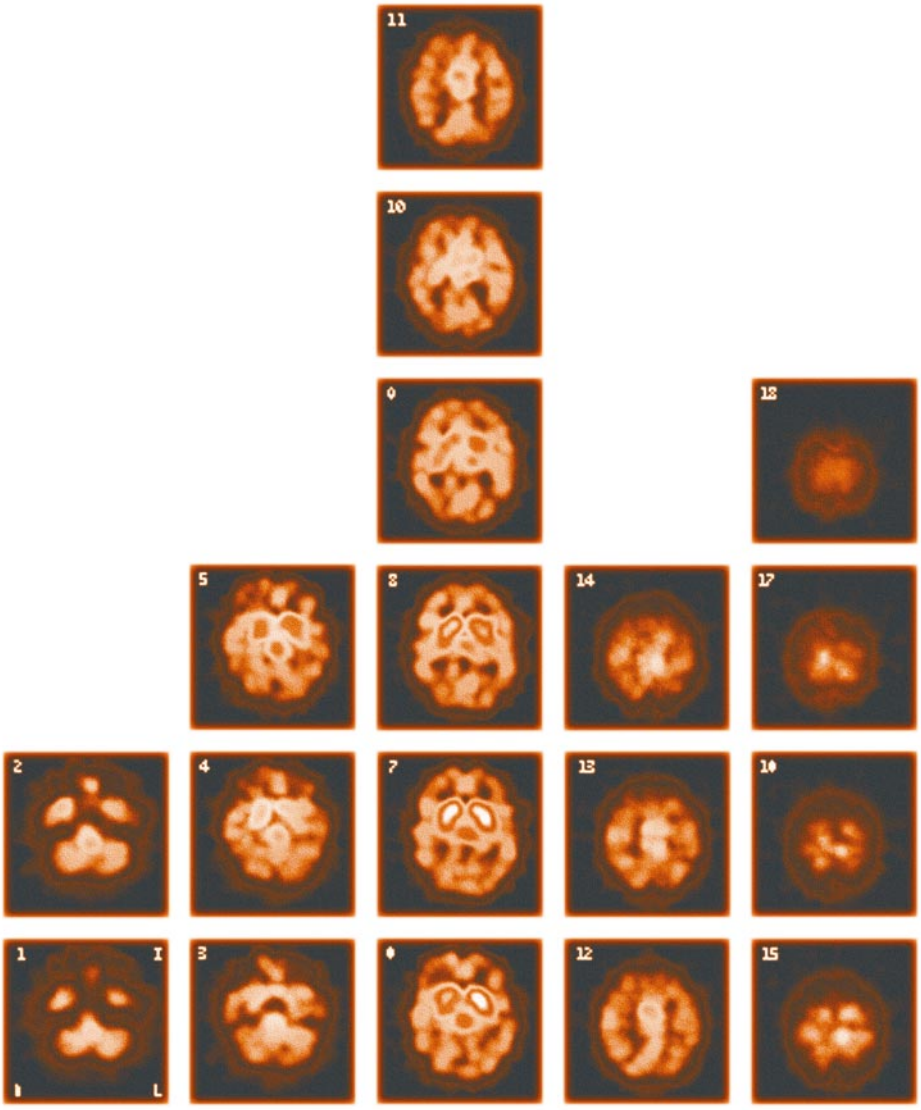
Neuroscience



An Audit of Research Activity

The Wellcome Trust

The Unit for Policy Research in Science and Medicine (**PRISM**) was established by the Wellcome Trust in 1990 as a centre for independent analysis and advice on science policy. Its mission is to help inform decisions on the most effective means of supporting scientific research. It supports evidence-based policy making particularly by:

- evaluating research outcomes;
- auditing scientific activity in different research fields and countries;
- applying novel approaches to strategic planning and priority setting.

As well as carrying out independent policy research, **PRISM** offers two unique services to funding organizations, policy makers, government departments, universities and industrialists:

- **SPIN** (Science Policy Information News) – a weekly round-up of news in biomedical science policy;
- **ROD** (Research Outputs Database) – developed by the Wellcome Trust to rack research outputs in biomedical sciences. For the first time, research-funding agencies are able to identify and acquire details of research papers attributable to them

NEUROSCIENCE RESEARCH

AN AUDIT OF RESEARCH ACTIVITY

Policy report no.10

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Neuroscience is one of the fastest growing areas of biomedical research. To counter the economic and humanitarian burden of diseases of the nervous system, significant funding initiatives are in place worldwide. To assess the UK's neuroscience research activity in a worldwide context, the study examined the incidence and economic burden of diseases of the nervous system; the funding inputs to neuroscience research internationally; and the published outputs and development of new therapeutic products. Opinion was sought on the barriers limiting research activity, on measures to tackle these obstacles, and on strategic objectives for future research.

Main stages of the study

The study comprised five stages:

- a survey of the latest estimates of the burden of diseases of the nervous system both globally and in the UK;
- a survey of the funds available for neuroscience research support;
- bibliometric analyses of research publications in eight subfields of neuroscience, and of patents that cite these publications;
- an opinion survey of neuroscience experts, to determine their perceptions of the field and of ways to strengthen research infrastructure;
- a workshop meeting attended by nearly 150 neuroscientists, of all disciplines, as well as representatives from the Wellcome Trust, industry and other funding agencies, to identify specific scientific and infrastructural opportunities that would strengthen the UK's neuroscience research base.

Main findings

Global burden of disease

Diseases associated with disorders of the nervous system are a major burden worldwide. Current estimates indicate that the majority of this burden is in developed countries. A World Health Organization (WHO) study predicts that this burden will increase dramatically over the next 30 years, with most of the increase occurring in developing countries.

UK burden of disease

These diseases have a considerable impact on the UK healthcare system. Mental illness is the leading cause of illness and disability in the UK, accounting for approximately 25 per cent of the UK government's total payments on sickness and disability benefits (approximately £6.1 billion out of £24.2 billion in 1990/91).

Executive Summary

Research-funding initiatives

There are significant research-funding and strategic initiatives worldwide to battle against the diseases in this field. The initiatives include the 'Decade of the Brain' programmes in the USA and European Union, and the Japanese government's Human Frontier Science Program. In the UK, there are special initiatives by the Wellcome Trust and other medical charities, the Medical Research Council (MRC), the Biotechnology and Biological Sciences Research Council (BBSRC), and the Department of Health's (DoH) research and development programme. Also within the UK, neuroscience research has been identified as a priority area by the UK government's Foresight Panel on Health and Life Sciences.

Research publications profile

Bibliometric analyses of eight neuroscience subfields indicate that the UK is generally in a strong position in this area, with growth in all the fields studied (none of the other 11 OECD countries can claim this). However, while it appears that UK cognitive behavioural psychiatry has a relatively large share of the world output of publications, this area does not produce publications of the general high quality of the other subfields selected for study. There is some evidence that UK clinical research in this field may need specific attention.

Exploitation of research

Patent analysis indicates that UK inventors account for 13 per cent of all inventors cited on US patents based to some extent on UK research, but only 3.5 per cent of these patents are owned by UK companies or individuals. This 'exploitation gap' in UK neuroscience – a failure to take advantage of commercially relevant research – needs to be addressed. The establishment of the UK University Challenge Fund (a £60 million venture capital fund for universities) is a major step in addressing the problem.

Perception of researchers

UK experts feel that this country has a strong base of neuroscience research. However, a number of infrastructural changes need to be made to maintain or strengthen this position. In particular, the career structure of UK neuroscience researchers needs to be improved – with clearer progression paths and increased mobility within the field.

The workshop meeting identified the following points:

Multidisciplinarity

There is a need for multidisciplinary research throughout neuroscience, and for funding mechanisms to encourage multidisciplinary research programmes. A new 'breed' of scientists is required – individuals highly skilled in more than one discipline. Examples cited included molecular biologists who could pursue their investigations in electrophysiological laboratories, cognitive psychologists at home in functional imaging laboratories, and computational scientists who are aware of the key biological questions.

Scientific opportunities

Researchers felt that the next incremental advance would be to study a further level of organizational complexity within their experimental system. For example, in developmental neurobiology, scientists see the next important step as attempting to understand how functional circuits develop; molecular neuroscientists foresee the study of intracellular signalling focusing on the single cell; and cellular neuroscientists predict a move towards studying the interactions between networks of neurons. There was a common recognition of the increasing importance of neuroimaging, particularly functional imaging. As biological systems are being explored in ever-increasing complexity, the need for studies of non-human primates was emphasized.

Genetic technology

Newly developed genetics technologies need to be applied throughout neuroscience research, from the development of new transgenic models, to the eventual introduction of gene therapy for the treatment of psychiatric disorders. Again, the training of multi-skilled research workers will be required to bring genetics into neuroscience.

Infrastructure

Significant advances in the field are possible, but high-quality infrastructural support is required. There were calls for refurbished laboratories, 'state-of-the-art' equipment and computing facilities. JIF – the Joint Infrastructure Fund recently set up by the UK government and the Wellcome Trust – will provide an extra £1.1 billion for infrastructure development. This will have a significant impact on this issue in the UK.

1 Introduction

1.1 Background

Neuroscience: An audit of research activity presents the results of a study of past activity and future options in neuroscience research. The study aimed to give a clear picture of the state of research in the field in the UK, how it compares with work being done elsewhere, and the resources needed in the future if the UK is to have a strong position in neuroscience research.

The specific objectives of this audit are:

- to review the demand for neuroscience research, in terms of the humanitarian and economic burden resulting from such diseases;
- to review the funding inputs into neuroscience research;
- to analyse the supply of neuroscience research, both in the UK and worldwide, as far as it can be measured through the quality and quantity of published papers;
- to undertake patent analysis in order to demonstrate the relevance of neuroscience research to commercial applications;
- to solicit the views of some of the leading researchers and funding agencies in the field.

In order to undertake this task:

- the burden of disease and level of funding was surveyed;
- bibliometric analysis of publications in the field and some subfields was performed;
- a questionnaire survey of 93 neuroscientists asked for views on the infrastructure needs of UK neuroscience;
- a workshop brought together 150 scientists to discuss the frontiers of development in neuroscience. Delegates were also asked for their views on the future for neuroscience.

1.2 Scope

Neuroscience research covers a wide range of disciplines, with many different subfields. As a comprehensive investigation into all subfields would be difficult an 'audit approach' was used. Eight subfields were chosen, spanning molecular and cellular research, systems research and clinical research. The subfields chosen were those regarded by the Wellcome Trust's scientific staff as important in terms of the number of funding applications received by the Trust; each subfield was then defined by experts in that particular area. The eight subfields investigated were:

1. molecular neuroscience;
2. cellular neuroscience;
3. overlap area between molecular and cellular neuroscience (this subfield was selected for analysis after the February 1997 workshop meeting because the general opinion was that it was impossible to separate the two subfields fully and that it was important to assess the 'overlap' area);
4. developmental neuroscience;
5. systems neuroscience;
6. cognitive neurology (analysed separately as a subset of systems neuroscience);
7. cognitive behavioural psychiatry;
8. drug-related behavioural psychiatry.

Subfields 1–6 were classified as 'basic', and subfields 7 and 8 as 'clinical'.

2 The Need for Neuroscience Research

2.1 Introduction

How widespread are diseases associated with disorders of the nervous system? What are the economic costs of treating such diseases in the UK and worldwide? In assessing these questions, an important indicator is 'burden of disease' – an assessment of the amount of ill health (including premature death and disability) attributable to specific deseases.

2.2 Worldwide patterns of burden of disease and death (1990 and 2020)

The World Health Organization (WHO) has conducted a major project designed specifically to look at how health problems such as disease or injury impact on the global society. The Global Burden of Disease (GBD) study[1] describes the patterns of global disease in 1990 and makes projections for the burden of disease in the year 2020.

2.2.1 Volume of disease burden

A key measure of disease burden is 'time lost' (in terms of years of life lost) due to premature death. In measuring the global burden of disease and injury, the GBD study used a relatively new incidence perspective called a DALY (disability-adjusted life year; see Box 2.1). A description of the methods used in the GBD study is presented in Appendix 1.

Table 2.1 presents the main findings of the GBD study and indicates the relative importance of neurological disorders to the global burden of disease. A detailed analysis of the incidence of all neurologically related health states is presented in Table 2.2. It should be noted that this latter table does not include any communicable diseases that may affect the brain or central nervous system (for example, bacterial meningitis), as the neurological damage resulting from such illnesses is often a by-product of the disease. The GDB figures that were identified as being relevant to this study were those relating to non-communicable, neuropsychiatric conditions.

Box 2.1 Disability-adjusted life years (DALYs)

DALYs are an expression of the time lost through premature death, and time lived with a disability – a disease or injury). This measure shows how populations are affected by important, non-fatal but disabling conditions such as some mental illnesses, in addition to the impact of premature death. One DALY represents one year of healthy life lost; the larger the number of DALYs, the greater the disease burden.

The GBD study used DALYs as an incidence perspective to describe the global burden of disease for three main reasons:

- the method of calculating time lived with a disability is more consistent with the method for calculating time lost due to premature death;
- an incidence perspective is more sensitive to current pidemiological trends;
- measuring incidence or deriving it from other data on fatality rates and rates of re-occurrence of disease, gives the calculation a degree of consistency.

As a measure of disease burden DALYS have significant benefits over simple death rates because of the sophisticated method of their calculation, so they can be used to inform health policy.

1 Murray C J L, Lopez A D (eds) (1996) *The Global Burden of Disease: A comprehensive assessment of mortality, injuries, and risk factors in 1990 and projected to 2020.* Harvard School of Public Health and the World Health Organization.

Table 2.1 Causes of DALYs in 1990 and 2020 (worldwide incidence).

'Top ten' diseases 1990	1990 DALYs (millions)	'Top ten' diseases 2020	2020 DALYs (millions)
Lower respiratory infections	113	Ischaemic heart disease	82
Diarrhoeal diseases	100	**Unipolar major depression***	**79**
Perinatal conditions	92	Road-traffic accidents	71
Unipolar major depression*	**51**	Cerebrovascular disease	61
Ischaemic heart disease	47	Chronic obstructive pulmonary disease	58
Cerebrovascular disease	39	Tuberculosis	43
Tuberculosis	38	Lower respiratory infections	43
Measles	37	War	41
Road-traffic accidents	34	Diarrhoeal diseases	37
Congenital abnormalities	33	HIV	36

*Unipolar major depression is clinical depression as opposed to manic depression (bipolar disorder).

Source: World Health Organization, 1996

Table 2.2 Incidence rate (per 100 000) of neuropsychiatric disorders.

	Demographic region*								
Disorder	**EME**	**FSE**	**India**	**China**	**OAI**	**SSA**	**LAC**	**MEC**	**World**
Parkinson's disease	17.0	11.1	4.3	2.4	3.9	2.5	2.1	3.5	5.8
Unipolar major depression	2319.0	2240.0	1961.0	2261.0	2014.0	1734.0	2029.0	1855.0	2079.0
Bipolar disorder	266.0	255.0	244.0	281.0	251.0	218.0	251.0	234.0	254.0
Schizophrenia	20.0	17.0	10.0	12.0	18.0	4.8	-	-	-
Epilepsy	63.0	131.0	131.0	120.0	185.0	234.0	280.0	20.0	155.0
Dementia	120.2	97.3	29.5	38.6	34.5	15.6	58.0	10.6	49.5
Multiple sclerosis	2.0	1.9	1.9	2.2	2.0	1.7	2.0	1.8	2.0
Post-traumatic stress disorder	103.0	105.0	118.0	115.0	120.0	124.0	120.0	121.0	116.0
Obsessive-compulsive disorder	720.0	707.0	698.0	752.0	720.0	660.0	718.0	683.0	713.0
Panic disorder	569.7	559.5	527.9	579.6	545.5	492.3	545.5	509.7	546.0
Cerebro-vascular disease	160.7	256.2	71.1	145.2	76.8	91.7	78.4	62.8	115.4

*EME (established market economies), including European and Australasian countries and the USA;
FSE (formerly socialist economies of Europe), including all former members of the USSR;
OAI (other Asia and islands);
SSA (Sub-Saharan Africa), including South Africa;
LAC (Latin America and the Caribbean);
MEC (Middle Eastern crescent), including Iran, Iraq, Israel, Pakistan and Turkey.

Source: World Health Organization, 1996

For eight of the 11 disorders considered in Table 2.2, the highest incidence rates were found in the established market economies (EME), and China (for a full description of the incidence rates, see GBD series). For six of the 11 disorders, the lowest incidence rates were found in the sub-Saharan Africa region. On a global scale, therefore, the burden of disease for neurological disorders appears to be greatest in the 'developed' world and lowest in the developing regions (where the incidence of pathogen-related communicable diseases is also likely to be high). However, these apparently lower incidence rates in the developing regions could be due to under-reporting or a lack of recognition of neuropsychiatric disorders. The relative contribution of neuropsychiatric disorders to the burden of disease in the developed world appears to be high (probably due to the generally older age profiles of the developed nations).

2.2.2 Projections of disease burden in 2020

One factor of the GBD study was the attempt to predict how mortality and disability figures would change between 1990 and 2020. As shown in Table 2.1, unipolar major depression (taken as a broad indicator of neuropsychiatric disorders) is predicted to move from the fourth to the second most important disease burden by 2020. The proportionate share of the global burden of disease due to neuro-psychiatric conditions is expected to rise from about 10.5 per cent in 1990 to 14.7 per cent in 2020. Although the relative contribution of neuropsychiatric conditions is unlikely to change substantially in the EME and FSE regions, major increases are expected in India, the OAI region, MEC region and SSA region (see Table 2.1). It is important to note that these changes are relative, and may arise due to real changes in disease rates, to demographic changes which alter the age distribution of the population, or to a combination of both.

2.3 UK burden of disease

The 1992 White Paper 'The Health of the Nation', published by the Department of Health, identified mental illness as one of the five key areas for action. Indeed, mental illness was stated as the leading cause of illness and disability in the UK, accounting for 14 per cent of certificated sickness absence, 14 per cent of NHS in-patient costs and 23 per cent of NHS pharmaceutical costs. An analysis of causes of death in the UK [using data provided by the General Register Office (GRO) in Scotland, the GRO in Northern Ireland and the Office of National Statistics (ONS) for England and Wales] has shown that, between 1980 and 1994, the mean number of deaths per year from the main neurological disorders was 24 699. Of these deaths, 31.9 per cent were due to organic psychotic conditions (such as schizophrenia) and 26.8 per cent were from hereditary and degenerative diseases of the central nervous system (such as Alzheimer's disease). It is important to note that these figures are constrained by adult attendances at health services and do not take full account of the burden of child psychiatric disorders. The UK disease burden can be identified both in terms of the economic cost to the National Health Service (NHS) and to the Department of Social Security (DSS).

2.3.1 Costs to the NHS

Table 2.3 shows the number of patients consulting health services for various health problems in England and Wales during 1991 and 1992. The number, and high incidence, of mental disorders or disorders of the nervous system or sense organs, indicates the major health problem presented by these neurological disorders in the UK. Table 2.4 presents the estimated economic cost to the UK NHS of the 14 different disease areas identified under the International Classification of Diseases (ICD). It should be noted that the figures in Table 2.4 comprise only 46 per cent of the total cost of disease to the NHS, excluding costs incurred elsewhere in the NHS that have benefits across all areas identified above (for example, community health services).

Table 2.3 Patients consulting per 10 000, England and Wales, 1991/92.

Disorder	Number consulting per 10 000
Acute respiratory infections	2420
Ear and mastoid process	**1012**
Inflammatory conditions of the skin	760
Neurotic disorders, personality disorders	**649**
Eye and adnexa	**637**
Rheumatism	490
Asthma	425
Hypertensive disease	419
Diseases of oesophagus, stomach and duodenum	353
Neurotic disorders	**344**
Ischaemic heart disease	170
Other disorders of the central nervous system	**166**
Benign neoplasms	126
Migraine	**115**
Diabetes mellitus	111
Depressive disorders	**110**
Cerebrovascular disease	66

Source: Compendium of Health Statistics, 1995 (Office of Health Statistics)

Table 2.4 Analysis of economic cost of disease to the NHS by ICD categories.

Disease area	Estimated cost in 1994 (£millions)	% of all NHS costs
Circulatory system	4 410	11
Mental disorders	**2 315**	**6**
Neoplasms	1 832	5
Respiratory system	1 796	5
Digestive system	1672	4
Musculoskeletal system	1321	3
Genito-urinary system	849	2
Nervous system and sense organs	**827**	**2**
Infectious and parasitic diseases	604	2
Skin and subcutaneous system	599	2
Endocrine and nutritional	572	1
Blood and blood-forming organs	327	1
Disorders of the eye	**238**	**1**
Ear and mastoid process	192	1
Total	**17 554**	**46**

Source: Compendium of Health Statistics, 1995 (Office of Health Economics)

The total assignable cost to the UK NHS of the three disease areas highlighted in Table 2.4 as related to neurological research amounted to approximately £3.4 billion in 1994. The true economic cost to the NHS is likely to be much higher, as this figure does not include costs related to these disorders within the 54 per cent of NHS expenditure that was unassigned.

