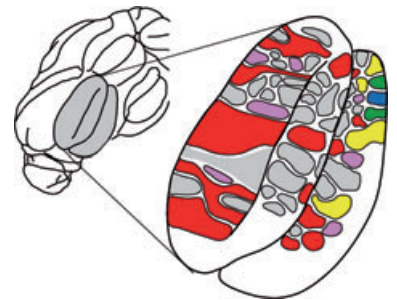
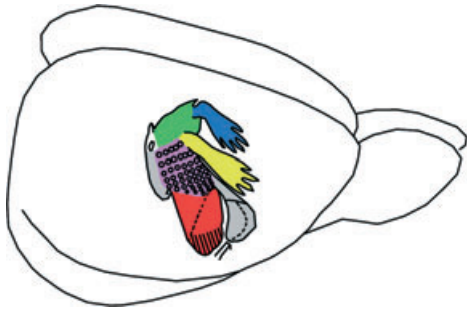


EJN

Volume 24 • Number 10 • November 2006



European Journal of Neuroscience



Blackwell
Publishing

Resource allocation to brain research in Europe – a full report

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Keywords: brain disorders, brain research, cost–benefit, Europe, funding, RABRE

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Executive summary

Background

Brain diseases are all diseases affecting the brain, spinal cord and peripheral nerves, and they include both neurological and psychiatric diseases. Brain research is all research relating to the nervous system

and thus covers the traditional concepts of clinical and basic neuroscience. We have previously assessed the burden of brain diseases in terms of disability-adjusted life years (DALY) and in terms of their economic cost. In Europe, brain diseases account for 35% of the overall disease burden and a conservative estimate of their cost is €386 billion per year. These costs will rise considerably in the coming years due to the ageing European population. One way of curbing this increase and possibly decreasing the cost of brain diseases is to intensify research. More brain research may lead to decreased disease

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Received 7 July 2006, revised 7 September 2006, accepted 14 September 2006

burden, but is also important in itself as it provides better knowledge about normal brain functions such as emotions, aggression, learning and memory. The aim of the present study was to collect information about spending on brain research in Europe and compare this to the burden and cost of brain diseases, research spending in other disease areas, and similar estimates for the US.

Methods

The present study examined all known sources of funding, including government grants as well as charitable and industry funding.

To estimate public spending on brain research across Europe (by both governments and charities), a survey was conducted of primary sources of research funding. This estimate represents the money spent by European institutions, rather than money invested in those institutions, because the latter may include money from outside Europe, for example research funding from the National Institutes of Health (NIH) in the US. Imputations were made for countries with inadequate response rates.

Industry funding was measured by three different approaches: (i) a worldwide survey of pharmaceutical expenditure by disease area; (ii) consideration of the published cost of developing a new drug as applied to the number of new chemical entities (NCEs) launched in Europe in past decades; and (iii) applying the share of drugs for brain diseases that have entered the market between 1985 and 2004 to total research and development (R&D) expenditure by pharmaceutical companies in Europe over the same period.

Furthermore, we assessed the cost–benefit of investment in brain research using different methods.

Results

Total spending on brain research in Europe in 2005 amounted to approximately €4.1 billion, of which €855 million came from the public sector (21% of total funding). Government funding constituted 78% of total public funding while 22% came from charitable foundations. The European pharmaceutical industry spent approximately €3.3 billion on brain research per year (range: €2.7–3.9 billion), corresponding to 79% of the total funding for brain research in Europe. In contrast, in the US, about €6.1 billion came from public sources (93.5% government and 6.5% charities) and €8.4 billion from industry funding (58% of the total funding).

Public funding for brain research varied between European countries, ranging from €60 000 in Malta to €312 million in the UK. Ireland had the highest level of public spending per inhabitant (€6.73), followed by the UK (€5.2) and Hungary (€2.7). The lowest level was found in Latvia (€0.14 per inhabitant). Hungary, the Netherlands, Norway, Sweden and France also had per capita spending above the European average, which was estimated at €1.2.

Fifty-three per cent of the total research spending could be attributed to specific brain disorders. Psychiatric disorders received one-third of investment in brain research while two-thirds went to neurological disorders. In our previous study on the cost of brain disorders, psychiatric disorders accounted for 67% of the overall cost and neurological disorders for 33%. In the present study we found considerable differences between research spending on brain disorders. Affective disorders received total funding of about €600 million, for example, whereas brain tumour received €70 million and traumatic brain injury (TBI) €12 million.

