

THE FUTURE OF THE BRAIN

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The brain has had a fairly uneventful past. It has evolved: millions of years of expansion and adaptation have added enormously to its capacity for controlling behaviour in the service of survival. But beyond this Darwinian miracle, it has been affected by little else. Such evolutionary changes have been incremental – as far as we know, the brain didn't undergo a quantum leap in complexity or function. Its future, on the other hand, may be very different. Sudden enlargement of faculties could become commonplace. In this article I allude to what that world might be like, and consider the philosophical implications of technological advances for the humble brain.

Sitting next to me while I type is a cup of filter coffee. The caffeine in the coffee is manipulating my brain chemistry by blocking receptors for the neurotransmitter adenosine, leading to increases in dopamine and making me more alert. I also had a cup two hours ago, so for most of this afternoon I have been and will be in a neurochemically altered state, due to something as innocent as a cup of coffee. By drinking coffee am I changing the “me” doing the writing? If it isn't me, who is it? Is this “not me” better or worse than me? This riddle probably doesn't strike you as tremendously important if the protagonist is coffee. But replace it with a chip implanted into my brain stem that occasionally offers up bursts of activity when I'm tired, and we seem to have an altogether more radical and unsettling proposition.

The brain is a tremendously complex system, made up of billions upon billions of interconnections between cells known as neurons. In the 1940s, Hodgkin and Huxley succeeded in isolating one of the larger neurons from a squid¹. They demonstrated in a series of elegant experiments that neurons communicate using the rapid movement of ionic currents, creating an electrical signal. At the junctions between neurons, and between motor neurons and muscles, this electrical signal becomes a chemical one, carried by one of many different neurotransmitters depending upon the type of neuron. In the form of semiconductors, we have

miniature electrical circuits that can mimic such neural activity, and interface with living tissue; in the form of drugs, we have increasingly specific molecular technology that can mimic neurotransmitter action, or modify existing activity. Despite not really understanding how the brain works, we are in a formidable position to alter it, both in health and disease.

The idea of modifying brain and behaviour through chemicals is certainly not a new idea – alcohol and other drugs of abuse have been in use for centuries. But the specificity with which we may be able to modify it in the future opens up some radical possibilities. Individual brain cells encode things as simple as bars of light and as complex as the sum of probabilities in a gambling task². It is now generally accepted in the neurosciences that the self – the I, me, and you of our everyday lives – is a product of the physical brain and its interactions with the environment. This viewpoint has profound consequences, because by probing these brain-environment interactions through technology, we can examine the very essentials of our inner, private worlds. Furthermore, the potential for modification through implants and drugs will challenge our traditional views of self, society and the law.

Lying with arithmetic

Earlier this year, John-Dylan Haynes and colleagues at University College London published a neuroimaging study that made quite a splash in the popular press³. The authors asked volunteers to undergo brain scans while they were performing either simple addition or subtraction of two numbers. It was down to the volunteer to choose, each time, whether to add or subtract. Before they were asked to reveal their answer, the researchers monitored changes in blood flow in different regions of the brain using functional magnetic resonance imaging (fMRI). Using a statistical technique that searches for patterns in these changes, they could train their decoding algorithm on both subtraction and addition trials. Then, impressively, they were able to classify subsequent arithmetic carried out by the same volunteers as either addition or subtraction, even before they revealed their answers. They were literally reading people's minds.

¹ Hodgkin A & Huxley A (1952) A quantitative description of membrane current and its application to conduction and excitation in nerve. *J. Physiol.* 117:500-544.

² Yang T & Shadlen MN (2007) Probabilistic reasoning by neurons. *Nature* 447: 1075-80.

³ Haynes JD et al. (2007) Reading intentions hidden in the human brain. *Curr. Biol.* 17: 323-8.

The natural fear for the future of the brain is that while we would not mind too much someone knowing whether we were adding up our shopping or subtracting our tax return, being subjected to Orwellian surveillance of our thoughts would be a step too far. *The Guardian* even claimed that “they [the researchers] may be able to spot people who plan to commit crimes before they break the law”⁴. But this is jumping to conclusions. Consider a suspected murderer who is subjected to a brain scan to assess whether he committed the crime or not. For Haynes’ pattern recognition algorithm to work, we would first have to ask him to think about being a murderer for a while, and then to think about not being a murderer. Then we would ask him to “think normally”, and assess whether he was a murderer or not! The absurdity of this situation is patently apparent. The sheer complexity and individual variation in our neural activity means that unwitting decoding of thoughts is unlikely to be in the future of the brain, unless the owner in question is fully cooperative. But the study beautifully demonstrates that our private stream of intentions is, in fact, a continually fluctuating coalition of neural activation. If we wanted to use these brain patterns to interface ourselves with technology, there is little stopping us.