Table 2.5 Percentage share of seven therapeutic groups, England, 1993.

	% of prescription items	% net ingredient cost
CNS	18	11
Cardiovascular	17	18
Infections	12	7
Respiratory	10	12
Gastrointestinal	8	14
Skin	7	5
Musculoskeletal	6	7
Total	**78**	**74**

Source: Compendium of Health Statistics, 1995 (Office of Health Economics)

Table 2.6 Average cost per in-patient per day in NHS hospitals by speciality, England, 1992/93.

Speciality	Cost per in-patient per day (£)
Child and adolescent psychiatry	216
Forensic psychiatry	184
Mental handicap	104
Mental illness	123
Neurology	181
Neurosurgery	297
Old-age psychiatry	102
Ophthalmology	321
Psychotherapy	128
Total average cost	**184**

Source: Compendium of Health Statistics, 1995 (Office of Health Economics)

Further indications of the economic burden of neurological disorders in the UK are illustrated by the costs of prescription drugs used to treat disorders of the central nervous system (Table 2.5) and the costs of in-patient treatments for neuropsychiatric conditions (Table 2.6). The most frequently prescribed drugs in 1993 were those used to treat disorders of the central nervous system – 92 million prescription items, of which 12 million were antidepressants. The net ingredient cost [NIC; the net cost of the chemical (or other) constituents of the various prescription drugs or other prescription items in each therapeutic group] of the central nervous system prescription items was £353 million, of which the antidepressants constituted £99 million.

The data in Table 2.6 indicate an average cost per in-patient per day of £184 for all neurological specialities. If this cost is extrapolated, the total cost per in-patient for such specialities for one year is approximately £67 000.

2.3.2 Costs to the DSS

Another indication of the cost to the economy is the number of days of certified incapacity. As can be seen from Table 2.7, neurological disorders were the second and fourth most important causes of incapacity in Britain in 1993. Table 2.8 shows the number of people claiming benefits for a neurological condition in 1990–91, the number of working days lost through sickness and the cost per year to the Department of Social Security (DSS).

As part of the Department of Health's action programme, the Office of Population Censuses and Surveys (OPCS) was commissioned to carry out a survey of psychiatric morbidity in the UK. The results of the survey, published in 1995, revealed that approximately one in seven adults aged 16–64 had some sort of psychopathology in the week prior to being interviewed. This figure provides compelling evidence of the importance of mental illness in terms of burden of disease within the UK.

Table 2.7 Days of certified incapacity, by cause, Great Britain, 1993.

Disorder	Days (millions)	% of all causes
Musculo-skeletal system	176	28
Mental disorders	**120**	**19**
Circulatory system	115	18
Nervous system/sense organs	**42**	7

Source: Compendium of Health Statistics, 1995 (Office of Health Economics)

Table 2.8 Claimants of sickness and invalidity benefits, 1990–91, for neurological disorders.

Cause	People	Days	Cost (£millions/yr)
Viral diseases of the central nervous system	2299	717 300	34
Organic psychotic conditions	571	178 200	9
Other psychoses	46 460	14 495 400	697
Neurotic and personality disorders	232 929	72 673 800	3494
Mental retardation	13 241	4 131 200	199
Inflammatory diseases of central nervous system	4654	1 452 200	70
Hereditary diseases of the central nervous system	12 036	3 755 300	181
Other diseases of the central nervous system	63 319	19 755 500	950
Disorders of the peripheral nervous system	9883	3 083 500	148
Disorders of the eye and adnexa	15 883	4 955 500	238
Disorders of the ear and mastoid process	7607	2 373 400	114
All neuro	408 882	127 571 300	6133
Total, all disorders	**1 612 074**	**502 967 100**	**24 181**

Source: DSS, Newcastle upon Tyne

2.4 US burden of disease

Table 2.9 illustrates the scale of the problem for a number of major uncured diseases in the USA. For Alzheimer's disease, depression, and stroke, the annual economic cost to the USA is approximately US$174 billion. A 1992 report by the firm Lewin-ICF (*The Cost of Disorders of the Brain*) estimated that the total economic cost of disorders of the brain to the USA was approximately US$401 billion per year (of which, neurological disorders cost $104 billion, psychiatric disorders $136 billion, alcohol abuse $90 billion, and drug abuse $71 billion). At that time, the US government's commitment to neurosciences research was approximately US$1.8 billion per year. In view of this economic impact, the report argued that more funding was needed in this area.

Table 2.9 Prevalence and cost of uncured disease in the USA.

Uncured disease	Approx. annual prevalence	Approx. annual econ. cost (US$billions)	Source
Cardiovascular disease	56 000 000	128	Am. Heart Ass.
Cancer	10 000 000	104	Am. Cancer Soc.
Alzheimer's disease	**4 000 000**	**100**	**Alz. Ass.**
Diabetes	16 000 000	92	Am. D. Ass.
Arthritis	40 000 000	65	Arth. Found., All. Aging Res.
Depression	**17 400 000**	**44**	**Nat. Dep. & Man. Dep. Ass.**
Stroke	**3 000 000**	**30**	**Nat. St. Ass.**
Osteoporosis	28 000 000	10	All. Aging Res.

Source: Pharmaceutical Research and Manufacturers of America, 1997

2.5 Conclusions

The worldwide burden of disease resulting from neuropsychiatric disorders looks set to increase, particularly in the developing nations, where shifts in the age distribution of populations may result in a greater proportion of the disease burden being associated with noncommunicable disorders such as mental and neurological illnesses. The resulting caretaking costs of such conditions worldwide will add to the economic burden in both developed and developing nations.

3 Funding Inputs to Research

3.1 Introduction

There is a clear indication of the increasing burden of neurological disease. What has been the response to this in terms of research funding commitments? The response of the major research-funding sources in the UK (central government, Research Councils, charities, and industry) are examined. Brief overviews of international programmes (in the USA, Japan and Europe) are also presented to place the UK's effort into perspective.

3.2 UK sources of neuroscience funding

3.2.1 UK central government

The UK central government has several sources of funding for neuroscience research. These include the Department of Health's Centrally Commissioned Research Programme (DoH), the National Health Service research and development programme (NHS), and the Research Councils – the Medical Research Council (MRC), the Biotechnology and Biological Sciences Research Council (BBSRC), and the Economic and Social Research Council.

A number of DoH research programmes have a particular focus on mental health and neuroscience research. These projects are contained in three strategic initiative areas: Research on Strategic Health Service Functions (for example, Policy on Mental Health Services); Public and Environmental Health (for example, the Health and Lifestyle Programme); and the Personal Social Services initiative. The NHS's Mental Health Programme, a part of its research and development programme, has identified five priority areas in this field to receive central funding: quality of life in residential care for the long-term mentally ill; community care of the severely mentally ill; a training package for use in primary care; the mental health of NHS workforce; and methodology to establish mental health needs of a particular population.

The MRC's expenditure on neurosciences and mental health for 1996–97 was £56.9 million. Within this field, the MRC invests in clinical neuroscience and mental health, behavioural science, cognitive science, neurobiology and the biology of brain disease. Research is supported not only at MRC Units and Institutes, but also in universities, medical schools and their equivalents via project grants and personal awards. The aims of the research strategy in this field are broadly fourfold:

- to understand the integrated biological basis of normal brain function and cognitive processes, and their development and ageing;
- to understand how genotype and social environmental factors contribute to normal and pathological development and function;
- to understand the interplay between social and cultural factors, psychological well-being and behaviour, brain biology in health and disease;
- to apply this understanding to the development of novel and effective approaches to the prevention, diagnosis and treatment of neurological and psychiatric disorders (including spongiform encephalopathies).

The BBSRC funds various themes in the area of neuroscience both by 'response mode awards' and by core funding to BBSRC-funded institutes. In 1996/97, the BBSRC spent approximately £11.5 million, of which £3.3 million was for research on transmissible spongiform encephalopathies. Certain themes in the area of neuroscience are funded (through response mode awards) by the Animal Sciences and Psychology Committee. These include senses, speech, biological clocks and locomotion. Core-funded programmes at the Roslin and Babraham Institutes include neuroscience themes relating to animal welfare and behaviour.

The Economic and Social Research Council currently funds projects in the cognitive neuroscience field, including funding of the Human Communication Research Centre (HCRC). Based at the Universities of Edinburgh and Glasgow, the HCRC is an interdisciplinary research centre that pursues cognitive science approaches to human communication.

Table 3.1 Wellcome Trust commitment in neurosciences as at 5 April 1998.

Grant type	Amount minuted (£millions)
Project grants	51
Programme grants	42
Equipment	6
Buildings	5
Junior research fellowships	29
Senior research fellowships	33
Studentships	3
Veterinary research	1
Other awards	2
Total	**172**

Source: Wellcome Trust Grants Administration Department

Although neuroscience research is not in the main remit of the Engineering and Physical Sciences Research Council (EPSRC), there are some areas where it provides underpinning support to medical research and the pharmaceutical industry. Examples are chiral chemistry, which enables novel drug compounds to be developed, and biomolecular sciences which, jointly with the BBSRC, aims to support, encourage and direct fundamental studies in chemistry and biology concerned with molecular structure and processes at the atomic level.

The life sciences work conducted at Chemical and Biological Defence (CBD) Porton Down (part of DERA, the Defence Research Agency) identifies medical countermeasures against chemical and biological agents and therefore requires that neurosciences research is supported. This work alone is valued in excess of £2 million per year, although work broadly defined as 'neurosciences' could fall into a number of categories including work carried out for the Ministry of Defence for which funding priorities are confidential. Plans are currently being discussed for the development of a Centre for Neurosciences whereby CBD facilities would be made available for project-based postgraduate training in the neurosciences.

3.2.2 UK charities

The largest charitable source of neuroscience funding in the UK is the Wellcome Trust, which at 5 April 1998 has committed itself to spending a total of £172 million to support such research through its various panels and schemes (this is a 'snapshot' of current commitments – the *annual* expenditure in this field is approximately £60 million). Table 3.1 analyses this expenditure by the various types of grant.

Many other organizations also play a major role in the funding of neuroscience research within the UK. Some of the largest organizations include: Action Research (annual expenditure £3.8 million), Multiple Sclerosis Society (£1.8 million), Stroke Association (£1.6 million), Ciba Foundation (£1.5 million), Parkinson's Disease Society of the UK (£1.3 million), Wellbeing (£1.2 million), Muscular Dystrophy Group (£1 million), Brain Research Trust (£816 000), Iris Fund for the Prevention of Blindness (£800 000), Guide Dogs for the Blind Association (£635 000), Motor Neurone Disease Association (£440 000), Mental Health Foundation (£410 000) and the Nuffield Foundation (£350 000). In January 1998, the Gatsby Charitable Foundation (affiliated with the Sainsbury family charitable trusts) donated £10 million over a period of ten years to University College London for research into cognitive neuroscience. The Gatsby Charitable Foundation also funds the Sainsbury Centre for Mental Health, and contributed £2.2 million to mental health projects in 1996/97.

This is not a complete list, but does give an indication of the wide range of sources for neurosciences research funding within the UK. It must be noted that in a number of examples cited above, only part of their total expenditure is spent on neurosciences research (such as the Nuffield Foundation); in other instances, all of an organization's expenditure is spent on research related to a disease of the nervous system and patient and carer support (e.g. the Parkinson's Disease Society).

3.3 US sources of neuroscience funding and the 'Decade of the Brain'

3.3.1 US central government

On 17 July 1990, President George Bush issued a 'Decade of the Brain' proclamation, calling on all public officials and the people of the USA to observe the decade with appropriate programmes and activities. In April 1991, the Subcommittee on Brain and Behavioral Sciences published a report, *Decade of the Brain 1990–2000 Maximizing Human Potential*, stating that the programme was established to "maximize human potential through studies of human behavior, senses and communication, learning and memory, genetic/chemical alterations, and environmental interactions. Progress in these areas should lead to reductions in mortality from brain and nervous system disorders and to improvements in the quality of life." The report identified nine research areas that could form the basis of an integrated programme in brain and behavioural sciences, and three areas that span the nine research areas (basic research, technology and international activities). The nine research areas were:

- drugs and the brain/addiction;
- ageing and the human brain;
- human behaviour and mental disorders;
- brain and spinal cord damage;
- communication and sensory disorders;
- development of the human brain;
- learning and memory;
- rehabilitation and restoration of function;
- environmental impacts on the human brain.

Table 3.2 Research and development budget allocations for US neuroscience-related institutes (US$millions).

Institute	*FY1995	FY1996	FY1997	FY1998
National Institute of Neurological Disorders and Stroke	626.5	659.8	701.6	722.7
National Institute of Mental Health	541.7	566.5	604.2	629.7
National Eye Institute	290.8	304.0	323.1	331.0
National Institute on Drug Abuse	289.8	305.0	328.3	358.5

*FY (financial year).

Source: American Association for the Advancement of Science Report XXII

The National Institutes of Health (NIH) Office of Financial Management has estimated that the NIH-wide spending related to the Decade of the Brain increased by 42 per cent between 1991 and 1995; after taking into consideration the effects of inflation on biomedical research funding, the real increase was in the order of 22 per cent in this period.

Four (of 21) NIH institutes and centres are responsible for the majority of neuroscience research funding: the National Institute of Neurological Disorders and Stroke, the National Institute of Mental Health, the National Eye Institute, and the National Institute on Drug Abuse. The research and development budget allocations for these four institutes (Table 3.2) indicate that, in 1995, there was a budget of US$1.78 billion potentially available to fund research into neuroscience. This budget rose to US$1.84 billion in 1996, US$1.96 billion in 1997, and is estimated to be US$2.04 billion in 1998.[2] These figures do not include the allocations for neuroscience-related research coming under the remit of other institutes such as the National Institute on Aging. The 1998 budgets for the NIH also show an additional and separate US$37 million allocated for research into the biology of brain disorders. To make best use of the large amounts of money available, a 1995 report by the National Institute of Mental Health set out a strategy for future research directions and developments that would cut across all subfields of neuroscience research (Box 3.1).

3.3.2 US charitable sector

There are many sources of medical biomedical research funding in the US charitable sector, and it would be difficult to provide a comprehensive list of those involved in funding neuroscience research. One of the main charitable sources is the Howard Hughes Medical Institute, which spends approximately US$67.4 million (£40.8 million) per year on neuroscience research, supporting 73 investigators (not all of whom are listed as being in the Institute's neuroscience programme, but all of whom are working on problems of current interest in the field). Other private organizations that are likely to contribute to the funding of neuroscience research in the USA include the Alzheimer's Association, the Amyotrophic Lateral Sclerosis (ALS) Association, the United Cerebral Palsy Association, the Depression and Related Affective Disorders Association, the Epilepsy Foundation of America, and others relating to specific neurological disorders.

2 Using US inflation figures of 2.2 per cent for the 1996–97 financial year and 2.9 per cent for the 1997–98 financial year (*The Economist*, 23–29 August 1997).

3 Funding Inputs to Research

Box 3.1 Future research directions in neuroscience and mental health

In October 1995, the National Institute of Mental Health published a report, *The Neuroscience of Mental Health II*, which included recommendations for future research directions and developments that cut across all subfields of neuroscience research. These recommendations included:

1. Research infrastructure

- continue to attract young, bright scientists to neuroscience research;
- enhance recruitment of bright scientists into the emerging field of computational neuroscience as well as into classical neuroscience fields of neuroanatomy and neurophysiology, which seem to be underrepresented.

2. Communication and interaction

- create databases, standard data formats, and the capability for sharing as well as processing data through electronic communications;
- establish intellectual networks to foster interactions among scientists from different disciplines and from both conceptual and experimental perspectives.

3. Modelling and theoretical neuroscience

- develop mathematical models to deal with complex systems involved in brain function;
- develop models for predicting molecular structures of membranes and other proteins important for signalling at the atomic level of resolution;
- develop appropriate models to study the brain mechanisms governing behaviour.

4. Neural circuitry

- completely map all connections within the brain and define these neurocircuits in terms of their functions, morphology and chemistry;
- develop new tools to trace tracts within the nervous system in living and *post mortem* material;
- enhance capability for dynamic, real-time image analysis and the visualization of specific neurochemicals;
- define the anatomic site of action of psychopharmacological or psychoactive drugs within the neural circuitry;
- focus in particular on the cerebral cortex and the limbic system and those subcortical systems that modulate their function.

5. Genetics

- develop effective vectors for delivery of genes to the brain;
- use gene 'knockout'/'knockin' techniques and antisense nucleotides to suppress gene expression, especially in behavioural and developmental studies;
- extend gene knockout/knockin capability from the mouse to the rat.

3.4 European Union Decade of the Brain

Following a number of failed attempts by the European Neuroscience Association to persuade the European Commission to incorporate neuroscience research into the Framework programme, the European Union (EU) Decade of the Brain initiative was established in 1992. A working party established by the then EU research commissioner Filippo Pandolfi was given the task of determining the needs of the European neuroscience community. The working party developed a proposal that would have cost the EU approximately ECU100 million per year of the initiative.

The present EU Framework biomedical research programme (December 1994 to December 1998) states its main aims as:

- to develop a better understanding of the human body's basic mechanisms for maintaining health;
- addressing the social aspects linked to healthcare;
- developing a basis for completing the European internal market in health services and for medical devices and pharmaceutical products.

The total budget for the present programme is ECU358 million (approximately US$430 million). Table 3.3 analyses the main areas of research, and shows that ECU43 million (US$52 million) has been budgeted for brain research. This does not include funding for neuroscience research under other headings such as age-related illnesses in the major socioeconomic diseases budget allocation. In addition to the Biomedicine and Health Programme budget, 6 per cent (ECU35 million) of the Biotechnology budget of the 4th Framework Programme is devoted to research into cell communication in neuroscience.

Table 3.3 European Union 4th Framework Programme (biomedical research) research and development expenditure, 1994–98.

Area of research	Budget (ECU million)	% of total
Pharmaceutical research	39.4	11
Biomedical technology and engineering	39.4	11
Brain research	43.0	12
Diseases with major socioeconomic impact (e.g. cancer, AIDS, TB, and age-related illnesses)	150.0	42
Human genome research	43.0	12
Public health research	36.0	10
Biomedical ethics	7.2	2
Total	**358.0**	**100**

Source: European Commission

3 Funding Inputs to Research

The primary objective of the brain research programme is to understand the functions of the brain, and the basic mechanisms underlying mental and neurological diseases. By integrating molecular, cellular and clinical approaches, the programme aims to promote appropriate and effective treatment and prevention. The tasks for the programme cover:

- the pathophysiology and basic mechanisms leading to disease, including the role of molecular signalling systems in disease development;
- nervous system damage and repair, including tissue banks, tissue transplantation and factors affecting cell growth and development;
- the establishment of cell cultures and, where necessary, animal models of the human brain diseases for the development of therapeutic agents;
- the genetic and immunological basis of mental and neurological diseases, including linkage studies;
- clinical research, including clinical trials of rehabilitation therapies, and neurosurgery;
- research on brain imaging;
- mechanisms of pain regulation and relief;
- illicit drugs, including biological effects and the role of genetic and environmental factors on drug use and addiction;
- epidemiological research, including population-based studies and the development of long-term prevention programmes;
- cognitive research, including memory processes, learning mechanisms and emotions.

An article in the *Lancet*[3] describes the disagreements between the 15 EU member states regarding the 1996 mid-programme supplementary budget. A 'top-up' amount of ECU700 million was proposed, but EU research ministers offered only ECU100 million, with ECU35 million intended for BSE-related research. This ECU35 million was allocated as follows:

- ECU7.5 million for biotechnological investigations of the infective agent, its detection, diagnosis and treatment;
- ECU16 million for biomedical and health research, including clinical and epidemiological research into human spongiform encephalopathies, diagnosis and vaccine research;
- ECU11.5 million for veterinary research.

This concentration of money into such a specific area of research reflects the considerable recent interest and controversy surrounding BSE. It is of particular interest to this study of neuroscience because of the proposed link between BSE and human Creutzfeldt–Jakob disease, which causes rapid and fatal neurological degeneration.

A recent article in *Science* (275, 7 March 1997) reports on an independent review of the 4th Framework Programme. This review claims that the programme supports too many projects and therefore lacks focus, but high-quality basic research is being produced. The review recommends that the next Framework Programme should be more concentrated, but remain flexible enough to deal with new scientific needs (such as BSE).

3 *Lancet* 349, 22 March (1997): 861.

3.5 Human Frontier Science Program (HFSP)

This Japanese initiative supports international research on the brain and molecular mechanisms of biological functions. The HFSP was established in 1989 by the Japanese government (who provided 80 per cent of the funding) with backing from six Western nations (USA, Canada, UK, France, Germany and Italy) and is based in Strasbourg. Since that date, the programme has attracted new members such as Switzerland and non-G7 members of the EU. In 1996, the HFSP budget was US$46 million, with Japan contributing US$37 million and the USA increasing its contribution to US$4 million from US$3.5 million in the previous year.