Public funding of brain research amounted to 0.2% of the cost of brain diseases per year and industry funding to 0.8%. Comparing

public research spending to the cost of individual brain diseases, brain tumour received proportionately the most funding, at 0.5% of its cost, while affective disorders and migraine received the least (0.035% and 0.025% of their costs, respectively).

Cancer research in Europe received about €1.5 billion of public funding (50% government and 50% charities) and around €2.5 billion of industry funding. The absolute funding of cancer research is approximately the same as the funding of brain research. However, public funding of brain research is smaller and, more significantly, the cost and burden of brain disease is almost double that of cancer.

Discussion and policy implications

This is the first evaluation of private and public funding of brain research ever to be conducted in Europe. We consider it an important accomplishment to have gathered the necessary information for these purposes. This would hardly have been possible for any single researcher or group of researchers. However, due to the extensive membership network of the European Brain Council (EBC), it was possible to secure cooperation from most countries. The results strongly suggest that funding of brain research must be increased in Europe, particularly public funding.

While these general statements certainly hold true, more precise conclusions must be drawn with care. In total, 71% of the public funding agencies contacted provided adequate responses to the survey, but only 53% of the countries included provided complete data. The imputations made for countries with no or incomplete data are by definition imprecise.

No data from universities were included in the total estimate, although universities make considerable investments, particularly in basic brain research. This was due to lack of data and the risk of double counting. In many cases we encountered difficulties in differentiating between expenditure on brain research and expenditure on other areas, so the imputations may overestimate research funding in some countries. On the other hand, because some organizations may have been omitted, and because we excluded universities, the results could represent an underestimate. Our best (but still highly uncertain) estimate of university-funded brain research is €700–800 million. Even after inclusion of this figure, public funding of brain research remains low compared to the US, and public brain research funding still constitutes only a minute fraction of the cost of brain disorders. Hence, the aforementioned caveats do not alter the overall conclusions.

Industry funding includes development costs as well as research costs. Our figures for industry funding of brain research may therefore be considered by some to be too high. However, both basic and clinical research is needed to bring new medicines to market and to provide the necessary information for their optimal use. In comparison to the US, there seems to be an under-funding of both basic and clinical brain research in the public sector in Europe. We have not been able to document the interaction between publicly and privately funded research, but this is a key factor for success in bringing new therapies to patients.

Several different analyses showed that increasing brain research would bring great benefits. Even using very conservative estimates, a high financial return on increased investment in brain research was predicted. This was true even within a 10-year period, although the benefits of increasing investment in brain research could endure long into the future, providing substantial annual returns. Our findings are in agreement with previous findings for the US.

Conclusions and recommendations

Spending on brain research in Europe, particularly public spending, is low compared to spending on other fields of research such as cancer, and it is particularly low compared to spending on brain research in the US. Increased public investment in brain research in Europe could be highly cost-effective and bring great benefits. The EC's prioritization of brain research in the Seventh Framework Programme is supported by the present data. Each European nation should follow the example of the European Commission (EC) and make the brain one of its research priorities for the years to come. It is important that both basic and clinical research receive adequate funding. Basic research is responsible for the most fundamental breakthroughs and often leads to subsequent paradigm shifts in drug development and patient treatment. Clinical research can direct basic research towards disease-related mechanisms and is instrumental in translating basic research findings into new products and treatments.

Using the same methodologies as in the present study, further studies should be undertaken in each European country to more precisely assess spending on brain research. To facilitate such studies, industry and public funding bodies should group funding for 'brain research' together, including research on stroke, brain tumour, developmental disorders, mental retardation, brain trauma and brain infections. This in turn would enable policymakers to prioritize investment in brain research in the most appropriate way.

Introduction

European research funding in general

Europe has a long tradition as a leader in R&D. Lately, however, it has been falling behind other major economies (Fig. 1). To strengthen R&D in Europe and bring it in line with other major economies, members of the European Union (EU) agreed to the Lisbon Strategy in 2000, which set out several R&D goals for 2010 (Eurostat, 2005b). Today, over halfway through the timeframe of the Lisbon Strategy, Europe is still far behind the US and Japan, in terms of both R&D intensity [i.e. R&D as a percentage of gross domestic product (GDP)] and number of agencies contributing to R&D investment (Eurostat,

2005b). China is also coming up fast from behind, with R&D expenditures of 1.3% of GDP in 2004.

In 2004, industry accounted for just over half of all R&D funding in Europe (54%). This is substantially lower than in both the US and Japan, where the industry contribution is two-thirds and three-quarters, respectively (Eurostat, 2005b). The Lisbon Strategy goal for R&D intensity was set at 3% of GDP, and the share of industry contribution at two-thirds of total investments (Eurostat, 2005b). Europe has an average R&D intensity below 2% today. This relationship between European and international R&D investments also holds true, in general, for biomedical research and, specifically, research productivity (Philipson, 2005). However, the EU and Switzerland still show a specialization in pharmaceuticals and biotechnology, the sector which showed the fastest growth in R&D spending in 2001–2004 [European Federation of Pharmaceutical Industries and Associations (EFPIA), 2006].

