3 Neuroscience and society

3.1 Benefits and opportunities

Professor Barbara J Sahakian, University of Cambridge

Background

Neuroscience is of growing importance in the 21st century given the rapid technological advances in this area and their impact on society. For example, neuroscience is critical to the understanding of the brain in health and disease and in developing more accurate diagnosis and new treatments across the lifespan. To illustrate, cognitive training treatments are under development for disorders such as attention deficit hyperactivity disorder (ADHD) (see Figure 5) and substance abuse, and drugs that protect the nervous system from degradation are being developed for Alzheimer's disease. Recent innovative proof of concept studies for drugs such as ketamine and scopolamine suggest that it might be possible to treat patients for depression effectively and very rapidly.

For neuropsychiatric disorders and also for brain injury, cognitive enhancing drugs are being used and further developed to improve functional outcome, quality of life and wellbeing (see also Section 2.2 and Box 2). This area of research in neuroscience raises important neuroethical issues, such as the increasing use of so-called 'lifestyle drugs' including 'smart drugs' by healthy people. The neuroethics of this and other areas is discussed in more detail in Section 3.3 (see also Section 3.2).

During the next decade, there will be marked advances in the use of neuroscience in education in helping children to learn in schools. This will lead to evidence-based programmes of individualised or personalised learning. This area, termed 'educational neuroscience', is addressed in depth in Module 2 of the *Brain Waves* project, Neuroscience: implications for education and lifelong learning.

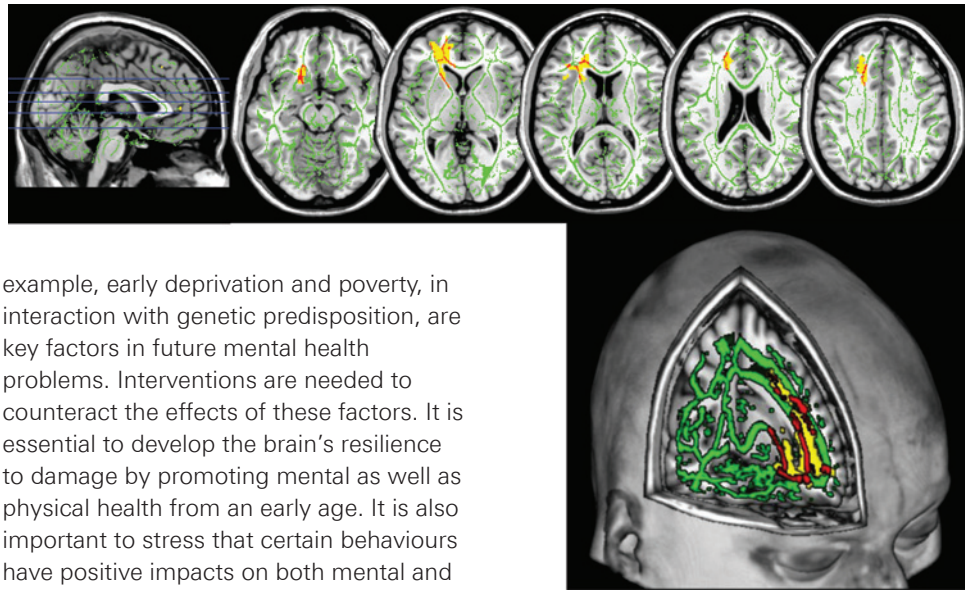
Other areas of neuroscience too will flourish, including those that intersect with social sciences and genetics, such as studies on whether, and under what conditions, we choose prosocial over antisocial or non-cooperative behaviour. The intersection of neuroscience with information technology will expand and further develop, including neural interface systems, neuroprosthetics and functional Magnetic Resonance Imaging (fMRI) feedback (see Sections 2.1, 2.3 and Box 3).