In 1996, a total of 45 research grants were awarded, of which 14 were to brain research projects. The Brain Research Program of the HFSP aims to promote research on the mechanisms of mind and behaviour, brain information processing, and neuronal function research; additional projects relating to neuroscience have also been funded by the Special Coordination Funds for Promoting Science and Technology (SCF).

The HFSP focuses on interdisciplinary research in the fields of molecular biology and the brain and mainly funds young scientists to collaborate with leading researchers based anywhere in the world. A recent article in *Science* (274, 13 December 1996) suggested that the popularity of the HFSP was primarily due to the fact that it has unique funding schemes. The article also highlights items targeted specifically by the HFSP – including postdoctoral salaries and travel expenses for exchange visits between collaborating laboratories or meetings between international research teams. The article reported on concerns raised by the Japanese government on its level of support for the programme. Collectively, the other partners in the programme receive the majority of the awards yet provide only one-fifth of the budget. For example, the USA receives more funds through the programme than any other country, but contributes only 9 per cent of the budget.

3.6 Japanese government research and development expenditure on neuroscience research

Aside from the HFSP, the Japanese government recently announced that, over the next five years, it would double its overall investment on science and technology. (The Japanese government's 1997 research and development budget proposals are presented in Table 3.4.) Neuroscience research gained significantly from this announcement, being allocated US$95 million for 1997 – an increase of 300 per cent on the previous year. As discussed in Box 3.2, this allocation includes funding for a new neuroscience institute at the Institute of Physical and Chemical Research (RIKEN). Other Japanese government ministries that have been intermittently involved with promoting neuroscience-related research and development are the Ministry of Education, the Ministry of Health and Welfare, the Ministry of Posts and Telecommunications, and the Ministry of International Trade and Industry.

Box 3.2 Japan's Brain Science Institute

Japanese government funding for a new neuroscience initiative will total US$125 million in 1997, with the potential to increase by 600 per cent over the next five years. The major new initiative has been the formation of a US$61 million Brain Science Institute that builds on an existing programme of neuroscience research at the Institute of Physical and Chemical Research (RIKEN) outside Tokyo. Officials hope that the institute will help to coordinate country-wide activities and help Japan to become a 'global powerhouse in neuroscience'.

Its head, RIKEN neuroscientist Masao Ito, hopes that the institute will help Japan to lead the world in exploring new research territory – for example theoretical neuroscience – as well as exploring applications in robotics and computer science. However, it is hoped that the allocation of resources will be fairly flexible to allow any areas of breakthrough to be explored. Ito also emphasizes that the new neuroscience effort is designed to complement other university and institute programmes, particularly in the field of clinical research.

Ito and his colleagues believe that the institute's focus on theoretical neuroscience may become its distinguishing characteristic, particularly its studies on the basic principles of information processing and how they apply to both the brain and computers.

The development of the new institute is being hailed by neuroscience leaders worldwide. Steven Hyman, director of the US National Institute of Mental Health said "The [worldwide] community will benefit from the investment", making a major contribution to what many already see as a 'golden age of brain science'.

Source: *Science* 275, 14 March (1997)

3.7 The pharmaceutical industry and commercial drug market

In the search for cures or preventative therapies, the pharmaceutical industry invests billions of dollars every year in research and development (estimated at US$37.3 billion in 1996). A comprehensive analysis of pharmaceutical company spending on neuroscience research and development is difficult – proxy measures such as using *c.* 15 per cent of sales to estimate research and development expenditure, and estimations based on the average cost of launching new products, can be misleading.

In 1994, the USA had 1465 pharmaceutical industry manufacturing establishments, employing around 195 000 people with an annual payroll of approximately US$9 billion. Over one-third of company-financed pharmaceutical research and development in the USA is devoted to the evaluation of promising drug compounds in human clinical trials, and 84 per cent of the US pharmaceutical research and development budget is devoted to finding and developing new products. In 1997, US research-based pharmaceutical companies will invest US$18.9 billion in research and development, and overall pharmaceutical revenues devoted to research and development almost doubled from 11.1 per cent in 1977 to 21.2 per cent in 1997. Table 3.5 shows how such research and development budgets are used, and the

Table 3.4 Japanese government 1997 research and development budget proposal.

Agency/Programme	1997 budget proposal (US$ millions)	% increase on previous year
Ministry of Education and Culture (Monbusho)		
Graduate schools programmes	226	27
Grant-in-aid research grants	1087	12
Postdocs and research assistantships	188	49
University/industry cooperation	962	15
Science and Technology Agency		
Neuroscience	95	300
Global climate change	544	35
New building materials	26	-
Next-generation supersonic aircraft	19	-
Oceanographic science and technology	228	20
Postdocs and STA fellowships	106	40
Regional research activities	135	66
Large research facilities	561	22
Public safety and disaster mitigation	471	24
Ministry of International Trade and Industry		
Research and development for new creative industries	3770	17
Information technologies	105	42

Source: *Science* 273, September (1996)

relative importance given to research into possible treatments for neurological disorders by the US pharmaceutical industry.

The Pharmaproducts database (a database of drugs/compounds in preclinical and clinical research by over 830 companies worldwide) provides an up-to-date analysis of current research and development being carried out by major pharmaceutical companies. Table 3.6 shows the number of compounds in development in the top five therapeutic areas for 1995 and 1996. The data on the percentage increases in Table 3.6 also indicate the increasing importance of the development of neurological drugs to the pharmaceutical industry. Box 3.3 presents an overview of some of the major pharmaceutical companies and their activities in the neurologicals market.

3 Funding Inputs to Research

Table 3.5 Domestic US research and development (US$000s) expenditure by product class.

Pharmaceutical preparations	**1991**	**1992**	**1993**	**1994**
Acting on cardiovascular system	1553	1689	1756	1964
Acting on central nervous system and sense organs	**1403**	**1836**	**2151**	**2097**
Acting on infective and parasitic disorders	1315	1409	1572	1537
Affecting neoplasms/metabolic diseases	1299	1624	1934	2586
Acting on respiratory system	459	526	656	670
Acting on digestive/genito-urinary system	404	377	453	367
Biologicals	301	414	410	436
Acting on skin	127	160	294	217
Diagnostic agents	103	145	154	124
Vitamins and nutrients	7.9	2.4	0.5	17.8
Other human use	721	858	864	842
Veterinary use	230	267	228	243
Total	**7923**	**9307**	**10 473**	**11 101**

Source: American Pharmaceutical Manufacturers Association

Table 3.6 Analysis of drugs in development by therapeutic area (top five categories).

Therapeutic category	**No. of compounds in development at 31/12/95**	**No. of compounds in development at 31/12/96**	**% increase on 1995 figures**
Neurologicals	**1195**	**1265**	**5.9**
Anticancers	1125	1196	6.3
Anti-infectives	1118	1184	5.9
Biotech products	915	954	4.3
Musculoskeletal	754	769	2.0

Source: *Scrip Magazine*, January 1996 and January 1997

Box 3.3 Major pharmaceutical companies and their activities in the neurologicals market

Abbott – has two neuroscience compounds under review for the treatment of epilepsy and schizophrenia, and is conducting early investigations on treatments for Parkinson's disease.

Boehringer Ingelheim – collaborated in 1995 with Cambridge NeuroScience, Inc. (USA) to develop Cerestat* for the treatment of stroke and traumatic brain injury. In 1996, BI also introduced a novel product talipexole onto the NCEs (New Chemical Entities) market for the treatment of Parkinson's disease.

Bristol-Myers Squibb – already markets six drugs for the treatment of various disorders of the central nervous system (CNS).

CoCensys – is developing drugs for the treatment of migraine, epilepsy and the treatment of stroke and head injury. Trials and research are being conducted on novel drugs for the treatment of insomnia, anxiety and neuro-degenerative disorders such as Parkinson's disease.

Glaxo Wellcome – already markets Imigran for the treatment of migraines, Lamictal for the treatment of epilepsy and Ultiva which is the company's new opioid analgesic. In the pipeline for 1997 is a new drug naratriptan for the treatment of migraines.

Lilly – already markets Prozac for the treatment of depression, Permax for Parkinson's disease and Zyprexa for schizophrenia. Investigational compounds are in testing for the treatment of Alzheimer's disease, migraines, sleep disorders, epilepsy and urinary incontinence.

* Drugs beginning with upper case denote the marketed name and lower case the product name.

Pfizer – markets Zoloft for the treatment of depression, obsessive-compulsive disorder and panic disorder, Aricept for the treatment of Alzheimer's disease and other cognitive disorders and Zeldox for the treatment of schizophrenia. Trials are being conducted on a new drug eletriptan for the treatment of migraines and on other compounds for the treatment of anxiety, sleeping and eating disorders.

Pharmacia & Upjohn – produces Xanax for the treatment of clinical anxiety, Halcion for acute insomnia and Sermion for the treatment of cognitive and behavioural disorders related to senile dementia. The company is seeking regulatory approval for Mirapex for the treatment of Parkinson's disease, reboxetine for depression, and Linomide is being tested for the treatment of multiple sclerosis.

Rhone-Poulenc Rorer – Rilutek was launched at the end of 1995 for the treatment of motor neurone disease, and was the first ever drug therapy for the disease.

Roche – of 40 prescription drugs in the company's portfolio, nine are available for the treatment of neurological disorders, including mood disorders, anxiety disorders and Parkinson's disease.

SmithKline Beecham – produces ropinirole for the treatment of Parkinson's disease and is investigating new compounds for the treatment of migraines.

Warner-Lambert – produces Cognex for the treatment of Alzheimer's disease.

Zeneca – markets five principal CNS products, and also produces Zomig, a new drug for the treatment of migraines and is developing Seroquel for the treatment of schizophrenia.

Table 3.7 Medicines for neurological disorders in clinical testing in the USA in 1995.

AIDS-related disorders	2
Alzheimer's disease	21
Amyotrophic lateral sclerosis (motor neurone disease)	6
Brain tumours	11
Cerebral palsy	2
Epilepsy	12
Cranial injuries	10
Migraine/headache	4
Multiple sclerosis	11
Peripheral neuropathies	6
Pain	6
Parkinson's disease	12
Spasticity	2
Spinal cord injuries	3
Stroke	16
Other	4

Of the 1265 neurological compounds in development during 1996, 266 were classed as neuro-protectives (used to treat actual nerve damage), and 220 were memory enhancers. These figures indicate that considerable effort is going into finding therapeutic products for Alzheimer's disease, Parkinson's disease, stroke and the treatment of damage to the peripheral and central nervous system.

Table 3.7 shows the numbers of medicines in clinical testing for a range of neurological disorders in 1995 in the USA. For mental illness, 64 medicines were in clinical testing in 1996, and 74 further medicines were in development (Table 3.8 shows the treatment areas identified as targets for these medicines in development).

The sales of drugs within the pharmaceutical retail sector (excluding drugs dispensed or used by hospitals) used in treating various diseases are monitored on a monthly basis in ten of the major industrialized countries. The countries surveyed are: USA, Japan, Canada, Germany, France, Italy, UK, Spain, Belgium and Holland. The total sales in 16 therapeutic areas between January and December 1996 in these countries are shown in Table 3.9. Over this 12-month period, therefore, approximately US$20 billion was spent on drugs for the treatment of disorders of the central nervous system – 14 per cent of the total retail sales of drugs in these therapeutic areas – and the retail sales figures grew by 14 per cent (US$2 billion).

However, an overview of some of the major developments in the pharmaceutical industry provides another perspective into activity in this area.

Table 3.8 Medicines for mental illness in development in the USA in 1996.

Anxiety disorders	12
Dementias	19
Eating disorders	3
Mood disorders	13
Psychotic disorders	17
Substance abuse/dependence disorders	8
Other disorders	2

Table 3.9 Retail drug sales in ten industrialized countries, January to December 1996.

Therapeutic area	Sales Jan.–Dec.1995 (US$ millions)	Sales Jan.–Dec.1996 (US$ millions)	% growth ('95. – '96) (ex. exchange)
Cardiovascular	25 564	25 527	3
Alimentary/metabolic disorders	23 449	24 594	9
Central nervous system	**18 194**	**20 295**	**14**
Respiratory	14 205	14 561	6
Anti-infectives	14 686	14 534	3
Blood agents	7212	7921	16
Musculoskeletal	7698	7604	4
Genito-urinary	7080	7502	8
Dermatologicals	6289	6260	2
Cytostatics	3613	3931	12
Sensory organs	3323	3378	6
Miscellaneous	3086	2880	(2)
Hormones	2173	2192	6
Diagnostic agents	1686	1768	10
Hospital solutions	644	561	(1)
Parasitology	251	283	15
Total	**$139 453 million**	**$143 791 million**	

Source: IMS International

3.8 Conclusions

Several major initiatives address research needs in the field of neurosciences: the US Decade of the Brain, the EU Decade of the Brain, the Japanese-led Human Frontiers Science Program, and the Japanese government's national research and development focus on neuroscience. In terms of actual expenditure, the US Decade of the Brain is the largest research initiative, while the HFSP plays the most active role in fostering international collaboration. The Japanese government is also set to increase its research expenditure in this field quite dramatically.

Within the UK, the major source of research funding in this area is from central government (via the DoH/NHS and the MRC). The commercial sector currently places great emphasis on its neuroscience research activity – this is reflected in retail sales of drugs for treating diseases of the nervous system and in the number of neurological drugs in development.

4 Opinion Survey

4.1 Introduction

The aim of the opinion survey was to assess the relative strength of UK neuroscience, identify current 'hot topics' in neuroscience research, consider any problems that neuroscience researchers encounter in the UK research environment, and look at areas of neuroscience where researchers feel the most progress is likely to be made over the next five to ten years.

The sample of experts consulted comprised those invited to a meeting at the Wellcome Trust in February 1997. This included all holders of Wellcome Trust and MRC programme grants, a number of industrialists, staff from funding organizations, and some eminent UK neuroscientists currently working abroad. The results presented here are based on 94 respondents to a questionnaire, a response rate of 54 per cent. The questionnaire covered perceptions of neuroscience research in the UK compared to the rest of the world, infrastructure needs and 'hot topics'. A full list of the questions asked, and the responses, is presented in Appendix 2.

4.2 Results

4.2.1 Sample

As shown in Figure 4.1, most of the respondents to the questionnaire were tenured academics (73 per cent) or university contract researchers (15 per cent). Of these, 27 per cent specialized in cellular neuroscience, 21 per cent in molecular neuroscience, 13 per cent in developmental neuroscience and 12 per cent in neurodegenerative disease. Most respondents had a great deal of experience as researchers, nearly three-quarters (73 per cent) had been in research for over 15 years – reflecting the fact that they were all holders of long-term funding or were representatives of funding organizations. (For the rest of this section, tenured academics or university contract researchers are referred to as 'active researchers'.)

The survey showed that 88 per cent of respondents had held Wellcome Trust grants in the last five years and 69 per cent had held MRC

Figure 4.1 Current occupational sector of respondents to neuroscience questionnaire.

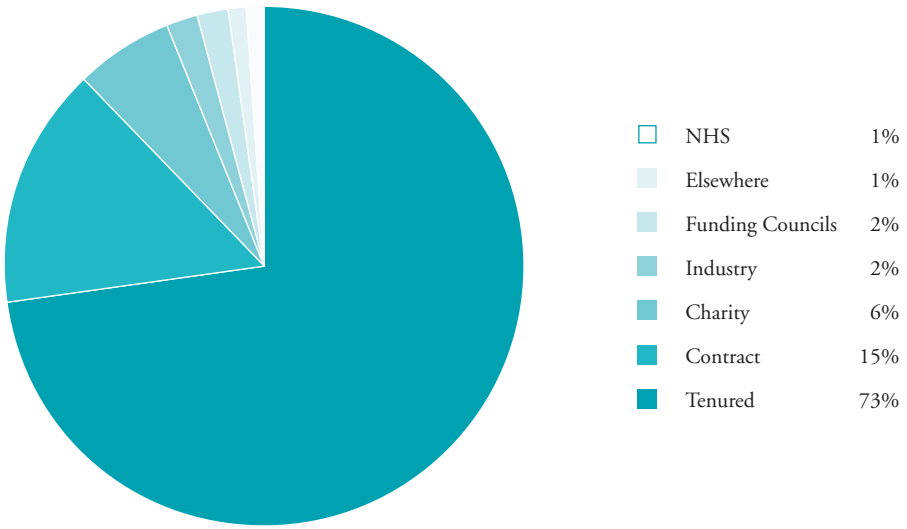
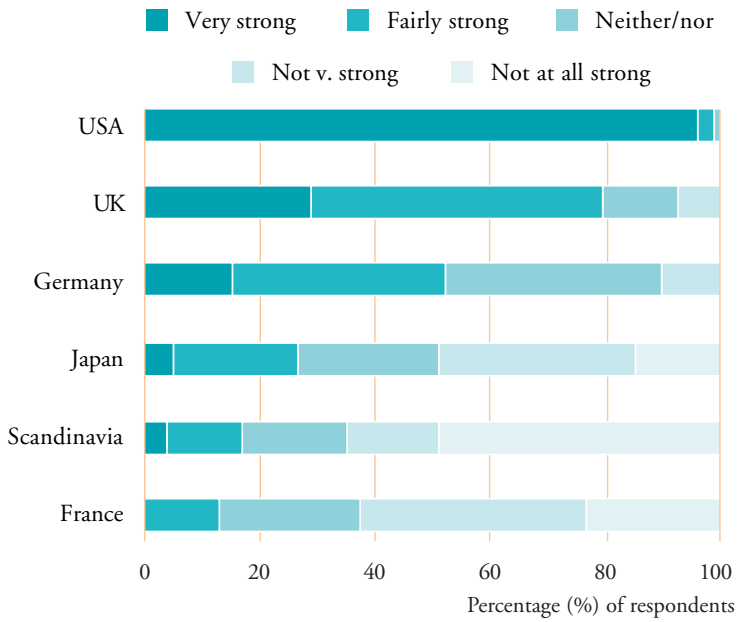


Figure 4.2 Relative strengths of countries in neuroscience.



grants in the same time period. Over half (55 per cent) had received money from other medical charities, 38 per cent from industry and 33 per cent from the EU. When asked where they were encouraged to look for funding by their host organization, 93 per cent identified the MRC, 65 per cent the Wellcome Trust, 60 per cent the EU and 60 per cent industry sources. Other Research Councils were highlighted by 49 per cent of respondents, other charities by 48 per cent, and NHS research and development funds by 41 per cent.

4.2.2 Relative strength of neuroscience research in the UK

Respondents were asked to rate several countries' strength in neuroscience research on a five-point scale, from 'very strong' to 'not at all strong' (Figure 4.2). The USA was rated as 'very strong' by almost everyone – 95 per cent. The UK was perceived as the second strongest of the countries listed, but a long way behind the US: 23 per cent rated it very strong and 64 per cent as fairly strong. Next came Germany, followed by Japan and Scandinavia. Compared to the analysis of publications in the next section, respondents may be underestimating the work of Japan and Sweden in this field. There was no general consensus of opinion on the strength of neuroscience research in France.

Some 84 per cent of respondents agreed with the statement that "The UK is strong in neuroscience research for a country with a relatively small population".

4.2.3 Top areas of UK neuroscience research

Respondents were asked to rank what they believed to be the top five areas of neuroscience research in the UK from one to five (Appendix 2, Q3–5). Of the respondents, 19 per cent said that the UK was good 'across the board', and 14 per cent stated that they did not feel that they knew enough about all the areas to answer the question. The remaining 65 respondents ranked cellular neuroscience as the top area, developmental research as second and neuroimaging as third – based on those respondents who placed each area first in their ranking and taking into account respondents' own speciality. In general, however, opinion was fairly well spread on where the strengths of the UK lie.

4.2.4 Areas where UK neuroscience research is perceived to lag behind

Molecular neuroscience research was rated as one of the five weakest areas by 41 per cent of respondents, computational neurology by 34 per cent, ophthalmology by 20 per cent and systems and neurology by 15 per cent.

4.2.5 Main problems in neuroscience research

Respondents were asked to indicate what they felt were the main problems facing those undertaking neuroscience research today – in the world and in the UK. As shown in Tables 4.1 and 4.2, UK researchers feel that they face similar problems to researchers abroad. The three most serious problems were considered to be a lack of career development for young scientists, lack of funding, and management load. In the UK, a lack of research-trained clinicians and teaching load were also felt to be key issues.

Table 4.1 The main issues that are confronting neuroscience research today worldwide.

