenal axis response to stress in infant macaques," *Biol. Psychiatry*, Vol. 55, 2004, pp. 733–738. Moreover, the serotonin transporter is not the only gene for which this new imaging genomics approach is producing such results; see Ahmad R. Hariri, and Daniel R. Weinberger, "Imaging genomics," *British Medical Bulletin*, Vol. 65, 2003, pp. 259-270.

30 Editorial, "New technologies and the loophole in the Convention," *Chemical Weapons Convention Bulletin*, Vol. 23, 1990, pp. 1-2.

be defined as an agent "which produces a disabling condition that persists for hours to days after exposure to the agent."[31] Specifically, the term has come to mean those agents that are highly potent and able to produce their effects by altering the higher regulatory activity of the central nervous system. As a recent NATO technical report on future peace enforcement operations noted,[32] incapacitating chemicals could act on "[t]he central nervous system by calmatives, dissociative agents, equilibrium agents." We are obviously, therefore, not discussing traditional riot-control agents here.

There is a long history of State interest in such chemical agents. In the United Kingdom, for example, substantial studies were made at Porton Down during the 1950s and 1960s of glycollates (which bind to one subcategory of acetylcholine receptors). The US also sought an incapacitating chemical capability, and for a while produced and stockpiled the delirium-inducing glycollate BZ.[33] At that time current knowledge of the neuroreceptor sub-types in the brain was not available, so it is unlikely that any agents of adequate specificity were developed. The use of an opiate from the fentanyl family to break the Moscow theatre siege in 2002[34] suggests continuing Russian interest. Although some 120 people died, it might be argued that the use of such an agent facilitated the release of 700 other people.

Evidence of an ongoing US military interest in new non-lethal chemical agents is apparent. A university group known to be closely linked to the US Joint Non-Lethal Weapons Directorate, for example, produced a report in 2000 entitled *The Advantages and Limitations of Calmatives for Use as a Non-Lethal Technique*,[35] which listed a variety of receptor sub-types of potential interest as targets for such new agents. This finding was hardly surprising given the history of US research on such agents,[36] and the United States is not the only country to have recently worked on them.[37]

The recent search for new non-lethal chemicals has taken place, of course, against a background of very rapid and intense civil research on agents affecting the brain.[38] Yet military interest is already directed towards the next

31 Graham Cooper and Paul Rice, (eds.), "Special issue — chemical casualties: Centrally acting incapacitants," *Journal of the Royal Army Medical Corps*, Vol. 148 (4), 2001, pp. 388–391.

32 Research and Technology Organization, *Non-Lethal Weapons and Future Peace Enforcement Operations*, TR-SAS-040, North Atlantic Treaty Organization, November 2004.

33 Martin Furmanski and Malcolm R. Dando, "Midspectrum incapacitant programs," in M. Wheelis, L. Rosza and M. Dando, *Deadly Cultures: Biological Weapons from 1945 to the Present*. Harvard University Press, Cambridge, 2006, pp. 236–251.

34 Robin Coupland, "Incapacitating chemical weapons: A year after the Moscow theatre siege," *The Lancet*, Vol. 362, 2003, p. 1346.

35 Joan M. Lakoski *et al.*, *The Advantages and Limitations of Calmatives for Use as a Non-Lethal Technique*, Applied Research Laboratory, College of Medicine, Pennsylvania State University, 2000. According to the report, the researchers identified several drug classes (e.g. alpha2-adrenoreceptor agonists) and individual drugs (...dexmedetomidine) found appropriate for immediate consideration as non-lethal [agents] involving e.g. unconsciousness or calming.

36 Malcolm R. Dando, *The Danger to the Chemical Weapons Convention from Incapacitating Chemicals*, First CWC Review Conference, Paper No. 4, University of Bradford, March 2003.

37 *A Survey of Biological and Biochemical Weapons Related Research Activities in France*, Country Study No. 2, Sunshine Project, November 2004.