Deep brain stimulation is another area which continues to develop rapidly for treatment for neuropsychiatric disorders, including depression, obsessive compulsive disorder and Parkinson's disease. This involves surgically implanting a medical device that stimulates specific parts of the brain. Similarly, stem cell research applied to the treatment of neuropsychiatric disorders continues to progress (see Section 2.3 and Box 4).

Application to policy

Certain areas of neuroscience will be important for public health policy. For

Figure 5 This image shows a) in green: major white matter tracts generated from a population of 32 subjects-16 healthy volunteers and 16 adult patients with attention deficit/ hyperactivity disorder (ADHD) b) in red: regions where these tracts were found to be abnormal in ADHD patients compared to controls and c) in yellow: regions of reduced white matter density in ADHD patients compared to controls. A, b and c are overlaid on a high resolution brain template acquired with magnetic resonance imaging (MRI). (Reproduced courtesy of Natalia del Campo, University of Cambridge.)



example, early deprivation and poverty, in interaction with genetic predisposition, are key factors in future mental health problems. Interventions are needed to counteract the effects of these factors. It is essential to develop the brain's resilience to damage by promoting mental as well as physical health from an early age. It is also important to stress that certain behaviours have positive impacts on both mental and physical health, and these behaviours should be promoted accordingly. For instance, exercise stimulates the development of nerve tissue in some regions of the brain (Olson *et al.* 2006).

Another example is the importance of early detection and treatment, as well as the need for new treatments, for neuropsychiatric disorders, such as depression and Alzheimer's disease. For example, genetic, cerebrospinal fluid (CSF) and blood, cognitive and neuroimaging biomarkers can play an important part in early identification of these disorders. This would enable some disorders to be prevented, while others could be treated effectively before they develop a chronic, relapsing or progressive course. Furthermore, new insights into underlying mechanisms, coupled with the use of more selective cohorts in clinical trials, is essential for the development of effective drugs in Alzheimer's disease.

Strong links should be fostered between academia and industry to allow valuable collaborations to facilitate drug development and evaluation. As we move further into the 21st century, it is important

to develop novel treatments, drug-based and otherwise, based on symptoms rather than the specific diagnosis. For example, it would be more productive to focus on symptoms, such as impulsivity, across diagnostic categories (such as mania, ADHD and substance abuse) or specific cognitive functions (eg impaired episodic memory) irrespective of disease diagnosis (Sahakian *et al.* 2010; MRC 2010). To illustrate this, a treatment that reduces impulsive behaviour may do so whether a person has a diagnosis of ADHD or substance abuse. Similarly, a treatment for certain memory problems may be useful for improving cognition and functional outcome in both mild Alzheimer's disease and first episode schizophrenia. Symptoms, such as impulsivity, reflect genetics and underlying neurobiology and are therefore more likely to be tractable targets for treatment, compared with a heterogeneous category from diagnostic manuals.

Industrial partnerships could promote the development of biomarkers and neurocognitive training research, as well as novel drug development. Proof of concept studies with ketamine and scopolamine indicate novel areas for the pharmaceutical industry to pursue which would result in great benefits for patients with depression (Berman *et al.* 2000; Zarate *et al.* 2006; Drevets and Furey 2010). Unlike the currently used selective serotonin reuptake inhibitors (SSRIs), with which depressed patients take weeks to show improvements, new drugs with different mechanisms work very rapidly. In addition, small molecule drug design is of growing importance as it holds potential to deliver better and more effective treatments. Translational medicine—the process of turning biological discoveries into drugs and medical devices that will help patients—is a UK strength. In addition, these partnerships could promote the development of pharmacogenomics, the discipline behind how genes influence the body's response to drugs. This might lead to a 'personalised medicine' approach to mental wellbeing, with individuals being given treatments tailored according to their genotype (see also Section 2.2).