Issue	Number	Percentage (%)
Lack of career development for young scientists	57	66.3
Lack of funding	42	48.8
Management load of best researchers	41	47.7
Cost of projects	37	43.0
Lack of research-trained clinicians	37	43.0
Poor interface between basic research and clinical development	34	39.5
Lack of interdisciplinary collaboration	28	32.6
Lack of trained technicians	27	31.4
Teaching load on best researchers	26	30.2
Lack of fellowships at all stages of career	22	25.6
Length of funding time	21	24.4
Lack of communication between industry and academia	17	19.8
Lack of facilities	14	16.3
Lack of diversity in research groups	14	16.3
Small size of research group	14	16.3
Lack of equipment	13	15.1
Quality of PhD training	13	15.1
Research effort spread too thinly	12	14.0
Quality of undergraduate training	11	12.8
Lack of focus	9	10.5
Lack of venture capital	7	8.1
Lack of good science	6	7.0
Total	**502**	

Table 4.2 The main issues that are confronting neuroscience research in the UK.

Issue	Number	Percentage (%)
Lack of career development for young scientists	64	77.1
Lack of funding	48	57.8
Management load of best researchers	45	54.2
Lack of research-trained clinicians	42	50.6
Teaching load on best researchers	42	50.6
Cost of projects	38	45.8
Lack of trained technicians	36	43.4
Poor interface between basic research and clinical development	31	37.3
Lack of facilities	30	36.1
Length of funding time	28	33.7
Lack of interdisciplinary collaboration	27	32.5
Lack of fellowships at all stages of career	26	31.3
Quality of PhD training	22	26.5
Small size of research group	22	26.5
Lack of venture capital	21	25.3
Lack of equipment	21	25.3
Lack of communication between industry and academia	18	21.7
Lack of diversity in research groups	18	21.7
Quality of undergraduate training	15	18.1
Lack of focus	11	13.3
Research effort spread too thinly	11	13.3
Lack of good science	4	4.8
Total	**620**	

Base: Active researchers

4.2.6 Research students

Immediately prior to the workshop meeting in February 1997, considerable publicity was given to the issue of poor-quality training received by undergraduates. The sample was therefore asked to identify the fundamental skills required by anyone intending to undertake research for a PhD. Most (84 per cent) identified scientific knowledge and 69 per cent identified laboratory skills. Over half (55 per cent) felt that research experience at undergraduate level was also important, 54 per cent thought that computing experience was required, and 47 per cent believed that familiarity with statistics was needed.

4.2.7 Staffing

Approximately three-quarters of the respondents agreed that every laboratory needs at least one permanent technician, and six out of ten agreed that it was difficult to recruit appropriately qualified laboratory staff.

4.2.8 Mobility

The questionnaire included a series of statements with which respondents were asked to agree or disagree (Appendix 1, Q23). Of these statements, five related to issues to do with either occupational or geographical mobility. Highlighting the importance of interdisciplinary teams, nine out of ten respondents agreed that "it is important to have people with training in different disciplines to each other" in research teams. Eight out of ten respondents perceived that there is value in young researchers being able to move between laboratories, but nearly three-quarters (73 per cent) believed that giving young researchers tenured positions will prevent that. Indeed, seven out of ten respondents agreed that "research staff should not have tenure in the first few years after completing their PhD". Two-thirds agreed that "postdocs should be encouraged to work abroad for at least a few years", and half agreed that "it is good to have foreign staff in a research group".

4.2.9 Finance

Respondents were asked if they felt there should be more money for neuroscience research and 86 per cent said yes. As this response was anticipated, respondents were asked whether they thought that there should be more money for neuroscience research even if it is taken from other areas of biomedical research; 44 per cent of the 86 per cent agreed with this question. Respondents were then asked how they would spend more money or re-allocate existing budgets; 81 per cent thought that more money should be spent on developing researchers' career structure, and 57 per cent indicated that there should be more money for fellowships.

Over half (54 per cent) of the respondents believed interdisciplinary collaboration should be supported, and 54 per cent thought that there should be special support for postdocs returning to the UK after a period abroad.

Perhaps the most surprising result of the survey is that nearly four out of ten respondents (39 per cent) did not say that funders should "just fund the best science as identified by peer review".

Table 4.3 Areas of neuroscience research that researchers perceive to be areas where significant advancement is likely in the next five to ten years.

Disease	**Total** (%)
Depression and anxiety	59
Neurodegenerative	56
Infections	51
Major psychoses, e.g. schizophrenia	43
Oncology	41
Eating disorders	37
Stroke	37
Inherited disorders	35
Rehabilitation following trauma	31
Child and adolescent psychopathology	15
Cognitive neurology	11
Substance abuse	11
Blinding disease	9

Base: 84 valid cases, ten missing cases

4.2.10 Promising areas of research

Respondents were asked to identify the subfields of neuroscience research most likely to lead to health treatments or therapies in the next five to ten years. Seventy-four per cent highlighted the advances being made in the study of neurodegenerative diseases, 66 per cent acknowledged the importance of molecular research, and 63 per cent identified neuropharmacological research. Other areas thought likely to be important were cellular and biological psychology and psychophysics.

4.2.11 Progression in treatment

Respondents were asked to identify the disease areas where they felt progress was likely to be made in the next five to ten years (Table 4.3). The main areas identified were neurodegenerative diseases, depression, infections, major psychoses and oncology. Although the number of administrators who returned questionnaires was small, it is interesting to note that they seemed more optimistic about the future of treatments than those currently active in research.

Six out of ten of all respondents said that they thought depression and anxiety would have improved treatments in the next five to ten years. Over half also thought that neurodegenerative diseases (56 per cent) and infections (51 per cent) would be treatable. Respondents were more despondent about major psychoses, oncology and strokes and least hopeful about child and adolescent psychopathology and cognitive neurology. Other diseases or illnesses that respondents felt to be treatable, not listed on the questionnaire, included Parkinson's disease, pain, chronic pain and spinal cord injury, sensorineural hearing loss, immune-mediated conditions, severe epilepsy and seizure disorders.

4.2.12 Future of UK neuroscience

Researchers were optimistic about the future of neuroscience research in the UK – eight out of ten saying that they thought it was very good or fairly good.

4.3 Conclusions

The opinion survey asked the UK neuroscience community to identify the main infrastructural barriers to maintaining and strengthening UK neuroscience research. It also gathered the perceptions of UK neuroscientists of the scientific strengths of UK research in this area.

Respondents felt that neuroscience research in the UK is fairly strong and they were optimistic for the future. Specific problems in day-to-day research work were identified, but these were all endemic to working within the UK university research system at the time of the survey. None appeared to be a specific problem of undertaking neuroscience research.

A major point to emerge is the need to promote mobility within a career structure and to stimulate and nurture researchers. An improved career structure is needed to ensure that researchers are not lost to other careers because of the uncertainty of contract research.

Depression, anxiety and neurodegenerative diseases were thought likely to see improved treatments or therapies in the next five to ten years, and the importance of molecular and neuropharmacological research was highlighted.

5 Academic Response to Research Need – A Bibliometric Analysis

5.1 Introduction

One method of assessing research activity in a field is the use of bibliometric analyses. Bibliometrics is the application of mathematical and statistical methods to scientific literature, patents and other forms of scientific communication in order to examine the state of research activity in a in a particular field. It provides information both on levels of research output and on research quality.

In this study, the publication output[4] of eight subfields of neuroscience was examined by bibliometric analysis: molecular neuroscience, cellular neuroscience, molecular and cellular neuroscience combined; developmental neuroscience, systems neuroscience, cognitive neurology, cognitive behavioural psychiatry and drug-related behavioural psychiatry. The first six of these subfields are collectively referred to as 'basic', while the latter two are referred to as 'clinical'. The field size and growth rates of each subfield in the UK was examined. The analysis then highlights a number of the general trends for the outputs in each of the eight subfields for the 12 countries studied.

A full description of the methodology used to undertake this analysis is presented in Appendix 3.

5.2 UK neuroscience research output

Approximately 227 000 scientific papers in biomedicine are published each year worldwide, of which approximately 16 per cent are neuroscience research. As shown in Table 5.1, the six basic subfields of neuroscience research considered in this analysis account for 41 per cent of all published papers in neuroscience, while the two clinical research subfields account for 10 per cent of all published papers in psychiatry/psychology (which account for about 5 per cent of the total output for biomedicine).

The UK produces 10.5 per cent of all biomedical papers and 9 per cent of all neuroscience papers. Among the six *basic* subfields, the UK share of world publications is higher in cellular and molecular neurosciences, molecular and cellular neurosciences combined, and cognitive neurology. Although the UK presence is not as strong in developmental neurobiology, there is a higher level of international cooperation (as measured by the index of multinational authorship; Table 5.1). In systems neuroscience, the UK presence is weaker still, and the level of international

4 'Outputs' are articles, notes and reviews (original scientific publications) in peer-reviewed serial publications from the Science Citation Index, Social Science Citation Index and the Neuroscience Citation Index.

Table 5.1 World and UK outputs of papers.*

Subfield	No. papers per year (World)†	Growth rate (%) 94/91‡	No.UK papers pa§	UK/world (%)	Index of multinational authorship
Cellular	659	10	64	9.7	8.4
Developmental	995	8	87	8.8	11.0
Molecular	865	12	84	9.7	10.2
Molecular and cellular	2244	13	212	9.4	10.1
Systems	8024	14	669	8.3	6.8
Cognitive neurology	1920	12	214	11.2	8.6
Neuroscience	**35 570**	**4**	**3186**	**9.0**	**9.0**
Cognitive behavioural psychiatry	513	8	74	14.5	4.9
Drug-related behavioural psychiatry	725	~4	55	7.6	5.4
Psychiatry/Psychology	**12 462**	**2**	**1350**	**10.8**	**6.4**
Biomedicine	**227 423**	**3.7**	**23 842**	**10.5**	**9.3**

* Comparisons of field size and growth rate are based on annual values for 1991–94 because for two of the subfields the data do not extend back before 1991.

† 1991–94 annual averages retrieved.

‡ Growth rate is defined as the annual average percentage growth between 1991 and 1994. For drug-related behavioural psychiatry the number of papers fluctuated between 1991 and 1994 and it is not possible to give a growth rate for this period, although it was +4 per cent per year between 1989 and 1995.

§ 1991–94 annual averages retrieved.

cooperation is the lowest of all the subfields. However, despite starting from the smallest base, the output of UK systems neuroscience research has the fastest rate of growth. In general, all of the basic neuroscience subfields are growing rapidly. In the clinical fields of psychiatry/psychology, the UK produces 10.8 per cent of all papers, and 14.5 per cent of all papers in the subfield of cognitive behavioural psychiatry, but only 7.6 per cent in drug-related behavioural psychiatry. The rate of growth in both these subfields is above average and the UK's strength in cognitive behavioural psychiatry is increasing four times faster than average. In both these subfields and in the field of psychiatry/psychology the level of international cooperation is relatively low.

Although Table 5.1 appears to show the psychiatry subfields as being treated separately from the rest of the neuroscience total, this is merely because the citation indexes used in the bibliometric analysis were different for the six basic subfields and the two psychiatry subfields (see Appendix 3).

5 Academic Response to Research Need – A Bibliometric Analysis

Table 5.2 Distribution of UK papers between journals of different levels of influence.

Subfield	Distribution of UK papers between journals				Mean level of influence of world papers
	Low-influence journals		High-influence jounals		
	1	2	3	4	
	%	%	%	%	
Cellular	25	29	40	5	2.16
Developmental	26	28	37	8.6	2.12
Molecular	30	30	43	5.7	2.15
Molecular and cellular	34	23	37	6.5	2.11
Systems	36	26	25	13	2.45
Cognitive neurology	18	37	18	11	2.34
Cognitive behavioural psychiatry	22	58	18	1.6	2.06
Drug-related behavioural psychiatry	19	33	43	4.4	2.33

Table 5.3 Comparison of the influence of UK publications with those of rest of the world.

Subfield	Ratio of UK papers to world papers				Mean level of influence of UK papers
	Low-influence journals		High-influence jounals		
	1	2	3	4	
Cellular	0.86	0.93	1.23	0.78	2.25
Developmental	0.87	0.83	1.26	1.32	2.28
Molecular	0.91	1.09	1.16	0.57	2.15
Molecular and cellular	0.90	1.00	1.21	0.73	2.16
Systems	0.89	0.99	1.17	1.09	2.58
Cognitive neurology	0.79	1.01	1.13	0.71	2.44
Cognitive behavioural psychiatry	0.92	1.18	0.79	0.45	1.99
Drug-related behavioural psychiatry	1.00	0.88	1.27	0.48	2.33

Table 5.4 Comparison of mean journal impact weighting and research levels.

Subfield	No. papers	No. journals	RL_{mean}	W_{mean} USA	W_{mean} UK	W_{mean} World	W_{mean} World (excl.– UK, USA)
Molecular	2379	421	3.80	2.46	2.15	2.16	1.84
Cellular	2038	318	3.83	2.54	2.25	2.16	1.79
Molecular and cellular	6213	688	3.79	2.33	2.16	2.11	1.85
Developmental	3589	589	3.75	2.31	2.28	2.12	1.84
Systems	10018	1828	2.87	2.68	2.58	2.45	2.24
Cognitive neurology	2181	1240	3.12	2.57	2.44	2.34	2.10
Cognitive behavioural psychiatry	1393	262	1.31	2.24	1.99	2.06	1.77
Drug-related behavioural psychiatry	2180	260	1.89	2.55	2.33	2.33	1.93

5.3 Weighting and influence of UK papers

Tables 5.2 and 5.3 show the distribution of UK papers between journals according to the level of influence or impact of the journal.[5] In molecular neuroscience, molecular and cellular neuroscience combined, and drug-related behavioural psychiatry, the influence of the journals in which UK papers are published is similar to that of the world. It is superior in cellular neuroscience, developmental neurobiology and systems neuroscience, but is slightly inferior in cognitive behavioural psychiatry. These results indicate the high standing of UK developmental neurobiology, and the standing being higher in cellular neuroscience than in molecular neuroscience.

Table 5.4 shows the mean journal impact weighting and research level[6] scores for world publications, UK publications, US publications, and the world when the USA and UK publications are removed from the profile. In every subfield, US publications tend to be found in the journals with higher impact factors. For three of the eight subfields, UK publications are on a par with the world publications. When the analysis is conducted with the US publications removed from the world profile, the position of the UK publications improves considerably compared with publications from the rest of the world.

5 A weighting of 4 is given to the top 10 per cent of journals, 3 to the next 20 per cent, 2 to the next 30 per cent and 1 to the bottom 40 per cent, in terms of citation impact.

6 Research level is used to describe the type of research being conducted (1=clinical research, 4=basic research) and can also indicate the relative levels of research with different subfields of research.

5 Academic Response to Research Need – A Bibliometric Analysis

5.4 General trends in outputs of papers

In order to compare the relative strength of each neuroscience subfield in the UK, the output from 12 OECD countries was analysed (see Appendix 3). For each of the eight subfields, both the percentage share of world output and productivity – measured as papers per year per million of population – were examined. It should be noted that the US output in all the 'per cent shares of world output' graphs is divided by five for scaling purposes. (Appendix 4 presents graphical analyses of two sample subfields comparing the UK against the world distribution of papers according to research level – on a scale of 1–4, where 1 indicates clinical research and 4 indicates basic research – and journal weighting.)

5.4.1 Developmental neurobiology

As shown in Figure 5.1, the USA dominates this subfield, with over 50 per cent of the output. Japanese output is now the second highest and is increasing at the fastest rate in the period studied. The UK, Germany, Canada and Sweden show growth in their share of output over the period, while French and Dutch shares have declined. Per head of population, Switzerland and Sweden appear to be producing the greatest number of papers per year. All countries show increasing productivity in the period studied, except for Australia.

Figure 5.1 Developmental neurobiology outputs.
Scientific papers from 1988 – June 1996 (articles, notes and reviews in the Science Citation Index)

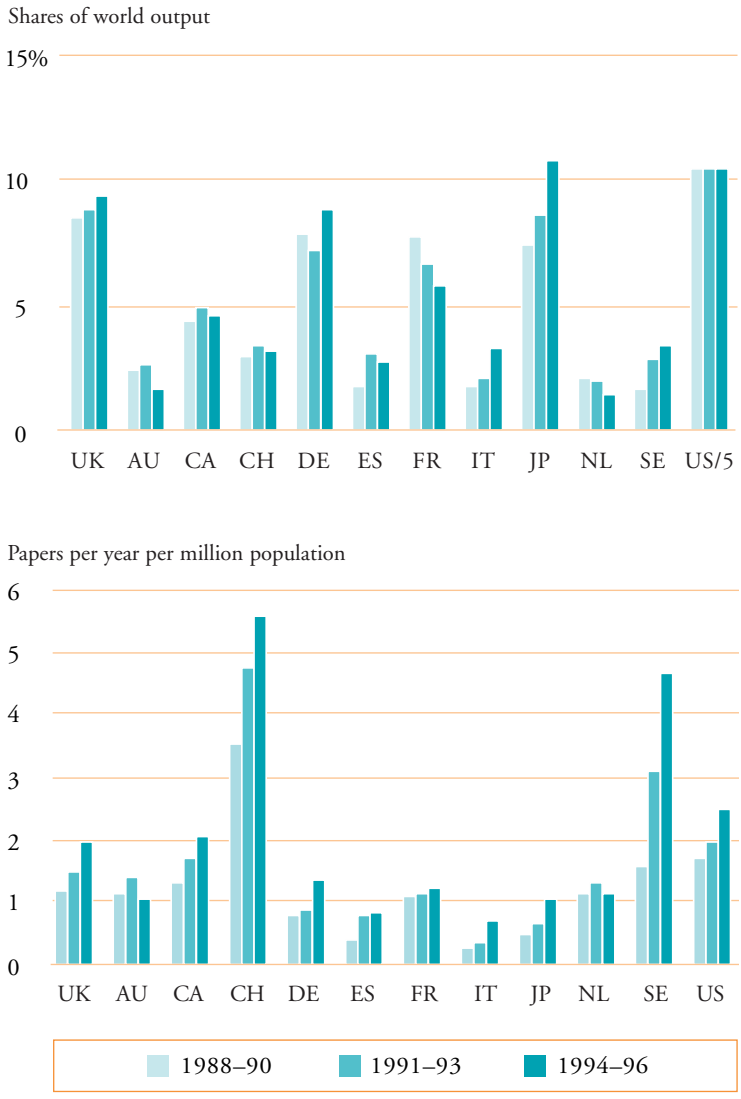


Figure 5.2 Molecular neuroscience outputs.
Scientific papers from 1991 – October 1996 (articles, notes and reviews in the Neurosciences Citations Index)

UK – United Kingdom
AU – Australia
CA – Canada
CH – Switzerland
DE – Germany
ES – Spain
FR – France
IT – Italy
JP – Japan
NL – The Netherlands
SE – Sweden
US/5 – USA (÷5)

5.4.2 Molecular neuroscience

The USA is dominant in terms of output in this subfield (Figure 5.2). Japan and UK are in joint second place, although the UK's share has risen substantially while Japan's share has declined. Other major players include Germany, France and Canada; of these, only France has shown a decline in its share of output. Switzerland and Sweden are the most productive per head of population. The UK, USA and Canada were similar in their productivity of papers (about half the level of Switzerland and Sweden).

5.4.3 Cellular neuroscience

Although the USA is dominant in terms of output in this subfield, its share appears to be declining (Figure 5.3). Japan and the UK are in joint second position; as in molecular neurosciences, the UK's share has risen while Japan's share has declined. Germany, Canada and France are other major contributors to this field. Switzerland, the UK and Canada appear to be most productive per head of population. The USA, Australia and Sweden were less productive, but ahead of Japan, The Netherlands, France and Germany.

Figure 5.3 Cellular neuroscience outputs.
Scientific papers from 1991 – October 1996 (articles, notes and reviews in the Science Citation Index)

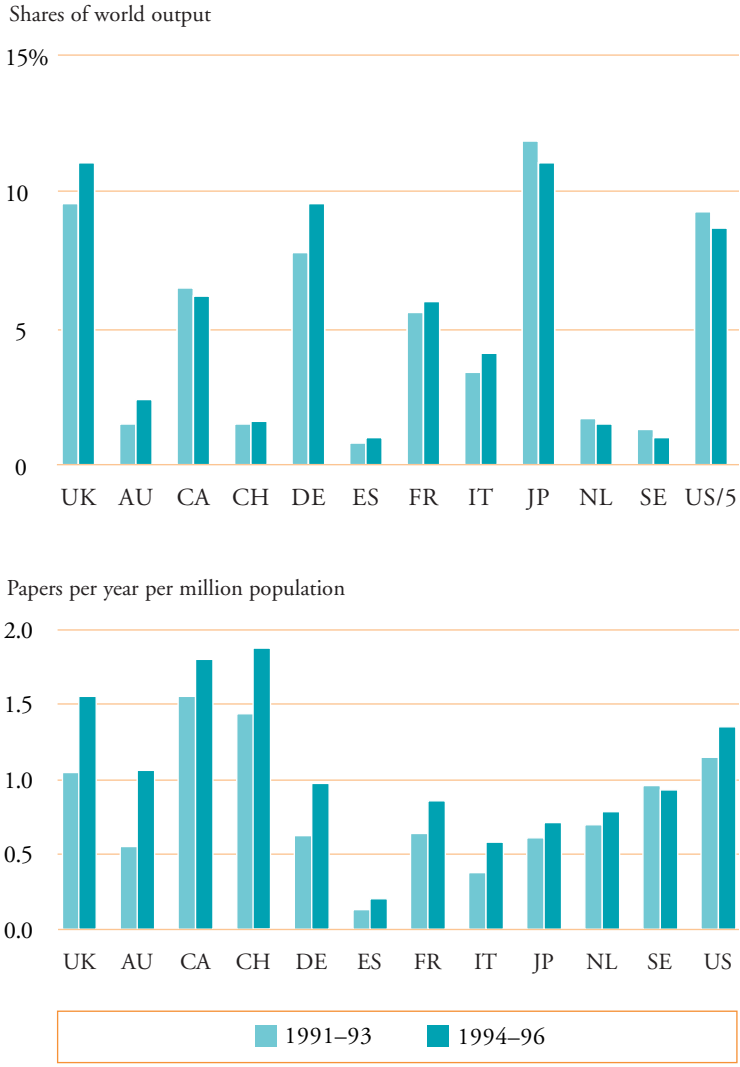


Figure 5.4 Molecular and cellular neuroscience outputs.
Scientific papers from 1991 – October 1996 (articles, notes and reviews in the Science Citation Index)

5.4.4 Molecular and cellular neuroscience combined

The USA is dominant in terms of output in this subfield, although its share is declining (Figure 5.4). Japan and the UK are again in joint second position although the UK's share has risen faster over the same time period than has Japan's share. Germany, France and Canada are other major contributors to this field, while Italy's contribution also appears to be quite strong. Switzerland is the most productive per head of population, with a rapidly increasing trend. Sweden, the USA, Canada and the UK were less productive, but ahead of Australia, France, The Netherlands and Germany.