38 Michael Williams et al., "Same brain, new decade: Challenges in CNS drug discovery in the postgenomic, postproteomic era," *Annual Reports in Medicinal Chemistry*, Vol. 36, 2001 pp. 1–10.

generation of agents. A 2004 US Broad Area Announcement stated the objective as follows:[39]

> "The Joint Non-Lethal Weapons Directorate (JNLWD) is soliciting proposals for research, development, integration, and demonstration of next-generation non-lethal weapons (NLW) and capabilities... "

Amongst efforts requested were:

> "Studies/Analyses to address technology-specific legal/treaty/public acceptability issues associated with: (1) extended duration incapacitation (...) and (3) precision long-range engagement of threats..."

In addition to drugs causing calming or unconsciousness, compounds on the horizon with potential as military agents include noradrenaline antagonists such as propranolol to cause selective memory loss, cholecystokinin B agonists to cause panic attacks, and substance P agonists to induce depression. The question thus is not so much when these capabilities will arise — because arise they certainly will — but what purposes will those with such capabilities pursue.

## Implications

The above analysis sketches the current status of mechanistic neuroscience, and suggests that in the near future a sufficiently detailed understanding of brain function will be gained to allow greatly expanded intervention for benign, or malign, purposes. We have also shown that there is continuing military interest in the weapons potential of emerging agents. We now return to our original question: What will the near and mid-term future be like if the gathering momentum for the militarization of biology is not stemmed?

### Present potentialities

Of course, military utility will go beyond weapons to performance-enhancing agents for use by one's own troops. Amphetamines have long been used to extend alertness, and manipulation of the sleep/wake cycle is currently used to enhance the performance of air crews (and probably special forces teams) on long missions. But as a recent National Academies report[40] noted, within a few decades we will have performance enhancement of troops which will almost certainly be produced by the use of diverse pharmaceutical compounds, and will extend to a range of physiological systems well beyond the sleep cycle. Reduction of fear and pain, and increase of aggression, hostility, physical capabilities and alertness could significantly enhance soldier performance, but might markedly

39 Broad Area Announcement, Non-Lethal Weapons Science and Technology: Applied Research and Technology Development Efforts, M67854-05-R-5009, 2004, Contracts Home Page, US Marine Corps.

40 National Research Council, *Opportunities in Biotechnology for Future Army Operations*, National Academies Press, Washington, DC, 2001.

increase the frequency of violations of humanitarian law. For example, increasing a person's aggressiveness and hostility in conflict situations is hardly likely to enhance restraint and respect for legal prohibitions on violence.

Given the kinds of operations other than war that are the increasingly common pattern of military engagement, we will also probably see soldiers armed not only with traditional lethal weapons, but also with a range of "non-lethal weapons" — acoustic, electromagnetic and chemical. Among the chemical weapons will be traditional riot control agents such as CS ("tear gas") and OC ("pepper spray"), as well as various pharmaceutical compounds that cause unconsciousness, paralysis or delirium at very low doses. Whether the traditional laws of war — for instance, protection of civilians and of soldiers "hors de combat" — will withstand these changed circumstances is unsure.[41] Certainly the historical record gives little comfort, as the major military use of "non-lethal" chemical compounds has traditionally been to amplify lethal force, not to replace it. In Vietnam, for instance, the US used approximately 10,000 tons of CS. The purported use was for humanitarian purposes, for situations in which combatants and non-combatants were intermixed, or where extensive property damage would result from attacking the enemy in urban environments. However, a 1973 Army report[42] reviewed after-action reports on the use of CS, and found no record of humanitarian use.

Currently in Iraq, the US is using acoustic beam weapons to flush snipers from cover, who are then killed.[43] And in the previously mentioned example of the Moscow siege, Chechen hostage-takers rendered comatose by the fentanyl derivative were shot dead.[44] It is credible that novel agents would find similar military uses, and that these "non-lethal" agents would often be used to increase the lethality of other weapons, rather than to replace them.