Thinking yourself better

fMRI measures changes in cerebral blood flow, which is an indirect and sluggish indicator of the firing of neurons; by contrast, brain-computer interfaces (BCIs) directly decode neural activity using surgically implanted electrodes. In 1982, Apostolos Georgopoulos, a neuroscientist then at John Hopkins University, recorded the activity of several different neurons in the primary motor cortex of a macaque monkey⁵. He and his colleagues found that when the monkey made arm movements in different directions, each cell had a particular direction for which its rate of firing was highest. When the firing of a population of cells, each with a different preferred direction, was examined, the vector sum of firing rates could predict with substantial accuracy where the monkey’s hand actually went. More recently, a team of researchers in California succeeded in decoding this population vector from motor cortex in

real time⁶. By using an implantable micro-array of electrodes, they showed that an owl monkey could move a robot arm by thought alone. In a final flourish, they even demonstrated that these decoded signals could be sent to a remote robot via the internet. Controlling technology through thought had become a reality.

Matt Nagle, a tetraplegic left unable to move after being attacked and stabbed, was one of the first patients to receive the benefit of this technology in 2002. After receiving an implant made by a commercial company, Cyberkinetics, he learned to control his brain activity to move a computer cursor and change TV channels by thought alone⁷. In the future, miniaturisation will allow BCIs to become wireless, transmitting signals to an external processor worn on the belt of the user. Such implants could be used to operate an unlimited range of appliances, even artificial muscles, restoring movement and sensory abilities to disabled patients.

Most currently used implant technology actually stimulates, rather than records from the brain. Deep brain stimulation (DBS) is becoming increasingly common in the treatment of Parkinson’s disease, ameliorating the symptoms of the movement disorder by applying regular pulses of activity to part of the thalamus. In DBS, millions of neurons are non-specifically disrupted, and the staggering success of the treatment is probably due to the fact that such a diffuse facilitation is all that is needed to restore basic function to the basal ganglia, the brain areas associated with movement initiation that are damaged in Parkinson’s. In the future, implant technology will have to be more precise, and ideally less invasive. The answer may be found in the form of a recent discovery where neurons can be controlled through use of light.

Channelrhodopsin-2 is a genetically engineered ion channel that produces an excitatory current on exposure to blue light; halorhodopsin is its antagonistic cousin, producing inhibitory currents in response to yellow light. By expressing these proteins in neurons (which can be done *in vivo* using harmless viral vectors), their activity can be controlled at will by

⁴ *The Guardian*, February 9th 2007

⁵ Georgopoulos AP et al. (1982) On the relations between the direction of two-dimensional arm movements and cell discharge in primate motor cortex. *J. Neurosci.* 2: 1527-37.

⁶ Wessberg J et al. (2000) Real time prediction of hand trajectory by ensembles of cortical neurons in primates. *Nature* 408: 361-5.

⁷ Hochberg LR et al. (2006) Neuronal ensemble control of prosthetic devices by a human with tetraplegia. *Nature* 442: 164-71.

miniature fibre optic cables inserted into the brain⁸. And as the targeting of the channels can be restricted to particular types of neuron, the unwanted spread of activity inherent in DBS is not seen. It may even be possible to use light to record from the brain without direct electrical contact and the associated drawbacks of inflammation and scar tissue. A protein known as green fluorescent protein (GFP) can be linked to a variety of chemicals, providing an optical signal of molecular processes. As the level of calcium within a brain cell is a relatively accurate measure of the state of its activity, expression of a GFP-tagged molecule that interacts with calcium can provide a visual montage of neural activity, possibly allowing remote control of devices in a similar manner to traditional BCIs.

It is true that even optical technology would require surgery, and the associated risks and recovery involved might dissuade healthy people. But what if the operation became commonplace early in life? Indeed, deep implants are unnecessary – a technique known as electrocorticography (ECoG) uses a sheet of electrodes placed on the brain surface to record signals, and is often used to assess epileptic patients before surgery. What is astounding about current BCIs is that they usually achieve sufficient decoding accuracy with signals from less than 100 neurons – a tiny percentage of the cells in even a millimetre square of cerebral cortex. It seems that a principle of neural networks, known as distributed coding, means that the exact placement of the implant is relatively unimportant – adaptation of both the decoding algorithm and the user could lead to the same BCI being able to serve many functions. We might imagine a future where a few scattered ECoG sheets put in place early in life, using non-invasive optical recording and stimulation, could be used to control personal computers, entertainment systems and cars by thought alone. Having interface capacity would protect against future disability later in life. And even more tantalisingly, we could interface with each other.