5.4.5 Systems neuroscience

The USA is dominant in terms of output in this subfield, although its share is declining (Figure 5.5). Japan and the UK are again in joint second position; Japan's share has risen faster over the same time period than the UK's share. Germany, Canada, France and Italy are other major contributors to this field. In this subfield, Sweden is the most productive, closely followed by Switzerland and Canada. The Netherlands is also strong, followed by the UK and USA. All the countries studied have a rapidly increasing trend in this subfield.

Figure 5.5 Systems neuroscience outputs.
Scientific papers from 1991 – October 1996 (articles, notes and reviews in the Science Citation Index)

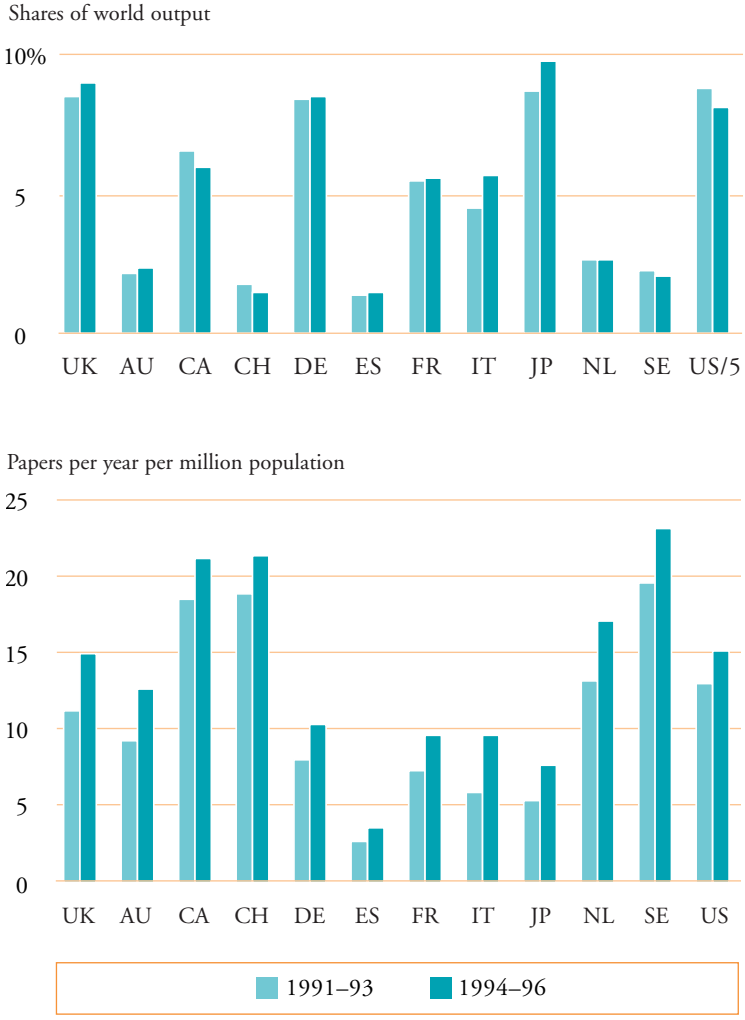
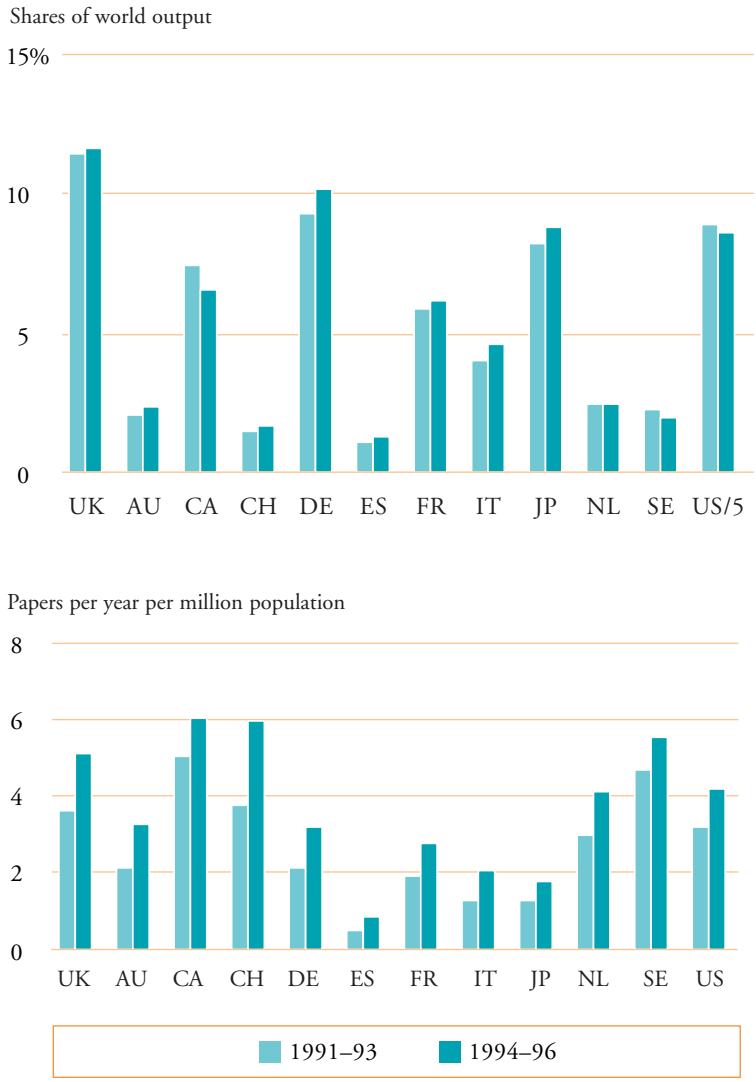


Figure 5.6 Cognitive neurology outputs.
Scientific papers from 1991 – October 1996 (articles, notes and reviews in the Science Citation Index)



5.4.6 Cognitive neurology

The USA is dominant in terms of output in this subfield, although its share is declining (Figure 5.6). The UK is in second position, with Germany third, although Germany's share has risen faster over the same time period than has the UK's share. Japan, Canada, and France are other major contributors to this field. Canada is the most productive, closely followed by Switzerland and Sweden. The UK is very strong, and its productivity is increasing rapidly. The USA and The Netherlands are the next most productive, although all the countries studied have a rapidly increasing trend in this subfield.

5.4.7 Drug-related behavioural psychiatry

The USA is especially dominant in terms of output in this subfield, with almost 60 per cent of the world total (Figure 5.7). The only other countries producing significant shares of output were the UK, Canada and Germany. Japan was particularly weak in terms of its share of output. The USA was the most productive country, followed by Canada; the UK and Switzerland are less productive. Japan and France produce very few papers per head of population in this subfield.

Figure 5.7 Drug-related behavioural psychiatry outputs.
Scientific papers from 1988 – June 1996 (articles, notes and reviews in the Social Science Citation Index)

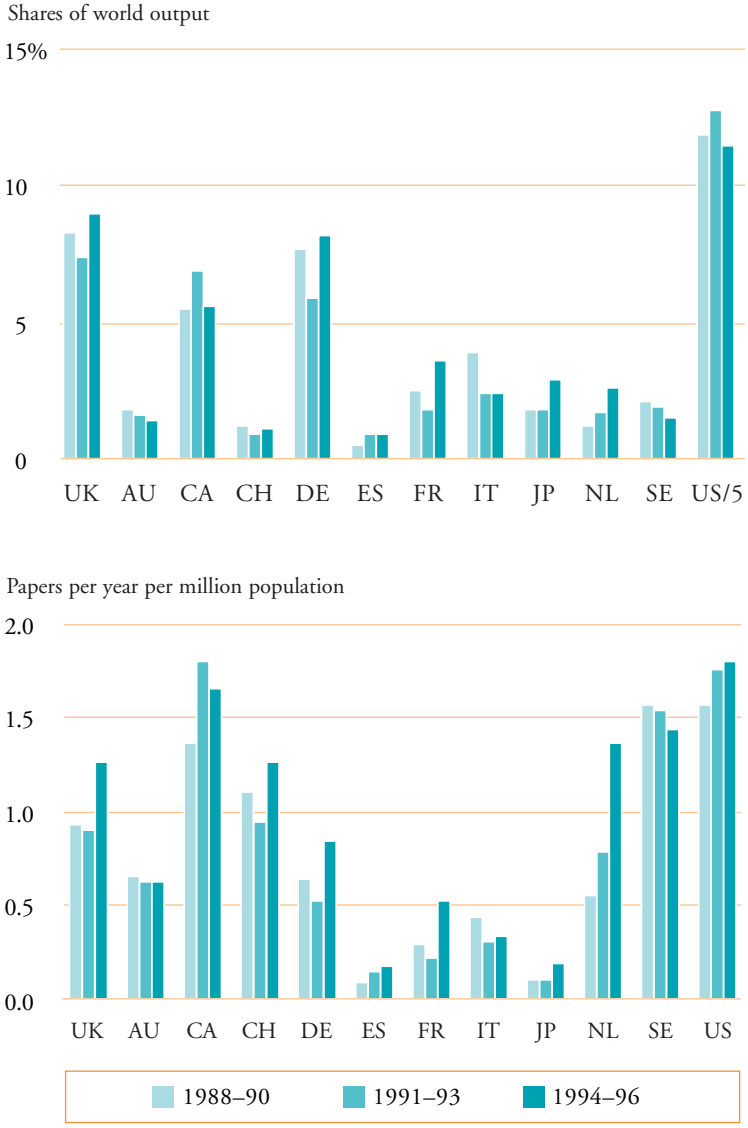
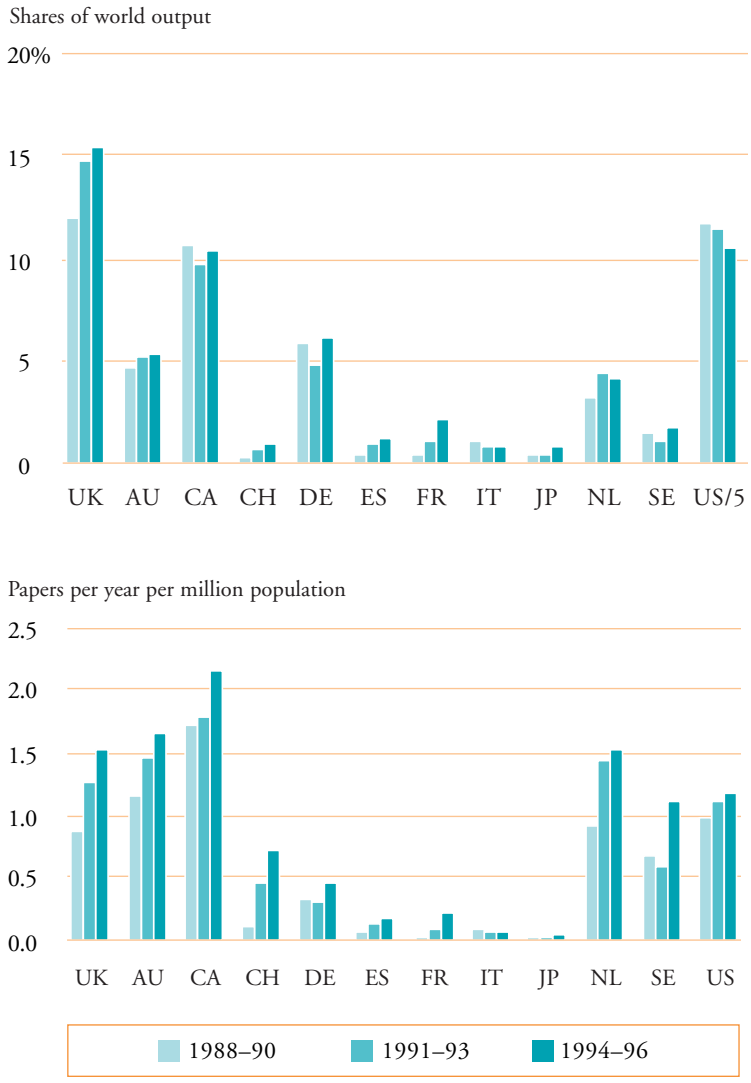


Figure 5.8 Cognitive behavioural psychiatry ouputs.
Scientific papers from 1988 – October 1996 (articles, notes and reviews in the Social Science Citation Index)



5.4.8 Cognitive behavioural psychiatry

The USA is dominant in terms of output in this subfield, although its share is declining (Figure 5.8). This appears to be a strong area for the UK, which is second in terms of share of papers and well ahead of the third-placed country, Canada. Germany and The Netherlands have about half of Canada's share with very little identified for the other countries. Canada, Australia, the UK and the Netherlands appear to be quite productive in this field. USA and Sweden are less so and there is very little output per head of population for Spain, Italy, France and Japan.

5 Academic Response to Research Need – A Bibliometric Analysis

5.5 Conclusions

The tables of outputs and the sample charts in Appendix 4 show that the eight subfields of neurosciences reviewed here are all growing quite rapidly. There are some significant differences between the basic and clinical subfields examined.

Basic research

The UK presence in the six basic research subfields does not differ greatly from the average for neurosciences as a whole (9 per cent). While the UK presence in developmental neurobiology appears to be low, in terms of numbers of papers, this is counteracted by the greater influence of the journals in which the articles appear. In all five subfields, the UK share of world papers is increasing steadily: none of the other 11 OECD countries can claim this. Japan's output is growing in developmental neurobiology and systems neuroscience, but declining in cellular and molecular neurosciences.

In terms of papers per million of population, the UK is typically in third or fourth place behind Switzerland, Sweden (but not in cellular neuroscience or systems neuroscience) and Canada. This mirrors the situation in most other subfields of biomedicine.

Clinical research

The UK appears to have a strong presence in the two behavioural psychiatry subfields – cognitive behavioural psychiatry and in drug-related behavioural psychiatry. However, the US has an unusually dominant position, with almost 60 per cent of world output (it should be noted that there may some bias in the SSCI because of the selection of journals). In terms of publications per unit population, the UK ranks fourth for cognitive behavioural psychiatry and sixth for drug-related behavioural psychiatry. Germany is also strong in both subfields, and the Canadian and Australian presence in cognitive behavioural psychiatry is striking, although papers in this subfield may be more subject to language biases in the SSCI than in many others.

In these two clinical subfields, UK papers tend not to be published in the most influential journals – there are fewer than half as many UK papers in the top-rated journals as one would expect on the basis of the world distribution.

6 How Research is Developed – A Patents Analysis

6.1 Introduction

This section contains the results of a study of the impact of neuroscience research on the innovation process – as measured by research publications cited on patents. The methodology used is that described in detail in an earlier study carried out by PRISM,[7] and the results relate to the publications cited (or 'prior art') on US patents. This analysis focuses on the following areas:

- the number and nature of neuroscience papers cited on the US patents;
- analysis of the citing US patents by frequency (including the top-citing patents);
- analysis of the country of origin of the inventors named on the citing patents;
- analysis of the assignees (or owners) named on the citing patent.

6.2 Neuroscience papers cited on US patents

A total of 21 590 papers were extracted from the Research Outputs Database (ROD) using an electronic keyword filter for neuroscience research. These papers were analysed using TechTrac[8] to determine those being cited on US patents as prior art. The 'hit rate' was 322 papers cited on 371 US patents (although it must be noted that a number of papers are cited on different patents and vice versa).

The percentage of UK neuroscience papers cited on US patents is 1.5 per cent – this is significantly lower than the 2.3 per cent of all biomedical papers (funded by either the Wellcome Trust, MRC or the CRC) cited on US patents (a previous PRISM study). Recent work has suggested that papers cited on patents tend to be highly cited in the biomedical literature themselves. The body of neuroscience papers contain a significant number of papers which have no funding acknowledgements. Such papers tend to have lower citation levels, which could explain the difference between the hit rate recorded for the three funding bodies compared to the neuroscience papers extracted.

There is also some variation between different biomedical subfields with respect to the percentage of UK papers in a particular subfield cited on US patents: the citation rate for neuroscience is 1.5 per cent; genetics 3.3 per cent; gastroenterology 1.4 per cent; oncology 1.7 per cent; gerontology 1.1 per cent; cardiology 1.6 per cent; and nursing research 0.05 per cent. PRISM is currently conducting a study to investigate the reasons for this variation.

7 Anderson J, Williams N, Seemungal D, Narin F, Olivastro D (1996), Human genetic technology: Exploring the links between science and innovation. *Technology Analysis and Strategic Management* 8(2).

8 TechTrac is a database developed by PRISM to track those biomedical papers contained in the Research Outputs Database that are cited as prior art on patents from both the US and European patent systems.

6.3 Analysis of cited neuroscience papers

The 322 papers cited on US patents were analysed to identify whether they were clinical or basic research. Each paper was assigned a 'research level' between 1 and 4, where 1 indicated purely clinical research and 4 indicated purely basic research. As shown in Table 6.1, more than 75 per cent of the neuroscience papers were at a research level of 3 or 4.

An analysis of the date at which the neuroscience papers were published mirrored the findings of previous PRISM studies showing that it takes, on average, four to five years for biomedical papers to be cited on a patent (Table 6.2).

It is interesting to note the variation in the number of papers cited as prior art on patents. As shown in Table 6.2, most patents cite one paper only. Four papers were cited on nine or more patents (Box 6.1).

Table 6.1 Cited neuroscience papers by research level.

Research level	No. of papers	Percentage (%)
None	6	1.9
1	17	5.3
2	39	12.1
3	110	34.2
4	150	46.6
TOTAL	**322**	**100.0**

Table 6.2 Year of publication of cited papers (*n*=322).

Year	No. of papers	Frequency (%)
1988	71	22.0
1989	61	18.9
1990	66	20.5
1991	51	15.8
1992	36	11.2
1993	29	9.0
1994	8	2.5

Box 6.1 Very highly cited neuroscience papers

1. Benwell M *et al.* (1988) Evidence that tobacco smoking increases the density of (-)-[^{3}H] nicotine binding sites in human brain. *Journal of Neurochemistry* 50: 1243–1247.
   Cited on 13 patents.

2. Nordberg A *et al.* (1989) The role of nicotine receptors in the pathophysiology of Alzheimer's disease. *Progress in Brain Research* 79: 353–362.
   Cited on 12 patents.

3. Costall B *et al.* (1989) The effects of ACE inhibitors captopril and SQ29,852 in rodent tests of cognition. *Pharmacological and Biochemical Behaviour* 33: 573–579.
   Cited on 11 patents.

4. O'Neill M F *et al.* (1989) Morphine induced analgesia in the rat paw pressure test is blocked by CCK and enhanced by the CCK antagonist MK-329. *Neuropharmacology* 28(3): 243–247.
   Cited on nine patents.

Box 6.2 Patents citing more than five UK neuroscience papers

Patent number: 05514680
Number of ROD neuroscience papers cited: 12
Total number of papers cited on patent: 63
Issue date: 7 May 1996
Title: Glycine receptor antagonists and the use thereof
Assignee: University of California, Regents

Patent number: 05506257
Number of ROD neuroscience papers cited: 7
Total number of papers cited on patent: 23
Issue date: 9 April 1996
Title: Aminocyclohexylamides for antiarrhythmic and anaesthetic uses
Assignee: University of British Columbia, Canada

Patent number: 05538844
Number of ROD neuroscience papers cited: 7
Total number of papers cited on patent: 26
Issue date: 23 July 1996
Title: Transport protein gene from the Huntington+3 s disease region
Assignee: None identified

Patent number: 05556969
Number of ROD neuroscience papers cited: 7
Total number of papers cited on patent: 44
Issue date: 17 September 1996
Title: Benzodiazepine derivatives
Assignee: none identified

Patent number: 05436272
Number of ROD neuroscience papers cited: 6
Total number of papers cited on patent: 65
Issue date: 25 July 1996
Title: Treatment of obesity
Assignee: Boots Co.