There is also a serious potential for misuse of pharmaceuticals during interrogation.[45] During the Cold War the CIA, for example, sought substances that would change personality and thus induce increased dependence on others.[46] The recent abuses of prisoners under interrogation by US forces in the aftermath of the second Gulf War remind us that even democratic countries with long traditions of support for humanitarian laws may act unlawfully when it appears to be vital to security. Accounts claiming forced medication with

41 David P. Fidler, "'Non-lethal' weapons and international law: Three perspectives on the future," *Medicine, Conflict and Survival*, Vol. 17, 2000, pp. 194–200.

42 Paul L. Howard, *Technical Report: Operational Aspects of Agent CS*, Deseret Test Center, Fort Douglas, Utah, April 1973, DTC-FR-S700M. The principal use of CS was for terrain denial (persistent CS was applied in enormous amounts on the Ho Chi Minh Trail, and around the perimeter of isolated US firebases). The most common combat use was to drive enemy troops from cover to increase their vulnerability to lethal fire, and to break combat when US troops were ambushed.

43 Bryan Bender, "US testing nonlethal weapons arsenal for use in Iraq," *Boston Globe*, 5 August 2005.

44 John Hart, Frida Kuhlau and Jacqueline Simon, "Chemical and biological weapons developments and arms control," Chapter 16, in *SIPRI Yearbook 2003: Armaments, Disarmament and International Security*, Oxford University Press, Oxford, 2003, pp. 645–682.

45 Mark Bowden, "The dark art of interrogation," *Atlantic Monthly*, Vol. 292, October 2003, pp. 51–76.

46 Julian P. Perry-Robinson, *Disabling Chemical Weapons: A Documented Chronology of Events, 1945-2003*, Harvard Sussex Program, University of Sussex, 2003, pp. 8–9.

psychoactive drugs have come from detainees released from US custody,[47] and detainee medical records have been made available to interrogators.[48] Progress in understanding the biological basis for repression[49] may allow the selective deletion of specific memories, which could not only protect sensitive information from unfriendly interrogation but also protect interrogators from effective oversight.

Torturers in all countries will have a greatly expanded repertoire of capabilities. "Non-lethal" police devices such as electric batons and OC sprays are now widely used for torture, and there is no reason to think that future devices and chemicals will not be similarly used.[50] In the hands of the sophisticated torturer or the interrogator willing to use torture to gain information, chemical agents will offer the ability to induce at will panic, depression, psychosis, delirium and extreme pain — and to offer instant relief as well, or even euphoria.

Even greater might be the danger of such capabilities in the hands of dictators to quell dissent. In addition to expanding the ability of dictatorships to use torture to gain information during interrogations, the possibility may exist of pacifying entire populations through additives to food or water.

Of course, anything developed for the use of States is likely to become readily accessible to criminals and terrorist groups, who may be able to use them as effectively as States, but for different purposes. They may even find these weapons more suited to their purposes than to the purposes of States. States are constrained by their own laws and by their international treaty commitments; criminals and terrorist groups partake in none of these constraints. There is thus potential for them to use these weapons with disproportionate effect.

This brief review of potential misuses of pharmaceutical compounds as weapons may seem far-fetched, but our review of the state of the art suggests they are only a slight extrapolation from known neuropharmacology. The capabilities seem to be nearly upon us, and we know that the militaries and justice departments of several nations are keenly interested. As we have noted, Russia has already used an incapacitating chemical as a weapon in the 2002 Moscow hostage rescue, and the US has funded much exploratory research. Other countries are certainly interested as well. Clearly at least some, perhaps most, of the capabilities we outline above are within reach, or will be in a matter of only a few years. And equally clearly, they will be used for military purposes unless there is active intervention of governments to prevent the development of pharmaceutical weapons.

47 James Meek, "People the law forgot," *The Guardian*, 3 December 2003, available at <http://www.guardian.co.uk/g2/story/0,3604,1098391,00.html> (visited 24 August 2005).