Telepathy

In 2002, Kevin Warwick, Professor of Cybernetics at Reading University, had an array of 100 microelectrodes surgically implanted into the median nerves above his left wrist. The chip intercepted the nervous activity going to Professor Warwick's hand, giving computer algorithms the required information to operate an artificial hand. "Sensory" feedback was provided in the form of

⁸ Zhang F et al. (2007) Circuit breakers: optical technologies for probing neural signals and systems. *Nat. Rev. Neurosci.* 8: 577-81.

microstimulation of the afferent nerves running from his arm to the brain. In an audacious experiment, he persuaded his wife, Irena, to have a similar implant, allowing them to communicate wirelessly simply by opening and closing their hands.

This demonstration gives a glimpse of what might be possible in a few years time. It is only a small step to wirelessly link cortical BCI implants between two or more people. By placing transmitting electrodes in Broca's area, the region of the brain responsible for generating speech, and a receiver in a partner's auditory cortex, speechless communication could become a reality. What would that type of communication be like? It is possible that it would have the quality of talking to oneself, especially if the brain regions selected are part of the network usually responsible for generating speech. But language is notoriously slow – it is serial, requiring one idea to be presented at a time, and it has elaborate grammatical constraints to ensure meaning is conveyed accurately. Could we bypass language altogether and directly link two brains with wireless BCIs, achieving something akin to broadband telepathy? This too is a possibility, but one which would depend on the architecture of thought itself. The philosopher Jerry Fodor has argued that there is an innate language of thought structured in a similar manner to normal language⁹, and thus massively parallel communication via BCIs might not be possible. By interfacing the mind with technology, this and other philosophical questions could become empirically testable.

If it isn't me, who is it?

Let us return to the conundrum of the effects of coffee on the self, but replace it with methylphenidate (Ritalin), a drug used to treat attention-deficit hyperactivity disorder (ADHD) in young children. In 2004, 5.1 percent of 16-18 year old high-school students in America used methylphenidate for non-prescribed purposes, presumably for its ability to help them concentrate and remain alert at school¹⁰. If it improves their performance, and is proved safe, should they be banned from taking it? There is obviously an important socioeconomic component to this argument: rich kids able to afford the drug

⁹ Fodor JA (1979) *Representations. Philosophical Essays on the Foundations of Cognitive Science.* Cambridge, Mass.: MIT Press.

¹⁰ NIDA InfoFacts, Methylphenidate (Ritalin). *National Institute on Drug Abuse* (2005). Available at: www.drugabuse.gov/pdf/infofacts/Ritalin05.pdf (accessed 6 September 2007).

shouldn't get an unfair advantage. But suppose for a moment it was legal and freely available. I suspect a natural reaction from many people is a nagging doubt that these students are somehow inauthentic. However, we have already seen that in all probability, there is nothing special about the particular biochemical makeup of our nervous systems; many of us change it on a regular basis with drugs such as coffee and alcohol.

This fluid view of the self may be hard to stomach, but it is one that will in all likelihood become more and more dominant as brain science progresses. Neurotechnology will have the potential to link us to computers, everyday appliances and each other in ways that will fundamentally challenge popular concepts of the relationship between mind and brain. Disability and cognitive disorder will enter a new era of treatment. In turn, the question of what should or should not be improved upon will doubtlessly become more relevant for society¹¹. I have no concrete answer to the question of smart drugs ethics, or, for that matter, that of brain implants; it is, after all, a matter of debate for a properly informed society. But my hunch is that evolutionary factors will lessen their impact. We have evolved to a near-optimal balance of flexible functionality; photoreceptors in the retina, for instance, contain a biochemical cascade of such exquisite sensitivity that they are each capable of detecting a single photon. By disturbing this balance, we might potentiate some functions at the expense of others in the short term, but it is improbable that a single drug or implant will have the ability to surpass millions of years of evolution. The history of the brain might have been dull, but it has certainly set the bar high for what we might want to improve upon in its future.

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¹¹ Persaud R (2006) Does smarter mean happier? In P Miller & J Wilsdon (Eds): *Better Humans? The politics of human enhancement and life extension*. London, UK: DEMOS Collection 21. Available at: www.demos.co.uk/files/File/BH-13.pdf (accessed 6 September 2007).