Patent number: 05565186
Number of ROD neuroscience papers cited: 6
Total number of papers cited on patent: 52
Issue date: 15 October 1996
Title: Method of detecting prions in a sample and transgenic animal used for same
Assignee: None identified

6.4 Analysis of US patents citing neuroscience papers

A total of 371 patents cited one or more of the neuroscience papers, and six patents cited more than five neuroscience papers (Box 6.2). These six patents were heavily reliant not only on neuroscience research, but also on research in other areas – as illustrated by the large number of papers cited (the average number of papers cited on biomedical patents is typically in the range of 5–10; data from TechTrac and CHI Inc.).

An analysis of the date on which the patents citing these neuroscience papers were filed shows that the neuroscience papers tend to appear on the more recent patents (Table 6.4). This is likely to be due not only to the lag time between publication and patent filing dates, but also to the increasing level of reliance on science references in US patents (CHI Inc., personal communication).

6.5 Inventors and assignees named on citing patents

The patents citing neuroscience papers were analysed to determine the relationship between the named assignees and inventors. As shown in Table 6.5, the UK formed the second largest group – after the USA – of named inventors listed on the set of neuroscience papers. Yet an analysis of the 132 different assignees cited on 321 of the patents (in some patents it is difficult to determine the assignee's name) shows that UK assignees owned only 11 of these 321 patents (or 3.4 per cent). The list of assignees named on five or more patents (Table 6.6) is dominated by US industrial corporations.

Table 6.4 Citing patents – filing year.

Year filed	Frequency	Percentage (%)
1989	1	0.3
1990	3	0.8
1991	11	3.0
1992	26	7.0
1993	68	18.3
1994	69	18.6
1995	83	22.4
1996	110	29.6
TOTAL	**371**	**100.0**

Table 6.5 Citing patents – inventors' country of origin.

Country	No. of inventors	% of total (*n*=840)
USA	561	66.8
UK*	110	13.1
France	50	6.0
Japan	29	3.5
Italy	20	2.4
No country	17	2.0
Canada	10	1.2
Denmark	9	1.1
Hungary	9	1.1
Switzerland	9	1.1
Sweden	6	0.7
Belgium	3	0.4
Spain	3	0.4
Germany	2	0.2
Republic of Ireland	1	0.1
Netherlands	1	0.1

* Due to difficulties in ensuring that subsidiaries and their companies were correctly linked, patents were assigned to the home country of parent companies. For example, patents owned by Glaxo Wellcome and its subsidiaries are labelled as UK.

Table 6.6 Citing patents – assignees.

Assignee name	No. of assignees named (*n*=321)
Warner Lambert Co.	19
Merck Sharp & Dohme Ltd	17
Merck & Co., Inc.	14
Lilly (Eli) & Co.	13
Reynolds (R J) Tobacco Co.	11
University of California, Regents	7
Pfizer Inc.	6
Squibb (E R) & Sons Inc.	6
University Pennsylvania, Trustees of	6
Adir Et Cie	5
Children's Med. Ctr. Corp., The	5
Du Pont (E I) De Nenours & Co.	5
Genentech, Inc.	5
Johns Hopkins University	5
Merrell Dow Pharmaceuticals Inc.	5
Rochester Medical Corp.	5

6.6 Conclusions

One of the routes via which basic research feeds into the innovation system is as underpinning science for filed patents. This section has measured the impact of UK neuroscience research papers on the US innovation system as measured by their citation on US patents. The cited research is heavily biased towards basic research papers rather than clinical investigation papers.

The citation rate on US patents for neuroscience papers (1.5 per cent) is significantly lower than for UK genetics papers (3.3 per cent) but on a par with papers from other biomedical fields – for example cardiology or oncology.

The impact of UK inventors (13 per cent of the inventors named on patents) is not reflected by the number of UK-based companies who own the citing patents (3.4 per cent of the assignees named) – there appears to be an exploitation gap in this field, a generic problem of UK academic research. The recent announcement by the UK government, the Wellcome Trust and the Gatsby Charitable Foundation of a £60 million University Challenge Fund to address this specific issue may well have a large impact in the longer term.

7 The Millennium Workshop Meeting – Strategies for Action

7.1 Introduction

The February 1997 'Millennium Workshop' meeting brought together more than 150 UK neuroscientists. In the four discussion sessions – covering developmental neurobiology, molecular neuroscience, cellular neuroscience and therapeutic strategies in psychiatric disorders – delegates were asked to focus on what the future might hold for neuroscience in the UK context, and what strategies for action would be required to increase the UK's presence in the field.

There was a common thread weaving together the future of the four subfields discussed – the prospect of boundaries between fields becoming increasingly blurred as each area takes on board both the technologies and theoretical constructs of other scientific disciplines. There was also a shared perspective of what the future might hold: in each field, scientists felt that the next incremental advance would be to study a further level of organizational complexity within their experimental system. For example, in developmental neurobiology, the next important step will be to attempt to understand how functional circuits develop; molecular neuroscientists foresee the study of intracellular signalling being raised to the level of studying the single cell; and cellular neuroscientists predict a move towards studies of the interactions between networks of neurons. There was a common recognition of the increasing importance of neuroimaging, particularly functional imaging. As biological systems are explored in ever-increasing complexity, the need for studies of non-human primates was also emphasized.

7.2 Summary of the key issues

7.2.1 Multidisciplinarity

All of the discussion sessions identified a need for funding mechanisms to encourage multidisciplinary research programmes. It was recognized that a new 'breed' of scientists is needed – individuals skilled in more than one discipline, for example, molecular biologists who can pursue their investigations in an electrophysiological laboratory; cognitive psychologists at home in the functional imaging laboratory; and computational scientists who are equally aware of the key biological questions.

7.2.2 Genetics

Common to the different sessions was the underlying theme of applying newly developed genetics technologies across the breadth of neuroscience research, from the development of new transgenic models, to the eventual introduction of gene therapy for the treatment of psychiatric disorders. Multi-skilled research workers will be required to bring this technology to neuroscience research.

7.2.3 Infrastructure

To achieve the significant advances which were felt possible, there was a need to underpin the advances in neuroscience with high-quality infrastructural support. There were calls for refurbished laboratories, 'state-of-the-art' equipment and new computing facilities.

7.2.4 Partnerships

A 'National Neuroscience Initiative' is being developed by the 'Health and Life Sciences Foresight Panel', sponsored by the UK government. As this initiative develops, there is an open opportunity in the UK to strengthen partnerships between government and funding agencies, scientists in the academic world and those in industry.

7.2.5 Conclusions

Neuroscience is characterized by the diversity of subfields which make up the discipline as a whole. The future holds promise of real progress being made towards understanding the great unknowns of brain and behaviour. The strategies for action identified by the workshop group point the way forward to achieving this goal.

7.3 Session overviews

7.3.1 Developmental neurobiology

Current understanding of developmental neurobiology has been advanced by studies of the nervous systems of non-vertebrate model organisms – in particular the fruitfly *Drosophila melanogaster* and, to a lesser extent, the worm *Caenorhabditis elegans*. The study of very early developmental events such as promotion of cell identity and patterning has been aided by previous work on the cell cycle and cancer, addressing questions relating to cell number and survival. Even though considerable progress has been made in understanding early developmental events, much work remains to be done; for example, it is still not known how individual neuronal cell types are determined.

Later events in the development of the nervous system, such as axon pathfinding and circuit formation, are even less well understood. These are areas that developmental neurobiologists are having to study *de novo*, as no contribution was available from non-neuronal systems in establishing baseline knowledge. The next decade is likely to see significant advances in these areas.

Many other areas of developmental neurobiology also require urgent attention. For example, how do developmental studies relate to the regeneration of the mature nervous system, what roles do developmental genes play in the subsequent refining of the activity of the mature central nervous system, and so on. Knowledge of developmental mechanisms is likely to have a significant input on the understanding of higher cortical function. It may be difficult to define how a complex system works by studying its individual elements, as the interaction between these elements makes important contributions to the function of the system as a whole. In that regard, cooperation and discourse between developmentalists and systems neuroscientists will be essential, and needs to be developed.

7 The Millennium Workshop Meeting – Strategies for Action

To study the function of specific neuronal pathways, systems neuroscientists use techniques such as selective lesioning to produce behavioural models. If transgenic technology could be used to mimic such models, associated genetic data would help the assessment of the developmental basis of the model. However, most behavioural work is currently carried out on rats, and transgenic techniques are currently focused on mice. Similarly, human developmental studies could also inform the production of transgenic models that may assist the study of the basic biology that underlies complex neurological and psychiatric disorders. However, transgenic technology will only be useful in the study of complex disorders such as schizophrenia and autism if the genes involved are highly conserved across species. In order to gain insight into higher cortical function, the use of non-human primates will be crucial, and the study of basic human neurodevelopment needs to be pursued. Cohorts can now also be followed longitudinally using functional neuroimaging techniques, as it is possible to study children as young as four years old using functional magnetic resonance imaging.

Key issues and funding implications

- Multidisciplinary research. It is essential to have a mechanism that encourages and enables collaboration between developmentalists and systems neuroscientists.
- Longitudinal human studies. These studies will require input from the areas of developmental neurobiology, neuroimaging, psychiatry and psychology.
- Continued resourcing of non-human primate studies. Although such studies are very expensive, they are vital and will inform and integrate with work in systems neuroscience and neuroimaging;
- Transgenic animals. It is important to develop transgenic technology that can be applied to the rat.

7.3.2. Molecular neuroscience

Molecular neuroscience is arguably more dependent upon advances in other areas of biology and transfer of new technologies from other disciplines than any other area of neuroscience. For example, the majority of intracellular signalling work was originally carried out in simple cell types such as fibroblasts, and it is only recently that these studies are being transferred into neuronal systems. This interface between general cell biology and neurobiology is vital, but has been underdeveloped in the UK, especially in the area of G-protein research, with few novel molecular genetic and structural approaches being adopted at an early stage in this country. Similarly, the majority of the original receptor cloning experiments of the early-to-mid 1980s were not undertaken in the UK.

This general failure to adopt cutting-edge molecular techniques as they became available may be attributed to a lack of flexibility in UK academic research and a shortage of secure funding in the 1980s. The new technology and methodologies meant work in this area necessitated a multidisciplinary approach, requiring appropriately qualified personnel to bring necessary expertise into the laboratory as rapidly as possible. At that time, it was difficult to find the resources to do this in the UK.

7 The Millennium Workshop Meeting – Strategies for Action

Despite the missed opportunities of the last decade, scientists in this country have made notable contributions to the functional analysis of receptors, biochemical signal transduction, and the role of glutamate in long-term potentiation. In the post-DNA-sequencing era, neuroscientists in the UK should be well placed to establish context and function, and to address relevant and pertinent cell physiology questions. With increases in the resolution at which inter- and intracellular signalling can be studied, the input from improvements in instrumentation technology will become increasingly vital and a multidisciplinary approach will be essential. So that the UK is successful in this arena, a mechanism for bringing together the expertise of cell biologists, molecular biologists, structural biochemists, protein chemists and physicists is necessary. It will also be important to enable new developments in any one field to be rapidly incorporated into others. This is particularly applicable to developments in physics and engineering which are currently slow to filter into biology.

New funding mechanisms may be needed to facilitate both a multidisciplinary approach and the rapid incorporation of new engineering technology into biology. The use of transgenic technology will continue to play a pivotal role in the elucidation of molecular mechanisms at a single-cell level, and will also inform more complex systems such as learning and memory. Again, multidisciplinary approaches will be required, and it will be important to find a mechanism to bring together the appropriate expertise. To this end, it will be imperative to train new personnel in new techniques.

There was some support for centralizing the production of transgenic animals, although it was generally felt that the commercial sector would increasingly adopt a role in this area. For example, companies in the UK and USA will soon be able to generate transgenics on a commercial basis. How the wider scientific community is to obtain access to the products of transgenic technology is a question that needs to be addressed.

It was felt that the current absence of rat 'knockouts' should not stop physiologists and behaviourists from using this model organism. The tools are now emerging to allow expression of 'dominant negatives' in an inducible fashion in specific groups of neurons. This technology is moving so quickly that the experimental power provided by mouse transgenics will soon be available in the rat, which will have a major impact on the study of systems neuroscience and animal behaviour.

Key issues with funding implications

- Multidisciplinary research. This may need to be facilitated by a specific funding scheme in order to overcome obstacles currently hindering progress in this area.
- Technology transfer. New developments in physics and engineering need to be transferred rapidly into neuroscience.
- Training requirements. Training of junior scientists should enable the acquisition of a breadth of skills. More established scientists should be encouraged to keep abreast of new technologies – for example, through Cold Spring Harbor-type courses;
- Transgenic facilities. Should the development of transgenic technology be left solely with industry?

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7.3.3 Cellular neuroscience

Many of the key developments of the last two decades in cellular neurophysiology have involved multidisciplinary approaches. For example, cellular imaging was dependent upon dye development by chemists as well as input from cell physiologists. The revolution in neurophysiology brought about by 'patchclamping' involved expertise from the area of electronics as well as physiology. Against this background, it is now increasingly important that appropriate funding mechanisms are devised which enable and encourage UK scientists to adopt a multidisciplinary approach. For example, as the limits of conventional patch-clamping are reached, computational neuroscience will gain in importance in order to take modelling methodology forward into the ever more complex area of systems and circuits. This will especially be the case if the now speedy translation of developments in cellular physiology into systems neuroscience is to be maintained.

Flexible research funding was thought vital, both to the fostering of multidisciplinary research and to the rapid exploitation of unforeseen research opportunities. There was little support for large, goal-orientated research institutions, as these were seen as inflexible and relatively unproductive. Instead, a 'virtual institute' – resourcing individual groups to facilitate independent collaborations – was thought to be potentially the most productive funding route. In order to exploit unforeseen research opportunities, qualified postdoctoral scientists must be recruited quickly, and it would be useful to have a funding mechanism in place that allowed the rapid assessment of the suitability of such personnel. Similarly, as raised in the discussion of molecular neuroscience, there is a need for a funding system that facilitates the transfer of technological developments into and across all areas of neuroscience. This could be achieved through the current programme structure, if it were possible to build into the system a small amount of funds that were specifically set aside for collaborative work. Such funding would have to be applied for, but the assessment could be rapid. In addition to the issue of personnel, it is vital to have quick and easy access to appropriate pieces of equipment. This could be attained by making funds available to allow personnel access to specialist equipment at centres of excellence, on an *ad hoc* basis.

To maintain both the continuity of staff and research momentum, there was support for encouraging young, less well-established investigators - who may also be less reticent in their approach to multidisciplinary research - to apply for modest long-term funding. An advertised multidisciplinary scheme may overcome the reluctance of more well-established groups to engage in multidisciplinary research.

At another level, support for interdisciplinary training of graduate students was high. Again, as with the discussion of molecular neuroscience, the availability of Cold Spring Harbor-type courses in the UK for both students – and more especially for group leaders – would provide another mechanism for fostering cross-disciplinary approaches.

Key issues with funding implications

- Flexible and rapid assessment procedures. Support for peer review was strong, but a method for the rapid assessment of additional funding, especially for additional personnel, would be welcome.
- Integration of new technology. A funding source that enables the assessment of the suitability of new technology to be applied to biological systems.
- Longer-term support for more junior academics.
- Training programmes for students, post graduates and group leaders.
- Funding scheme aimed at cross-disciplinary programmes.

7.3.4 Therapeutic strategies in psychiatric disorders

This session served to illustrate that the once disparate disciplines of genetic, psychosocial research and brain biology are now coalescing, as progress in one field is seen to inform work in others.

The influence of imaging studies is becoming all-pervasive, but little is known about the precise mechanisms and processes that underlie the changes in metabolic rate seen in functional imaging. In order to exploit and interpret human MRI data, intervention studies in non-human primates, such as single unit recording, are necessary. Indeed, the monkey is the only species that will allow a complete, vertically integrated neurobiological programme of work, incorporating genetics, environment, systems and cellular approaches, with obvious implications in man. Other European countries now look to the UK for such non-human primate studies, as it has become exceptionally difficult to carry out such work in countries such as Germany and Scandinavia.

Using animals to be predictive in man is not limited to non-human primates. The molecular and cellular basis of addiction has also been informed by studies in rodents, although most of this work has been carried out in the USA. The UK is stronger in the area of the psychology of addiction and the mechanisms involved in relapse. However, the study of addiction is a good example of how the interface between different disciplines can inform novel therapies. Work aimed at understanding the molecular and cellular basis of conditioning mechanisms has been combined with a systems level approach to drug-taking and drug-seeking behaviour. As a result, the problem of drug abuse is now being tackled by pharmacological strategies, cognitive behavioural therapy, and a combination of both.

The assessment of treatment regimes will become increasingly important as the number of alternative treatments for any one disorder increases. Such studies are invariably long term and costly, but their precise evaluation is vital if developments in research are to be exploited to the full in the clinic. Cross-disciplinary approaches are being exploited in these areas. For example, the study of the genetic basis of psychiatric disorders is increasingly being influenced by classical epidemiological methodology, as the necessity for large-scale, well-controlled and coordinated studies becomes obvious. In this way, it is hoped to deliver definitive evaluations of therapeutic strategies, which have hitherto been unavailable.

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The interplay between genetics and environment is particularly important, as the genetic component of most common psychiatric disorders is likely to be due to allelic variation. Although not every psychiatric disorder has a significant genetic component, it will be crucial to improve knowledge of how genetic factors influence both the susceptibility to environmental stresses and the shaping and selection of environment. Psychosocial research is a neglected area. For example, the rise in many types of psychopathology in adolescents seen in the last 50 years (for example suicide, drug abuse, crime and eating disorders), cannot be ascribed to a genetic basis. It is important that the mechanisms that underpin these psychopathologies are understood; there is little work being done in this area at present.

Key issues with funding implications

- The interplay between genetics and environment.
- Treatment trials.
- Imaging of humans and non-human primates.

8 Discussion and Conclusions

Diseases associated with the nervous system are a major burden worldwide. The WHO's estimates indicate that, at present, these are diseases of the developed world – probably because the demographic profiles of these countries contain larger numbers of older individuals, and there is an increased incidence of these diseases in older individuals. By the year 2020, however, there will be a significant increase in the overall burden of these diseases – with much of this increase in developing countries. The increase will be due to the changing demographic profiles of these developing countries, as improvements in healthcare lead to longer lifespans.

At the national level, mental illness is the leading cause of illness and disability in the UK. Diseases associated with the nervous system account for approximately 25 per cent of the total paid out each year by the UK government in sickness and invalidity payments. In the USA, these diseases have high prevalence rates – for example, depression alone accounts for 17.4 million cases per annum, stroke 3 million cases and Alzheimer's disease 4 million cases (cancer accounts for 10 million cases and cardiovascular disease for 56 million cases).

In recognition of the major burden associated with these diseases, many funding agencies and companies, both in the UK and worldwide, have established specific programmes to support research in this field. In the UK, funding for research in this area comes primarily from Government departments and agencies (the MRC, the DoH and the BBSRC), the charitable sector (including the Wellcome Trust, Action Research, Multiple Sclerosis Society and many other members of the Association of Medical Research Charities), and the pharmaceutical industry. In the USA, the 'Decade of the Brain' programme, announced in 1990, reflects the importance of this area. The NIH have a budget allocation for 1998 of approximately US$2 billion for neuroscience research, and the federal government has announced an additional US$37 million for research into the biology of brain disorders. The US pharmaceutical industry now spends more on developing medicines for treatment of diseases in this area than any other field apart from neoplasms and metabolic diseases.

The EU has also adopted the current decade as its decade of the brain, and this has resulted in neuroscience research being identified as one of its priority areas of research within the Framework Programme. The Human Frontier Science Program, a Japanese-led international research funding effort, has also focused on neurological research, whilst in Japan itself, a neuroscience initiative had a US$125 million budget in 1997, which is expected to increase by 600 per cent over the next five years.

Industrial funding of neuroscience research is difficult to quantify. One indicator of commercial priority in this field is reflected in the fact that, in 1996, a SCRIP survey indicated that neurologicals were the leading therapeutic area in terms of the number of drugs in development, ahead of anti-cancers and anti-infectives.

8 Discussion and Conclusions

With all this activity among funding agencies to invest in research in this field, are the funding strategies in the UK successful in terms of producing research publications in this field, and are these research findings being translated into improvements in healthcare and treatments in this field? Parts 4 and 5 of this study go some way to answering these questions. The analysis of the neuroscience research publications was restricted to eight subfields: molecular neuroscience, cellular neuroscience, the overlap area between molecular and cellular neuroscience, developmental neuroscience, systems and cognitive neurology at the basic research end of the research spectrum and cognitive behavioural psychiatry and drug-related behavioural psychiatry at the clinical end of neuroscience research. Together these eight subfields provide a broad picture of neuroscience research.