48 P. Slevin and J. Stephens, "Detainees' medical files shared: Guantanamo interrogators' access criticized," *Washington Post*, 10 June 2004, A01.

49 Michael C. Anderson *et. al*., "Neural systems underlying the suppression of unwanted memories," *Science*, Vol. 303, 2004, pp. 232–235.

50 *The Pain Merchants: Security Equipment and Its Use in Torture and Other Ill-Treatment*. Amnesty International, London, 2 December 2003.

## Future potentialities

If we look to a longer term, even more far-reaching manipulations of human beings are discernable. Work, for instance, on direct brain-computer interfaces in primates[51] has shown that animals can learn to control a robotic arm through electrodes connected to individual neurons not previously used for similar purposes. In other words, they can learn to fire specific neurons at will, which can in turn control an external device. This may lead to major breakthroughs in the management of patients with permanent spinal cord injuries, but it may also ultimately allow direct mental control of military equipment, and perhaps even remote control of human beings. Already insects and rodents have been "wired" to allow investigators to remotely control their movements, overriding any endogenous intentions.[52] Evidently such capabilities are a long way off, but it is not too soon to start anticipating the possible malign outcomes of such research.

Thus, we see the near-term future (10-20 years) possibly including militaries whose troops will go into action with chemically heightened aggressiveness and resistance to fear, pain and fatigue. Their memories of atrocities committed will be chemically erased in after-action briefings. They will be equipped with a range of weapons, including chemicals that incapacitate their opponents, who may then be executed in cold blood. Civilians will be targeted with incapacitating chemicals when they get in the way, and many will die of overdoses or secondary effects. Civilians in occupied territories will be pacified by chemicals included in food distributions (and civilians at home may also be so pacified). Enemy captives, and civilians suspected of collaboration, will be treated with psychoactive chemicals to extract information, including the use of devastatingly effective chemical torture when necessary. The chemical compounds will be rapidly metabolized and will leave no forensic trace. In this dire future scenario, many fragile democracies will have yielded to totalitarian rule, whose governments repress any dissent with brutal effectiveness, aided by chemical pacification of entire populations, use of incapacitating agents for crowd control and capture of dissident leaders, and use of chemicals for torture and interrogation of dissidents. A worldwide criminal underworld will be using similar technologies to deal with both victims and competitors. Terrorist groups worldwide will be finding frequent use for the force-amplifying effects of chemical agents.

Since the future possibilities become very difficult to discern with any confidence and cannot be defined at this point (unlike the near-term possibilities above, which we can discern with more clarity), we offer a few speculations only to hint at what is likely to be possible in the long term. We can imagine, however, that in the longer term (50 years?), soldiers could become wired for

51 Jose M. Carmena *et al.*, "Learning to control a brain-machine interface for reaching and grasping by primates," *PLoS Biology*, Vol. 1, No. 2, 2003, pp. 1–16.

52 Ben Harder, "Scientists 'drive' rats by remote control," *National Geographic News*, 1 May 2002.

rapid and direct communication with headquarters, and to control powerful military drones by their thoughts. They could be triggered remotely to enter specifically programmed behaviour patterns — evasive, suicidal, berserk, etc. Their memories and convictions would be subject to alteration and erasure.

We would like to hope that this is not the world we shall leave to our children, but we are not particularly sanguine. Human history gives ample grounds for pessimism about our ability to prevent widespread exploitation of the manipulative, hostile and malign possibilities that the emerging technologies will bring within reach.

## Responses

What we are suggesting here is that the biological, medical (and legal) communities should face the near certainty that unless active steps are taken to prevent it, biology will become the next major military technology, and that neuroscience — and by implication much of the rest of modern biology — will become highly vulnerable to use or abuse in entirely unintended, but clearly foreseeable, ways. We know of no major technology with military utility that has not been vigorously exploited for hostile purposes, and there is no reason to think that the revolution in biology will not be similarly bent to military ends. Of course, anticipating such an eventuality, and dealing effectively with it, are two very different things. We see three major generic strategies for attempting to contain the malign applications of biology.