Other novel approaches to understanding and treating brain diseases will include synapse proteomics. Irregularities in the sets of synapse proteins (chemicals in the junctions between nerve cells) cause particular clinical symptoms shared between diseases. This provides a novel route for the pharmaceutical industry, since 'blockbuster' drugs that have large markets and are useful in many individuals can be developed. Sets of synapse proteins can be targeted by drugs that should be useful in the treatment of multiple diseases.

The discovery of hundreds of new synapse proteins also provides a new set of potential drug targets. For example, to date, by far the greatest effort of pharmaceutical companies has been on the neurotransmitters (chemicals that send a signal from one nerve cell to the next) and their receptors and uptake systems. These comprise less than 10% of all synapse proteins, which leaves the other 90% to investigate. This provides an investment opportunity. The study of molecular functions at synapses and their

importance in behaviour is rapidly developing. Synapse proteomics will be of increasing importance in genomic diagnostics of brain diseases. For instance, from data on genetic disorders that affect the nervous system, it was found that over 130 brain diseases are caused by mutations in synapse proteins (Bayes and Grant 2009; Fernandez *et al.* 2009). It is already clear that autism, schizophrenia and bipolar disorder involve dozens of synapse proteins. This further emphasises the important point that future diagnostics will be likely to involve careful clinical phenotyping (classification of observable characteristics) using, for example, cognitive testing and brain imaging, but also genetic diagnosis.

Other novel neuroscientific approaches to understanding and treating neuropsychiatric disorders, such as Parkinson's disease, exist. For example, there are highly innovative techniques using optics to control neural activity (Gradinaru *et al.* 2010). These techniques allow for the control of cellular activity by exposure to light. Specific cells can be excited or inhibited by different wavelengths of light, a technique that is both spatially and temporally precise. These optogenetic methods (an emerging field that combines optics and genetics to probe neural circuits) have been demonstrated to be effective in many species and are likely to have wide applications in the future (Boyden *et al.* 2005). Optogenetics has been used to investigate synaptic connections within neuronal networks (Petreanu *et al.* 2007) and synaptic plasticity (Zhang *et al.* 2008). Used alongside Magnetic Resonance Imaging (MRI), it may prove especially valuable (Wells *et al.* 2010). Moreover, the technique has proved beneficial in restoring visual function in mice (Lagali *et al.* 2008) and so has applicability to treating forms of human blindness. Optogenetic therapy also holds promising potential for the treatment of neurological diseases. The technique has now been used in the study of Parkinson's disease where it can be used to investigate how symptoms are produced by different pathways in the brain (Kravitz *et al.* 2010). A recent study in *Nature* (Kravitz *et al.* 2010) indicated in a mouse model of Parkinson's disease that regulation of motor behaviours by optogenetic control was possible and that a modulation of circuitry may represent an effective therapeutic strategy for ameliorating motor deficits in patients with Parkinson's disease. While optogenetic techniques hold great promise for translational studies to aid understanding of neural mechanisms in neuropsychiatric disease, it remains to be determined whether these techniques can be used in humans.

Opportunities

The prospect of new technologies and new treatments for neuropsychiatric disorders and brain injury for the benefit of patients, society and the economy is extremely exciting. Many opportunities for their commercialisation exist, including those described above. These may be developed through public-private partnerships in some instances.

Important innovation in the area of neurocognitive activation (cognitive

training) could be exploited commercially for the benefit of society relatively rapidly. This is an important new technique which could easily be exploited through the UK Games Industry. It could be used in entertainment games for training impulse or cognitive control in children and adolescents with ADHD or substance abuse problems. It could also be used for training episodic memory in elderly people with amnestic mild cognitive impairment (aMCI), the onset stage of Alzheimer's disease. Klingberg (2010) has demonstrated the power of the technique by showing that training on a working memory task is associated with changes in brain activity in specific regions of the brain, as well as changes in the densities of certain types of receptors in healthy people. Therefore this technique could be useful for young and old healthy people, in addition to those with neuropsychiatric disorders and brain injury. The challenge for the games industry or other markets is to transform this training from a chore into a fun and enjoyable activity.