The UK presence in the six basic research subfields is close to its average share of world neurosciences publications (approximately 9 per cent), except for cognitive neurology where the UK's share is slightly higher (approximately 11.5 per cent). The UK's share of the world publications in these six subfields (dominated by the USA) is on a par with Japan's output. However, in all the six basic subfields the UK share of world publications is growing; none of the other 11 OECD countries studied can claim this. In terms of the number of papers per head of population, the UK is typically in third or fourth place behind Switzerland, Sweden and Canada – this is a general trend for most subfields of biomedicine. The journals in which UK papers are being published in these subfields appear to be of a lower journal impact weighting than US papers, but higher than the average for the world as a whole.

In the two behavioural psychiatry subfields, there appears to be a marked difference in the UK's record. While the UK's share of cognitive psychiatry is relatively high (14 per cent), the journals in which these papers are published have lower impact weightings compared with the world average for this subfield. In the drug-related psychiatry subfield, the UK produces relatively fewer papers (7.6 per cent; reflecting the unusually dominant position of the USA in this field), but these papers are published in journals of relatively high impact weightings on a par with the world output in this area.

Approximately 2 per cent of all the neuroscience papers produced by the UK was cited (as 'prior art') on US patents. Thus apart from the increase in the number of medicines coming on to the market this is another indicator that the investment in neuroscience is paying dividends (albeit indirectly) in terms of improvements in healthcare (through new treatments) and economically (through revenue generation and savings in treatment of chronic conditions). The most notable finding contained in the patent analysis was the fact that whilst UK inventors cited on US patents represented 13 per cent of all the inventors cited, UK companies or individuals represented only 3.5 per cent of the assignees or owners named on the patents. The overall message is that neuroscience research is feeding into patents but there is evidence that the UK is facing an exploitation gap in a very important and growing field. It is hoped that the recently launched UK University Challenge Fund will address this problem.

8 Discussion and Conclusions

It appears that the UK's general position in the neuroscience subfields is strong and growing. A survey of experts found that the UK was perceived to be the second strongest country (after the USA) in neuroscience research, a perception that appears to be reflected in the bibliometric analysis. The main theme that ran through the survey was the need to strengthen the research infrastructure if the UK's current strength is to be maintained or increased. The main infrastructure issues included increased funding for career development of researchers to keep them in the field, to promote mobility within a career structure and acquisition of appropriately qualified laboratory technicians.

The 'live' discussion of the workshop meeting revealed a common thread drawing together the future of the four subfields discussed – the prospect of the boundaries between fields becoming increasingly blurred as each area took on board the technologies and theoretical constructs of other scientific disciplines. There was a shared perspective of what the future might hold; in each field scientists felt the next incremental advance would be to study a further level of complexity within their experimental system.

In conclusion, it appears that the field of neuroscience research is growing rapidly with relatively large sums of funding available worldwide. This growth is important in view of the projected increase in importance (both in terms of human welfare and economic impact) of diseases associated with disorders of the nervous system. In the UK, the overall picture is of a research base in a relatively strong position, being eclipsed only by the US effort (to a greater extent by quantity of output and to a lesser extent by quality of output). This is not surprising in view of the large financial investment to neuroscience research in the USA. The general view of UK experts is that the field is strong but this will not be maintained unless there are some changes to the research environment – their recommendations reflect the generic problems of the UK university system, including lack of adequate infrastructure and career development. The recent injection of £1.1 billion into a UK university infrastructure fund by the UK government and the Wellcome Trust will have a considerable impact on at least one of these issues.

Appendix 1
The Global Burden of Disease Study – methods

Some projections of disease burden are made only for mortality rates encompassing all diseases or injuries; these rates are sometimes broken down into component causes. Others use cause-specific mortality rates for cancers, coronary heart disease, HIV and many of the more major conditions. Some methods are based on extrapolating past trends while others consider the relationship between mortality and a set of independent variables (factors which may make an individual more susceptible to disease). Projecting mortality can be considered simultaneously for all age groups, or based on the assumption that the relationships between mortality rates and the independent variables will vary by age and sex (as is often the case).

The mortality rate due to all causes is limited in that it assumes that future trends will continue in the same pattern as in the past, but as the composition of causes of death changes, so the trends in mortality rates for all causes will also change. Cause-specific projections are based on the assumption that trends in the determinants of health (such as the incidence of smoking) will continue in the future, and that the relationships between these determinants and the incidence of mortality from specific diseases will be approximately the same in the future, which will not necessarily be the case.

In the WHO's Global Burden of Disease study, the researchers' health projections were calculated using age-, sex- and cause-specific models based on a limited set of socioeconomic determinants of death rates, together with tobacco use (included as a major contributor to many health problems). They developed this method in order to try and produce valid figures without excessive complexity.

Data from this study have provided valuable background information on the relative contribution of neurological disorders to the overall picture of global disease burden, but there are a number of caveats which should be considered when consulting such data, particularly when projections of health outcomes are being used:

- Estimation of the burden of disease on a national, regional or global level relies on a reliable assessment of the size and distribution of population and deaths, by age and sex. Access to such information can be difficult, particularly in developing regions without good routine death registration systems, where mortality is estimated using census and survey data. The Global Burden of Disease study used demographic estimates of death and population in 1990, by age and sex, which were developed specifically for the World Development Report 1993.

- Estimation of causes of death are usually derived from routine death registration systems, sample death registration systems, epidemiological assessments and cause-of-death models. Death registration systems are not generally complete in developing regions, so the other methods must be used to supplement the data. The GBD study used cause-of-death models which were developed separately for males and females in each of seven age groups, but the primary data had to come from different sources depending on the region.

- Mortality rate estimates for sub-Saharan Africa were adapted from the routine death registration data for South Africa (because only this information was available) and estimates were then made for the rest of Southern Africa, and then for the whole of the region.

- Estimation of the incidence, prevalence, remission, duration, case-fatality and mortality for each disease or injury was made using community-based epidemiological studies and, where such information did not exist, the estimates made in the Global Burden of Disease study were obtained in close collaboration with a large number of experts familiar with specific diseases or injuries.

- The researchers involved in the Global Burden of Disease study acknowledge that the reliability of some of the above estimates is variable and requires cautionary interpretation, particularly for sub-Saharan Africa, India, other Asia and Islands and parts of Latin America and the Caribbean, where very little is known about causes of mortality, disease incidence, prevalence and duration.

Appendix 2
Tabulated results for neuroscience questionnaire

Q1 Present occupation of respondents to neuroscience questionnaire.

Occupation	No.	Percentage (%)
Tenured university post	68	73
University contract researcher	14	15
Administrative staff	7	8
Researcher in industry	2	2
NHS researcher	1	1
Scientific researcher	1	1
TOTAL	**93**	**100**

Base: All respondents

Q2 Length of time active researchers have been involved in postdoctoral scientific research.

Time	No.	Percentage (%)
Between 5 and 10 years	11	13
Between 10 and 15 years	12	14
Between 15 and 20 years	26	30
Over 20 years	37	43
TOTAL	**86**	**100**

Base: All active researchers

(Definitions: 'Actives' are those currently involved in research, while 'inactives' are administrators in either the Research Councils or medical charities.)

None of the administrative staff answered this question.

Q3 Specialisms within neuroscience ranked according to activity level in research.

	Actives			Inactives		Combined		
Specialism	**No.**	**%**	**Rank**	**No.**	**Rank**	**No.**	**%**	**Rank**
Cellular	**23**	**26**	**1**	**1**	**4**	**24**	**27**	**1**
Molecular	**16**	**18**	**2**	**3**	**1**	**19**	**21**	**2**
Developmental	**12**	**13**	**3**	**0**	**0**	**12**	**13**	**3**
Neuropharmacology	**9**	**10**	**4**	**2**	**2**	**11**	**12**	**3**
Neurodegenerative disease	**9**	**10**	**4**	**2**	**2**	**11**	**12**	**5**
Biological psychiatry	8	9	6	1	4	9	10	6
Systems	8	9	6	0	0	8	9	7
Neuroimaging	6	7	8	0	0	6	7	8
Vision	6	7	8	0	0	6	7	8
Neuroanatomy	5	6	10	0	0	5	6	10
Neuropsychology	5	6	9	0	0	5	6	10
Psychopharmacology	4	4	11	1	4	5	6	10
Auditory	4	4	11	0	0	4	4	13
General psychiatry	4	4	11	0	0	4	4	13
Neuroendocrinology	4	4	11	0	0	4	4	13
Neurology	4	4	11	0	0	4	4	13
Child psychiatry	3	3	16	0	0	3	3	17
Ophthalmology	3	3	0	0	0	3	3	17
Computational neurology	2	2	17	0	0	2	2	19
Clinical psychology	1	1	18	0	0	1	1	20
Psychophysics	1	1	18	0	0	1	1	20
TOTAL	**80**			**10**		**90**		

NB No respondent put behavioural psychology or cognitive psychology as their specialism.

Appendix 2

Q4 Perceived top areas of neuroscience in the UK.

	Actives		Inactives		Combined	
Specialism	**No.**	**Rank**	**No.**	**Rank**	**No.**	**Rank**
Cellular	**18**	**1**	**1**	**2**	**19**	**1**
Developmental	**10**	**2**	**1**	**2**	**11**	**2**
Neuroimaging	**6**	**3**	**2**	**1**	**8**	**3**
Neuropharmacology	**5**	**4**	**1**	**2**	**6**	**4**
Cognitive psychology	**4**	**6**	**1**	**2**	**5**	**5**
Molecular	**5**	**4**	**0**	**0**	**5**	**5**
Neuropsychology	4	6	0	0	4	7
Neuroanatomy	3	8	0	0	3	8
Psychopharmacology	2	9	1	2	3	8
Child psychiatry	2	9	0	0	2	10
Clinical psychology	2	9	0	0	2	10
Neurology	1	13	1	2	2	10
Vision	2	9	0	0	2	10
Neurodegenerative disease	1	13	0	0	1	13
TOTAL	**57**		**8**		**65**	

Q4 cont. Areas of neuroscience in the UK ranked top by respondents taking into account the respondent's own specialism.

	Actives	
Specialism	**No.**	**Rank**
Cellular	7	1
Developmental	7	1
Neuroimaging	7	1
Cognitive psychology	5	4
Molecular	4	5
Neuroanatomy	3	6
Child psychiatry	2	7
Clinical psychology	2	7
Neuropsychology	2	7
Neurology	2	7
Neuropharmacology	2	7
Psychopharmacology	2	7
Vision	2	7
TOTAL	47	

NB Neurodegenerative disease is no longer considered a top area of neuroscience.

Q4 cont. Top areas of neuroscience when combined recoding is performed.

	Combined		Combined recoded	
Specialism	**Score**	**Rank**	**Score**	**Rank**
Developmental	**126**	**2**	**106**	**1**
Neuroimaging	**106**	**3**	**101**	**2**
Cellular	**146**	**1**	**86**	**3**
Neuropharmacology	**102**	**4**	**82**	**4**
Molecular	**81**	**5**	**76**	**5**
Vision	71	6	71	6
Cognitive psychology	67	7	67	7
Neuroanatomy	43	9	43	8
Neurodegenerative disease	39	10	34	9
Neuropsychology	44	8	34	9
Child psychiatry	24	11	24	11
Biological psychiatry	22	12	22	12
Systems	22	12	22	12
Behavioural psychiatry	19	15	19	14
Psychopharmacology	22	12	17	15
Clinical psychology	16	16	16	16
Neurology	12	17	12	17
Psychophysics	12	17	12	17
Computational neurology	11	19	11	19
Auditory	9	20	9	20
Neuroendocrinology	5	21	5	21
General psychiatry	4	22	4	22

NB Combined recoded represents new scores and ranks after those individuals who ranked their own speciality as top have been removed.

Appendix 2

Q5 Areas of neuroscience where the UK is perceived to be lagging behind other countries.

	Actives			Inactives		
Specialism	**No.**	**%**	**Rank**	**No.**	**%**	**Rank**
Molecular	**24**	**41**	**1**	**4**	**7**	**1**
Computational neurology	**20**	**34**	**2**	**2**	**3**	**5**
Ophthalmology	**12**	**20**	**3**	**3**	**5**	**2**
Neurology	**9**	**15**	**4**	**2**	**3**	**5**
Systems	**9**	**15**	**4**	**2**	**3**	**5**
Cellular	7	12	6	2	3	5
Developmental	7	12	6	1	2	0
Neurodegenerative disease	7	12	6	0	0	0
Auditory	6	10	9	0	0	0
Biological psychiatry	6	10	9	3	5	2
General psychiatry	6	10	9	1	2	0
Neuroendocrinology	6	10	9	0	0	0
Vision	6	10	9	1	2	9
Child psychiatry	4	7	14	0	0	0
Neuroanatomy	4	7	14	0	0	0
Neuropsychology	4	7	14	0	0	0
Neuroimaging	4	20	14	0	5	2
Psychopharmacology	4	7	14	0	0	0
Behavioural psychiatry	3	5	19	0	0	0
Neuropharmacology	3	5	19	0	0	0
Psychophysics	3	5	19	1	2	9
Clinical psychology	2	3	22	0	0	0
Cognitive psychology	1	2	23	0	0	0
TOTAL	**157**			**20**		

Q6 Perceived relative strengths of countries in neuroscience.

Country	Very strong	Fairly strong	Neither/ nor	Not v. strong	Not at all strong	Mean score (+2 to -2)
UK	15.9	28.0	7.4	4.0	0	1.100
USA	65.2	1.9	0.7	0.0	0	1.900
Germany	9.1	21.3	21.5	6.0	0	0.740
France	0.0	14.0	26.7	42.0	25.0	0.045
Japan	4.5	17.9	20.7	28.0	12.5	0.380
Scandinavia	5.3	16.9	23.0	20.0	62.5	0.333

Q7 Respondents' (*n*=87) mean score for the overall contribution of UK neuroscience research to the understanding of biological mechanisms was 7.2 (on a ranked scale of 1–10).

Q8 Respondents' (*n*=69) mean score for the contribution of UK neuroscience to the development of new therapies was 6.15 (on a ranked scale of 1–10).

Q9 Degree of agreement with the statement that "The UK is strong in neuroscience research for a country with a relatively small population".

Response	No.	Percentage (%)
Agree strongly	23	25
Agree	54	59
Disagree	11	12
Disagree strongly	1	1
Don't know	3	3
TOTAL	**92**	**100**

Base: All respondents

Appendix 2

Q10 The main issues that are confronting neuroscience research generally today ranked in descending order.

Issue	No.	Percentage (%)
Lack of career development for young scientists	57	66
Lack of funding	42	49
Management load of best researchers	41	48
Cost of projects	37	43
Lack of research-trained clinicians	37	43
Poor interface between basic research and clinical development	34	40
Lack of interdisciplinary collaboration	28	33
Lack of trained technicians	27	32
Teaching load on best researchers	26	30
Lack of fellowships at all stages of career	22	26
Length of funding time	21	24
Lack of communication between industry and academia	17	20
Lack of facilities	14	16
Lack of diversity in research groups	14	16
Small size of research group	14	16
Lack of equipment	13	15
Quality of PhD training	13	15
Research effort spread too thinly	12	14
Quality of undergraduate training	11	13
Lack of focus	9	11
Lack of venture capital	7	8
Lack of good science	6	7

Base: All respondents

Appendix 2

Q11 The main issues that are confronting neuroscience research in the UK today ranked in descending order.

Issue	No.	Percentage (%)
Lack of career development for young scientists	64	77
Lack of funding	48	58
Management load of best researchers	45	54
Lack of research-trained clinicians	42	51
Teaching load on best researchers	42	51
Cost of projects	38	46
Lack of trained technicians	36	43
Poor interface between basic research and clinical development	31	37
Lack of facilities	30	36
Length of funding time	28	34
Lack of interdisciplinary collaboration	27	33
Lack of fellowships at all stages of career	26	31
Quality of PhD training	22	27
Small size of research group	22	27
Lack of venture capital	21	25
Lack of equipment	21	25
Lack of communication between industry and academia	18	22
Lack of diversity in research groups	18	22
Quality of undergraduate training	15	18
Lack of focus	11	13
Research effort spread too thinly	11	13
Lack of good science	4	5

Base: Active researchers

Appendix 2

Q12 Problems with conducting neuroscience research in the UK today.

Problem	No.	Percentage (%)
Too heavy teaching and administrative workload in universities	72	79
Lack of funding for new lecturers	56	62
Lack of researchers of international quality	37	41
Loss of postgraduates to the USA	36	40
Lack of methodological flexibility of UK researchers	24	26
Lack of training to exploit new developments	24	26
Insufficient mobility inside and out of the UK	14	15
Loss of postgraduates to countries other than the USA	5	6.0

Base: All respondents

Q12 Problems with conducting neuroscience research in the UK today.

Problem	No.	Percentage (%)
Too heavy teaching and administrative workload in universities	66	79
Lack of funding for new lecturers	52	62
Loss of postgraduates to the USA	36	43
Lack of researchers of international quality	33	39
Lack of training to exploit new developments	24	29
Lack of methodological flexibility of UK researchers	21	25
Insufficient mobility inside and out of the UK	12	14
Loss of postgraduates to countries other than the USA	5	6

Base: Active researchers

Q13 Regarding funding for neuroscience research.

- 85.7 per cent of all the respondents felt that more money should be spent on neuroscience.
- 88 per cent of those active in research felt that more money should be spent on neuroscience (*n*=83).
- 57.1 per cent of those in administration felt that more money should be spent on neuroscience (*n*=7).

Appendix 2

Q14 Regarding funding priorities.

- 44.2 per cent felt that there should be more money even if it meant taking it away from other areas, 32.5 per cent said no and 23.4 per cent said don't know.
- 44.4 per cent of active researchers felt that there should be more money even if it meant taking it away from other areas, 31.9 per cent said no and 23.6 per cent said don't know.
- 25 per cent of administrators felt that there should be more money even if it meant taking it away from other areas, 50 per cent said no and 25 per cent said don't know.

Q15 How respondents would spend new money or (re)allocate existing funds to support or improve UK neuroscience research.

Response	No.	Percentage (%)
Develop an alternative career structure	75	81
Just fund the best science by peer review	59	63
Increase funding of individuals through fellowships	53	57
Ensure postdoctoral students going abroad have funding for their return	51	55
Encourage interdisciplinary collaboration on specific topics	50	54
Encourage key players back to the UK	48	52
Encourage foreign researchers to move to the UK	43	46
Focus on centres of excellence, whether in universities or other institutes	42	45
Fund long-term posts for lab technicians	42	45
Fund longer PhDs	39	42
Fund projects for longer	38	41
Fund training of clinicians in laboratory techniques	35	38
Develop supergroups	34	37
Pay differential salaries to reward the better/best researchers	31	33
Identify areas most likely to be fruitful and concentrate funding on those	29	31
Identify up-and-coming techniques and set up facilities to support them	28	30
Identify strong areas and concentrate funding on those	23	25
Fund MRes in advance of PhDs	15	16
Try to stop postdoctoral students moving abroad	4	4
Identify weak areas and concentrate funding on those	3	3

Base: All respondents

Appendix 2

Q15 How respondents would spend new money or (re)allocate existing funds to support or improve UK neuroscience research.

Response	No.	Percentage (%)
Develop an alternative career structure	68	80
Just fund the best science by peer review	56	66
Increase funding of individuals through fellowships	49	58
Ensure postdoctoral students going abroad have funding for their return	48	57
Encourage interdisciplinary collaboration on specific topics	45	53
Encourage key players back to the UK	45	53
Encourage foreign researchers to move to the UK	39	46
Fund long-term posts for lab technicians	39	46
Focus on centres of excellence, whether in universities or other institutes	38	45
Fund longer PhDs	37	44
Fund projects for longer	34	40
Fund training of clinicians in laboratory techniques	34	40
Develop supergroups	30	35
Pay differential salaries to reward the better/best researchers	30	35
Identify areas most likely to be fruitful and concentrate funding on those	26	31
Identify up-and-coming techniques and set up facilities to support them	26	31
Identify strong areas and concentrate funding on those	21	25
Fund MRes in advance of PhDs	14	17
Try to stop postdoctoral students moving abroad	4	5
Identify weak areas and concentrate funding on those	2	2

Base: Active researchers

Appendix 2

Q16 Organizations from which active researchers have obtained funding in the last five years.

Organization	No.	Percentage (%)
The Wellcome Trust	75	88
MRC	59	69
Other medical charities	47	55
Industry sources	32	38
EU	28	33
BBSRC	14	17
NIH	9	11
NHS R&D	8	9
Other US foundations	7	8
Other Research Councils	6	7
Howard Hughes Institute	4	5

Base: Active researchers

Q17 Organizations from which researchers' institutions encourage them to obtain funding.