The first would be what we would describe as the "free-market" approach.[53] In essence, this approach accepts that the knowledge needed for benign applications is the same as for malign ones, and posits that there is essentially no way to prevent the development of the capabilities we have outlined. This approach recommends that we let the market drive the technology, and trust to self-interest to restrict the malign applications. We are sceptical that this will work; certainly it hasn't worked that way for any previous technology, probably in large part because the development of hostile applications of new technologies is largely done by governments behind closed doors, with non-competitive funding, with little public oversight or policy advice, and with very large financial benefits to many.

Another approach would be the neo-Luddite one — to attempt to halt the biological revolution in its tracks, or at least give pause to it, before it produces any more problems for society. This too seems unworkable to us; there are simply too many constituencies dependent on and anticipating the benign applications that are promised by biology. Furthermore, stopping the progress of biology would require that all countries with an active biomedical research community and pharmaceutical industry come to the same conclusion. Obviously this is no solution, as desirable as it might be to some.

53 Robert Carlson, "The pace and proliferation of biological technologies," *Biosecurity and Bioterrorism*, Vol. 1, 2003, pp. 203–214.

This leaves, as the only viable option for controlling the malign applications of biology, a middle road of imposed national and international regulation of biological research and of military development. This would build on long-standing norms against the hostile use of chemistry and biology and on an existing international treaty regime including the 1925 Geneva Protocol, the 1972 Biological and Toxin Weapons Convention, and the 1993 Chemical Weapons Convention. It would, however, require greatly enhanced transparency in biodefence and chemical defence, and in research in areas of concern.[54] Moreover, whilst we have concentrated here on the military because it is most likely to have the resources needed to effect the disquieting changes outlined above, it is obvious that once the process is under way many more dangers could arise. Many alliances are therefore conceivable with those who have misgivings about the potential threats to international humanitarian law and human rights in general. Yet the approach we support would require biologists themselves to become much more aware of, and concerned about, the misuses of their science. These are issues that few in the biological or medical communities have even been conscious of, at least since the anti-biological warfare activism of microbiological societies in the 1960s. A major change is therefore necessary in the culture of the biomedical sciences. Failing this, the wholesale militarization of biology will be an integral part of the continuing revolution in modern biology.

Fortunately, those concerned do not have to start from scratch. The aforesaid three treaties effectively outlaw the development, production, stockpiling or use of all biological and chemical weapons, lethal or incapacitating. Nonetheless, there are loopholes (for instance, for law enforcement), and there are ambiguities; together, these provide countries determined to develop new biochemical weapons with a legal opportunity to take at least the first steps. Given the potential of these new weapons to expand military options and the interest in them shown mainly by the most powerful States, many arms controllers fear that the international legal regime banning such weapons may crumble. Concerned scientists do not have to invent a new arms control regime, but they will need to bring their expertise to bear on strengthening the existing regime and the norms enshrined in it against the hostile use of biology and chemistry.

Biomedical scientists in particular could become active, through their professional societies or individually, in efforts to implement systems of oversight, such as the recommendations of a recent report from the US National Research Council.[55] The first tentative steps to implementation have been taken in the US by the establishment of the National Science Advisory Board for Biosecurity,[56] but the system will have to become much more intrusive and international — and will have to effectively include military laboratories — before

54 Mark Wheelis, and Malcolm R. Dando, "Back to bioweapons?", *Bulletin of the Atomic Scientists*, January/February 2003, pp. 40–46.

55 National Research Council, *Biotechnology Research in an Age of Terrorism*, National Academies Press, Washington DC, 2004.

56 See <http://www.biosecurityboard.gov> (visited 24 August 2005).

it will be an effective constraint.[57] Another important opportunity is offered by the current international interest in codes of conduct for bioscientists,[58] which may help to prevent the misuse of the life sciences for hostile purposes. Thoughtful input from scientific societies and national academies of science could be quite influential in the outcome of these discussions.