European brain research

Europe led in brain research until 10–20 years ago (Murphy & Topel, 2003). For the past decade, however, the US has been and continues to be the leading region in terms of brain research funding. The gap between European and American brain research is widening (Murphy & Topel, 2003). If Europe is to be a competitive region in brain research, this trend must be reversed. More information is therefore needed on resource allocation to brain research in Europe and on the potential benefits to be gained from increasing the funding of brain research.

The 'Cost of Disorders of the Brain' study (Andlin-Sobocki *et al.*, 2005) evaluated the cost of brain disorders in Europe and is a starting point for understanding the economic impact of brain disorders on European society. The study focused on the cost of the 12 most prevalent brain disorders [for definitions see appendix to the present study at <http://www.europeanbraincouncil.org/publications>] and included mental, neurological and neurosurgical disorders. It estimated all costs to society, including healthcare costs (hospital care, ambulatory care and drugs), private and public costs outside the medical sector (nursing home costs and services and goods for private homes) as well as indirect costs (productivity losses due to sick leave, absenteeism and early retirement; Andlin-Sobocki *et al.*, 2005). The study showed that 127 million Europeans suffer from brain disorders, at a cost of €386 billion in 2004 (Andlin-Sobocki *et al.*, 2005). In another study, brain disorders were estimated to constitute 35% of the burden of all diseases in Europe in 2003 (Olesen & Leonardi, 2003). According to the World Health Organization (WHO), mental disorders imposed the highest burden on European society, followed by cardiovascular diseases (CVD) and cancer (Table 1), even though many brain disorders were not included. The burden of disorders was measured in DALY (WHO, 2004).

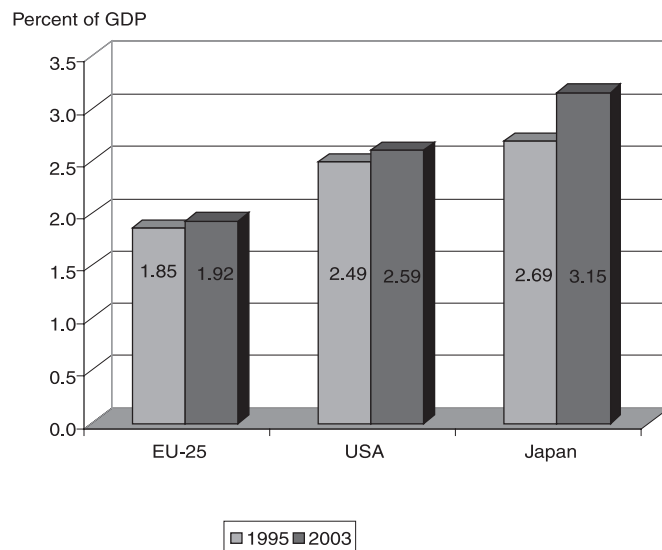


FIG. 1. Gross expenditures in R&D as a percentage of GDP for the EU-25, the US and Japan (1995 and 2003). Source: Eurostat (2005d).

TABLE 1. Top five disease groups in terms of burden of disorders in Europe (2002)

DALY	EU-25 countries			EU-15 countries		
	Total	Per 1000	(%)	Total	Per 1000	(%)
Mental	14 857 720	32.8	25.3	12 379 282	32.7	26.3
CVD	10 088 093	22.2	17.1	7 637 493	20.1	16.2
Cancer	9 839 035	21.7	16.7	7 989 864	21.1	16.9
Injuries	5 099 011	11.2	8.7	3 644 620	9.6	7.7
Respiratory	3 523 243	7.8	5.9	3 167 675	8.4	6.7
All disease groups	58 807 846	129.7	100.0	47 092 868	124.2	100.0

Brain disorders are therefore prevalent and costly to society, yet they receive only 15% of direct healthcare spending (Andlin-Sobocki *et al.*, 2005).

These cost data (Andlin-Sobocki *et al.*, 2005) on the burden of brain disorders support the results of the 1990 WHO/Harvard University Global Burden of Disease Study (Murray & Lopez, 1996), which emphasized the need for new initiatives to ensure optimal treatment of brain disorders, including initiatives in R&D. Today, brain disorders represent the single largest future indication for drug treatment [Centre for Medicines Research International (CMR), 2006]. An important recent initiative for the advancement of brain research was the creation of the EBC in 2002. The EBC unites neurologists, psychiatrists, psychologists, neurosurgeons, basic neuroscientists, patient organizations and industrial researchers with the primary purpose of promoting brain research (European Brain Council, 2006).