Organization	No.	Percentage (%)
MRC	66	93
The Wellcome Trust	46	65
EU	42	59
Industry sources	42	59
BBSRC	40	56
Other Research Councils	35	49
Other medical charities	34	48
NHS R&D	29	41
NIH	14	20
Howard Hughes Institute	12	17
Other US foundations	8	11

Appendix 2

Q18 Skills that are seen as fundamental for today's PhD students in advance of undertaking research.

Skills	No.	Percentage (%)
Scientific knowledge	72	84
Laboratory skills	59	69
Research experience at undergraduate level	47	55
Operating computers	46	54
Statistics	40	47
Mathematics, e.g. calculus	13	15
Computer programming	12	14
Clinical knowledge	8	9

Q19 The responses to this question (on composition of ideal research groups) were too diverse in order to carry out reasonable analyses.

Appendix 2

Q20 Areas of neuroscience most likely to lead to health therapies in the next five to ten years, including the development of drugs.

Response	No.	Percentage (%)
Neurodegenerative disease	56	74
Molecular	50	66
Neuropharmacology	48	63
Cellular	30	40
Biological psychiatry	27	36
Psychophysics	25	33
Neuroimaging	24	32
Developmental	19	25
Neuroendocrinology	14	18
Neurology	9	12
Child psychiatry	8	11
Systems	8	11
Vision	8	11
Behavioural psychiatry	7	9
Cognitive psychology	6	8
Neuropsychology	5	7
Ophthalmology	5	7
Auditory	4	5
Clinical psychology	4	5
General psychiatry	4	5
Neuroanatomy	3	4
Computational neurology	1	1

Q21

- 53.3 per cent of all respondents said that they would make use of a national information resource centre, 9.8 per cent said that they wouldn't and 37 per cent said that they did not know.
- Of those that are active in research 52.3 per cent said that they would use it, 9.3 per cent said no and 38.4 per cent said don't know.
- 80 per cent of those in administration said yes and 20 per cent said no.

Appendix 2

Q22 How an information resource centre might benefit the neuroscience community.

Benefits	No.	Percentage (%)
It would encourage collaboration	47	69
Reduce the need to respond to requests on current research programmes	24	78
Help potential postgrads identify the most appropriate places of study	53	16
Other	11	35

Base: All respondents (68 valid cases, 26 missing cases)

Q22 How an information resource centre might benefit the neuroscience community.

	Actives		Inactives	
Benefits	**No.**	**Percentage (%)**	**No.**	**Percentage (%)**
It would encourage collaboration	42	68	5	83
Reduce the need to respond to requests on current research programmes	22	36	2	33
Help potential postgrads identify the most appropriate places of study	50	81	3	50
Other	9	15	2	33

Base: Active researchers (62 valid cases, 32 missing cases), Administrators (six valid cases, 88 missing cases)

Q23 How much did respondents agree with the following statements
"It is important to have foreign staff in a research group"

Level of agreement	Actives (%)	Inactives (%)	Total (%)
Agree	26	14	25
Vaguely agree	26	14	25
Neither agree nor disagree	34	57	36
Vaguely disagree	2	0	2
Disagree	12	15	12

Base: 93 valid cases, one missing case

Appendix 2

"It is important to have people with training in different disciplines to one another"

Level of agreement	Actives (%)	Inactives (%)	Total (%)
Agree	64	17	62
Vaguely agree	27	83	30
Neither agree nor disagree	6	0	5
Vaguely disagree	1	0	1
Disagree	2	0	2

Base: 93 valid cases, one missing case

"Research staff should not have tenure the first few years after completing their PhD"

Level of agreement	Actives (%)	Inactives (%)	Total (%)
Agree	49	33	48
Vaguely agree	26	17	25
Neither agree nor disagree	18	17	19
Vaguely disagree	4	17	4
Disagree	3	16	4

Base: 92 valid cases, two missing cases

"Every permanent laboratory needs at least one permanent technician"

Level of agreement	Actives (%)	Inactives (%)	Total (%)
Agree	50	57	50
Vaguely agree	27	15	26
Neither agree nor disagree	12	14	12
Vaguely disagree	4	14	4
Disagree	7	0	8

Base: 92 valid cases, two missing cases

Appendix 2

"PhD students and postdocs should be encouraged to move between laboratories"

Level of agreement	Actives (%)	Inactives (%)	Total (%)
Agree	43	57	44
Vaguely agree	36	29	36
Neither agree nor disagree	17	0	15
Vaguely disagree	2	0	2
Disagree	2	14	3

Base: 92 valid cases, two missing cases

"Postdocs should be encouraged to work abroad for at least a few years"

Level of agreement	Actives (%)	Inactives (%)	Total (%)
Agree	32	43	33
Vaguely agree	36	14	35
Neither agree nor disagree	23	29	23
Vaguely disagree	7	0	6
Disagree	2	14	3

Base: 92 valid cases, two missing cases

"It is difficult to recruit appropriately qualified laboratory staff"

Level of agreement	Actives (%)	Inactives (%)	Total (%)
Agree	33	34	33
Vaguely agree	28	33	28
Neither agree nor disagree	16	0	15
Vaguely disagree	15	0	15
Disagree	8	33	9

Base: 88 valid cases, six missing cases

"PhD grants should be attached to projects or supervisors, not to academic departments"

Level of agreement	Actives (%)	Inactives (%)	Total (%)
Agree	50	60	50
Vaguely agree	27	40	28
Neither agree nor disagree	13	0	13
Vaguely disagree	4	0	3
Disagree	6	0	6

Base: 90 valid cases, four missing cases

Q24 The proportion of diseases that are seen as being treatable in the next five to ten years.

Disease	Actives (%)	Inactives (%)	Total (%)
Depression and anxiety	58	83	60
Neurodegenerative	57	50	56
Infections	49	67	51
Major psychoses, e.g. schizophrenia	43	50	43
Oncology	39	50	41
Eating disorders	36	33	37
Stroke	35	67	37
Inherited disorders	33	50	35
Rehabilitation following trauma	30	50	31
Child and adolescent psychopathology	16	17	16
Cognitive neurology	9	33	11
Substance abuse	12	0	11
Blinding disease	8	33	10

Base: 84 valid cases, ten missing cases

Other diseases/illnesses that respondents felt to be treatable included Parkinson's disease, pain, chronic pain and spinal cord injury, sensorineural hearing loss, immune-mediated conditions, severe epilepsy and seizure disorders.

Appendix 2

Q25 The overall future for neuroscience research in the UK is...

Level of agreement	Actives (%)	Inactives (%)	Total (%)
Very good	13	14	13
Fairly good	66	72	66
Neither good nor bad	18	14	18
Fairly bad	2	0	2
Very bad	1	0	1

Base: 90 valid cases, four missing cases

Appendix 3
Bibliometric analysis of research outputs in eight neuroscience specialist areas – methodology

Introduction

The eight specialist areas were named for analysis purposes as:

- cellular neuroscience (CELNE);
- developmental neurobiology (DEVNE);
- molecular neuroscience (MOLNE);
- molecular and cellular neuroscience (MOCEL);
- systems neuroscience (SYSNE);
- cognitive neurology (COGNE);
- cognitive behavioural psychiatry (COBEH); and
- drug-related behavioural psychiatry (DRUGB).

The first six of these areas involve mostly basic research; the latter two also involve the treatment of patients suffering from disorders.

In this analysis the position of the UK is judged according to its output of scientific papers relative to the world production and that of other leading countries within OECD, as follows:

Table A1 OECD countries used for the analysis.

AU	Australia	CA	Canada
CH	Switzerland	DE	Germany
ES	Spain	FR	France
IT	Italy	JP	Japan
NL	Netherlands	SE	Sweden
UK	United Kingdom	US	United States of America

Method

Subfield definition

The first task was to design a 'filter' consisting of a set of keywords that would selectively retrieve papers from one of the Citation Indexes published by the Institute for Scientific Information. These were as follows:

Appendix 3

Table A2 List of subfields used for analysis, with their five-letter codes.

CELNE	Cellular neuroscience	Neurosciences Citation Index
COBEH	Cognitive behavioural psychiatry	Social Sciences Citation Index
COGNE	Cognitive neurology	Neurosciences Citation Index
DEVNE	Developmental neurobiology	Science Citation Index
DRUGB	Drug-related behavioural psychiatry	Social Sciences Citation Index
MOLNE	Molecular neuroscience	Neurosciences Citation Index
MOCEL	Molecular and cellular neuroscience	Neurosciences Citation Index
SYSNE	Systems neuroscience	Neurosciences Citation Index

For the SCI and SSCI, only the titles of the papers were available for searching, but for the NCI it was also possible to search the keywords attached to each paper (both author-given and additional indexer-given ones) and the abstract. For the selective retrieval of papers in the closely related subfields of CELNE and MOLNE, it was considered that the greater amount of information in the NCI would be helpful in allowing a judgement into which subfield any given paper fell, and it was therefore decided to use this Index for these two subfields and for the overlap subfield of molecular and cellular neurosciences (MOCEL). An investigation of the relative merits of searches for papers either on the basis of their titles, or of their titles, keywords and abstracts, showed that the precision[1] of the latter was not much inferior to the former and the recall was much higher – typically twice as great – so a decision was made to base the search on the 'basic index' of titles, keywords and abstracts in the NCI. However, some of the papers in the NCI are not in refereed journals, and it only extends back to 1991, so it was not used for the three other subfields.

The process of defining a set of keywords which forms a filter is an interactive one[2] and involves the generation of sets of records consisting of paper titles and journal names which are then marked by an expert with a tick, query or cross to indicate that the papers are within the chosen subfield, on the borderline or can't say/don't know, or out of the subfield. Ideally, the filter should retrieve only papers that are relevant to the subfield, and it will often consist of both positive words (whose presence causes a paper to be retrieved) and negative words (which would cause a paper to be rejected). In practice there will be false positives (lack of precision, or type II errors) and false negatives (lack of recall, or type I errors). Normally, a precision of better than 0.9 is sought, but this was hard to achieve here because the subfields had such a large overlap. The final values of precision were as given in Table A3; clearly they are much better for the SSCI searches, where there are very specific words used by authors to characterize their work, than for the SCI/NCI ones, where the subfields overlap.

1 Precision = proportion of the papers retrieved by the filter that are relevant to the subfield; recall = proportion of the papers in the subfield that are retrieved by the filter.

2 For a full description of the process, see: Lewison, G. The definition of biomedical research subfields with title keywords and application to the analysis of research outputs. Submitted to *Research Evaluation.*

Estimates were also made of the degree of recall, based on the fraction of the papers by authors working within each subfield that were retrieved. These are much less satisfactory and only give a rough idea of the coverage of each of the filters. The recall values for CELNE and for MOLNE are particularly low because the objective was to separate these two subfields and avoid papers that spanned both subfields, although the considerably better figures for molecular and cellular combined demonstrate their similarity.

Table A3 Measures of precision and recall.

Subfield	Precision	Recall
CELNE	0.87	0.3
COBEH	0.92	0.5
COGNE	0.86	0.7
DEVNE	0.79	0.6
DRUGB	0.96	0.4
MOLNE	0.75	0.3
MOCEL	0.83	0.8
SYSNE	0.80	0.8

Counts of papers

For each subfield, the papers retrieved were limited to articles, notes and reviews in accordance with normal bibliometric practice for the analysis of substantive research outputs. The numbers of papers from each of the 12 OECD countries were determined for each year from 1988 to 1996 (for the NSI, only the last six years) on the basis of integer counts (i.e. a paper with addresses in both France and the UK would be counted as unity for each). They were plotted as three-year mean values for the percentages of the world total and as papers per million population.

The 12 OECD countries account for around 90 per cent of the world's scientific output in these subfields (it is typically 87 per cent in biomedicine as a whole) and the actual percentages are rising with time, largely because of increased international scientific co-authorship. This varies between the subfields. A measure of it is given by the non-dimensional factor **m**, defined as the ratio of the number of papers with international co-authorships to the total number of papers, where a paper with two countries represented contributes one to the number of international co-authorships, a paper with three countries represented contributes two, and so on. The value of **m** normally increases with time and it is correlated with the research level of the subfield: the more basic the research, the more the amount of international cooperation.

Appendix 3

Table A4 Definitions of research level and journal influence or weighting.

Research level (RL)	**Journal influence or weighting (W)**
1 = clinical observation	1: mean $C_{0\text{-}4}$ < C2; 40% of core journals
2 = clinical mix	2: mean $C_{0\text{-}4}$ > C2; 30% of core journals
3 = clinical investigation	3: mean $C_{0\text{-}4}$ > C3; 20% of core journals
4 = basic research	4: mean $C_{0\text{-}4}$ > C4; 10% of core journals

Research level and journal weighting

In order to characterize the research outputs, the journals in which the papers were published were classified into four categories both on the basis of the type of research they covered (research level, RL) and their influence or weighting (W), as shown by the mean numbers of citations received by their papers over a five-year period (mean $C_{0\text{-}4}$). The table below shows the categorization used.

The values of RL for each journal have been allocated by CHI Research Inc., a specialist bibliometric consultancy company in the USA, on the basis of inspection of the journal by experts and the citation pattern of the papers within it.[3] However, the weighting values need to have regard to the way citations are produced within each subfield. For example, papers in large basic research subfields with many researchers such as genetics will tend to receive more citations than ones in small subfields, especially clinical ones.

The procedure used for the allocation of weights to journals in each subfield was as follows. First, a list was made of all the journals used by researchers worldwide in the subfield over the whole period studied; they were ranked in descending order of frequency of use. From this list, a set of 'core journals' was selected, comprising about 10 per cent of the total but covering about 75–80 per cent of all the papers. The mean citation scores, $C_{0\text{-}4}$, for each of these journals were determined for 1990 papers cited in 1990–94 (these are published by the Institute for Scientific Information), and the core journals were then listed in descending order of mean $C_{0\text{-}4}$ value. The top 10 per cent of core journals were classed as W=4; the next 20 per cent as W=3; the next 30 per cent as W=2; and the bottom 40 per cent as W=1. These percentages were slightly modified if it was possible to detect a noticeable gap in the mean $C_{0\text{-}4}$ values so that the categorization corresponded to a natural division. The critical mean $C_{0\text{-}4}$ values needed for a core journal to receive a weighting of 4, 3 or 2 were then noted (denoting C4, C3 and C2 in the above table) and these were used to allocate weightings to the non-core journals. Table A5 below shows the values of C4, C3 and C2 for each subfield: they give an impression of its size.

3 Narin F, Pinski G and Gee HH (1976) Structure of the biomedical literature. *Journal of the American Society for Information Science* 27(1): 25–45.

Table A5 Critical journal citation scores.

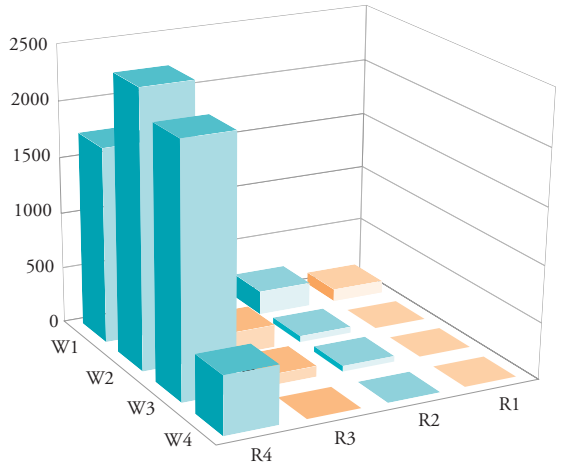
Subfield	C4	C3	C2
CELNE	40.0	16.0	9.8
COBEH	16.0	9.8	5.9
COGNE	17.0	10.3	5.8
DEVNE	50.0	16.9	9.1
DRUGB	13.3	9.1	5.6
MOLNE	40.0	16.5	10.0
MOCEL	40.0	16.4	10.0
SYSNE	16.3	9.5	4.4

There is a clear division between four of the basic science subfields (CELNE, DEVNE and MOLNE and MOCEL) and the two behavioural psychiatry ones (COBEH, DRUGB), with the formers' researchers using journals that are nearly twice as highly cited at the lower levels and nearly three times as highly cited at the top level. However, systems neuroscience (SYSNE) is much less highly cited, probably because it is a relatively new (but rapidly growing) field. Similarly, cognitive neurology has a relatively low citation rate.

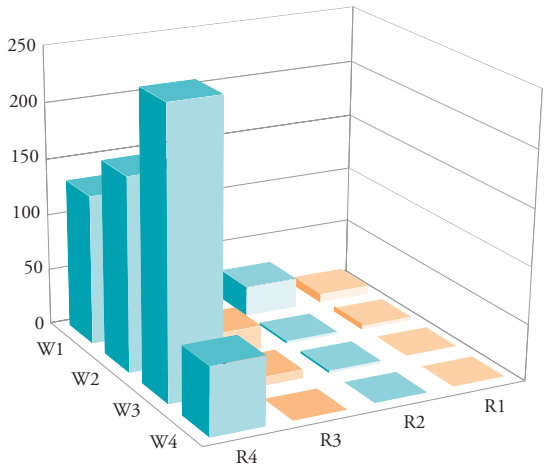
Once the journals had been categorized in this way, it was possible to compare UK output with that of the world in the form of 'carpet plots' showing the numbers of papers in each of the 4×4=16 cells of an RL/W matrix (see Appendix 4). The mean W value of the UK and the world papers gives an indicator of the quality of the UK output. Even if the W values are similar, the distribution of the papers between the four sets of journals may be different and indicate a different research activity and/or publication strategy.

Appendix 4
Distribution of research papers from basic and clinical neuroscience subfields

Developmental neuroscience – distribution of papers (world) according to research level and journal weighting.



Developmental neuroscience – distribution of UK papers according to research level and journal weighting.

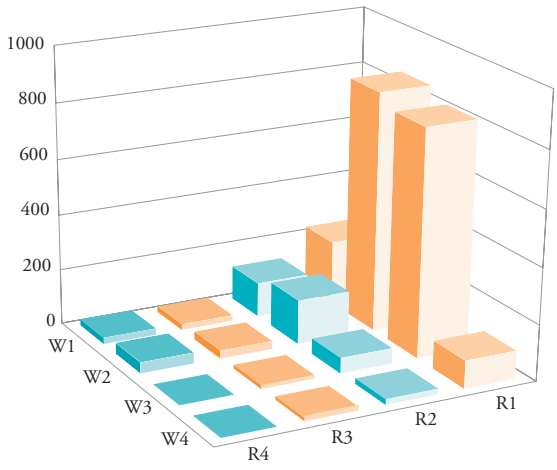


Comparison of weighting of journals for basic research papers for UK and world.

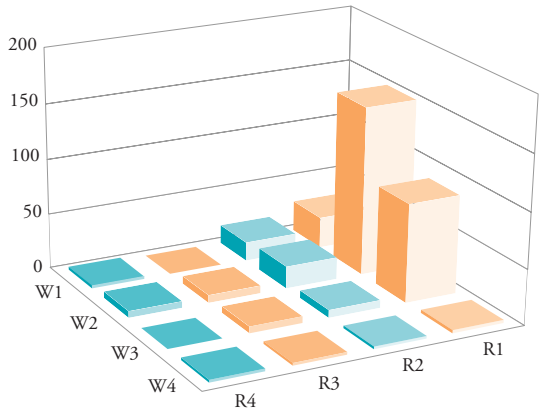
	W=1	W=2	W=3	W=4	Total	Mean
World	1738	2448	2228	520	6934	2.20
UK actual	133	172	253	61	619	2.39
UK pred.	155	218	199	46	619	2.20

Difference between actual and predicted totals significant on χ^2 test with $p < 0.001\%$.

Cognitive behavioural psychiatry – distribution of papers (world) by research level and journal weighting.



Cognitive behavioural psychiatry – distribution of UK papers by research level and journal weighting.



Comparison of weighting of journals for all papers for UK and world.

	W=1	W=2	W=3	W=4	Total	Mean
World	963	1934	909	139	3945	2.06
UK actual	127	326	103	9	565	1.99
UK pred.	138	277	130	20	565	2.06

Difference between actual and predicted totals significant on χ^2 test with $p < 0.01\%$.

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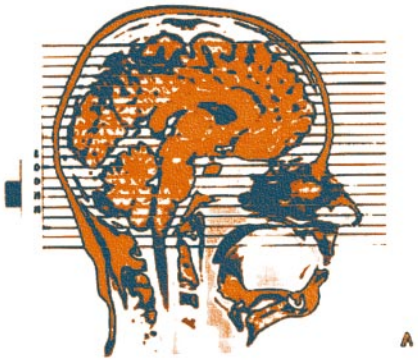
Neuroscience is one of the fastest growing areas of biomedical research. In this report *Neuroscience: An audit of research activity*, prepared by the Wellcome Trust's policy research unit PRISM, the UK's neuroscience research activity in a worldwide context is assessed. Also examined are the barriers that limit research, measures to tackle those obstacles and strategic objectives for future research.



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