Other areas provide financial opportunities for neuroscientific development, although the gain to society is unclear, such as neuromarketing (see Section 2.5). Studies in this area have used decision making and purchasing paradigms together with fMRI technology to indicate, for example, that a preference for the drink Coke may be influenced by brand image rather than by the taste itself.

Challenges and solutions

Neuroscience is coming of age and can be successfully applied to important problems in health and disease to ensure the UK is economically competitive and that our society flourishes. Therefore it is unfortunate that there has been a recent withdrawal of some drug companies, including UK-based ones, from the development of new drugs for the treatment of psychiatric disorders (Miller 2010) (see also Sections 2.2 and 3.2).

Two actions which might stimulate central nervous system (CNS) research and development enterprise are: i) to extend the patent life of a new drug for psychiatry to ensure that the enormous development costs are taken into account; and ii) to make new mental health treatments a priority by speeding access and development of new drugs/products for mental health, as is done for HIV/AIDS.

A more difficult problem to solve is the sensitivity of 'accepted outcome measures' to change and early stage disease, such as those used by the US Food and Drug Administration (FDA) and European Medicines Agency (EMA). This is particularly true where early detection is important and where neuroprotective drugs can be given. Treatments, including pharmacological ones, need to be given early—before the patient has marked impairments in occupational and social functioning and reduced quality of life and wellbeing. (The standard diagnostic manuals require a decline and impairment in social and occupational functioning for a diagnosis of dementia). Therefore this challenge may lead to an opportunity to innovate the drug development process, for instance targets for treatment may become closely related to genetics and neurobiology (eg impulsivity, episodic

memory) rather than diagnostic categories (eg schizophrenia, ADHD) (see Sahakian *et al.* 2010). Another challenge is the true translation of Proof of Concept studies to Phase 3 clinical trials, as it is difficult to replicate exactly the methodology used in these two stages. Finally, other challenges for research studies include extensive bureaucracy (such as paperwork for research and development funding, ethical reviews, and intellectual property rights protection) and the reluctance of research sponsors to tolerate risk.

Other European opportunities in response to this need to 'repair' the CNS research and development enterprise may include: funding via organisations such as the Innovative Medicines Initiative (IMI),a partnership between the European Community and the European Federation of Pharmaceutical Industries and Associates (EFPIA); grant funding from the EU via the national research councils; development of a capability cluster in mental health; and increased integration between disciplines, particularly psychiatry and neurology.

Conclusion

In summary, there are extensive opportunities for neuroscience to contribute evidence-based advice to policymakers, health professionals, the private sector and the public. Public engagement in neuroscience is a rapidly growing area. 'Smart drugs' or cognitive enhancing drugs (eg modafinil) and their benefits for healthy people have been of keen interest. If these drugs are shown by the pharmaceutical industry to be safe and effective in long-term studies, policy change might allow these to be marketed through the usual routes. This would reduce potential harms of current internet purchase of these 'smart drugs' and may be of particular aid to certain groups in society such as elderly people (see also Sections 2.2, 3.2 and Box 2).

Furthermore, there is a global market for adaptive learning technologies. Marketing e-books and TV programmes are thus far an unexploited area. These types of initiatives can have importance for lifelong learning. Education and learning are known to enhance cognitive reserve, and better cognitive function is associated with better wellbeing (Beddington *et al.* 2008). Both science and technology and higher levels of cognitive abilities and education are linked to increased prosperity (eg increased gross domestic product) (see, eg, Royal Society 2010; Rindermann 2008). Furthermore, investment in mental health has provided substantial economic benefit in the past and should continue to do so in the future (Health Economics Research Group, Office of Health Economics, RAND Europe 2008).

Neuroscience can provide us with the tools to make the most of our minds and also the necessary platform for an economically competitive and flourishing society. Now it is up to us as neuroscientists, the government and society to transform this potential into a reality.

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