In the end, it is likely that whether biology becomes an offensive military technology in the coming decades will depend to a significant degree on whether scientists become actively involved in legal discussions, and on the advice they give to policy makers.[59] It is to be hoped that the issues raised in this paper will receive the attention of the scientific community that they urgently deserve, and that scientists will join the arms control, diplomatic, and humanitarian law communities to explore mechanisms to protect humanity from the fearsome potential of abuse of the technologies they are developing, while preserving the beneficial applications.

57 Elisa D. Harris and John D Steinbrunner, "Controlling dangerous pathogens," *Issues in Science and Technology Online*, spring 2003, pp. 74-78.

58 For relevant developments related to codes of conduct see: <http://www.ex.ac.uk/codesofconduct/> (visited 24 August 2005).

59 Robin Coupland, and Kobi-Renee Leins, "Science and prohibited weapons", *Science*, Vol. 308, 2005, p. 1841.

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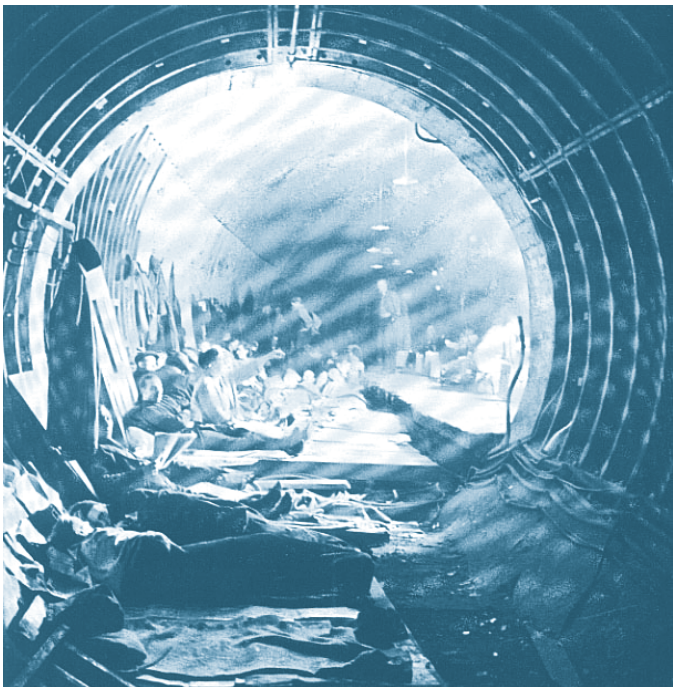
## Dresden

The city of Dresden on February 14th, 1945.
It was never possible to determine the exact number of deaths. Some historians of the time estimated 400,000 deaths, which turned out to be a gross exaggeration. Today, it is generally accepted by historians and by the city of Dresden that approximately 35,000 people died, 25,000 of which have been identified.



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## London

From beginning of September 1940 to May 1941, the Luftwaffe systematically bombed British cities in order to demoralize the enemy. The picture shows the underground of London transformed into a shelter during the battle for England.

**Gas used during the First World War**

British soldiers blinded by gas in April 1918.
Non-lethal tearing agents would be sent over to get soldiers to remove their gas masks thereby making them more vulnerable to a later attack with one of the more dreaded gas such as mustard gas, or asphyxiant gases.

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**Mustard gas**

Effects of mustard gas on a patient picked up by a Norwegian Red Cross ambulance during the Abyssinian war of 1935-1936.


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**Sarin gas attack on Tokyo's subway system**

Sarin gas attack on Tokyo's subway system in 1995 by the Japanese religious sect, Aum Shinriko.

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**Military gear worn to protect against sarin**

Sarin is a colorless, odourless, tasteless, human-made chemical warfare agent. The picture shows the military gear worn to protect against sarin (US Army).