It is widely recognized that funds for brain research are important for the development of new therapies and to increase knowledge about brain disorders (Olesen & Leonardi, 2003). However, to our knowledge, no previous study has evaluated the size and nature of funding of brain research in Europe. In the cancer field, however, a survey was carried out in 2003 by the European Cancer Research Managers forum (ECRM; European Commission, 2005a), which estimated the total public funding of cancer research in Europe. For this survey, information was obtained directly from public funding agencies. The present study has adopted methods used in the ECRM study to estimate public funding of brain research. Estimates of industry spending on brain research in Europe have been obtained using methods similar to those used in a previous study (Wilking & Jönsson, 2005), which assessed the size of industry funding of cancer in Europe.

The present study is therefore pioneering because it identifies the major funding agencies of brain research in Europe and evaluates the size of the investments made in this field, as well as the potential benefits. It is our hope that this study will enable further investigation of research activity and the impact of different funding agencies. The primary objective of the study was to provide the best possible estimates of the funding of brain research in Europe. The secondary objective was to assess the potential benefits of increasing investment in brain research.

Publicly funded brain research was defined as investments made in brain research by both government agencies (public institutions) and charities (by the public and transparent to the public). Charitable organizations (organizations for public benefit that rely on donations for financial support) and private not-for-profit organizations (whose securities are not offered to the public) were combined into the term 'charities' to avoid any confusion.

The neurological disorders included in this study are: dementia (including Alzheimer's disease), epilepsy, migraine, multiple sclerosis (MS), Parkinson's disease (PD) and stroke. The two neurosurgical disorders are brain tumour and TBI. The psychiatric disorders are: addiction (alcohol and illicit substance dependence), affective disorders (depression, bipolar disorder), anxiety disorders (panic disorder, generalized anxiety disorder, social phobia, agoraphobia, obsessive-compulsive disorder, any specific phobia) and schizophrenia. As we wanted to estimate total funding of brain research, it was important to include a category known as 'other brain disorders' (e.g. amyotrophic lateral sclerosis, attention-deficit hyperactivity disorder, neurodegenerative disorders, etc.) and 'basic research not related to specific disorders'.

For the purposes of this study, Europe is defined as the EU-25 (all the member states of the European Union) countries plus Norway, Iceland and Switzerland.

Materials and methods

Study design

The present study estimated the funding of brain research in Europe in 2005 and put it in relation to the burden of brain disorders. The study also assessed previous benefits of medical innovation as well as potential future benefits. Data on public funding was collected through a funding survey. The published literature and other available data were also used to assess total investments in brain research from all sectors, and to compare those investments to the current burden of brain disorders.

Although, globally, Europe is at the forefront of investment in research, it is far behind the US. To clarify this imbalance, an international comparison was made. We also wanted to compare brain research funding to funding in another medical field, and chose cancer as the comparative disorder. The assessment of current and future benefits of brain research was illustrated by case studies, as well as by calculations of potential gains in quality of life (QoL) from new treatments.

Data collection

Public funding survey

For the purposes of the public funding survey, the major government and charity funding bodies across Europe were identified and sent a questionnaire, in which they were asked to provide data on their annual direct spending on brain research in 2004. [See appendix to present study at: <http://www.europeanbraincouncil.org/publications> for details about the funding survey method and listing of participants in the survey.] They were also asked to divide their annual spending into disorder-specific categories (plus a category for basic research not related to specific disorders), and to state their organizational classification. Direct research spending was defined as salaries of researchers, laboratory equipment and any consumables and other costs of research.

Follow-up e-mails were sent and multiple phone calls were made to those organizations which did not respond to the initial survey invitation, in order to obtain the requested data. Homepages were also thoroughly searched for financial information when no other contact was established. The absence of any reply or any available financial record of brain research funding on the different organizations' websites was noted in our database, which was structured to provide updatable reports on the data received.

The financial information was reviewed and cross-checked, giving comparable listings across countries and disorders. If the data were given in a currency other than euros, they were converted using average annual rates from Eurostat (2005a). All data presented in this study are in 2005 values, though the data themselves are based on the year 2004 or earlier years if 2004 was not available. The inflation rates used were taken from Eurostat (2005e).

As illustrated in Table 2, adequate financial information was obtained from 161 of the 226 funding agencies identified, giving a total response rate of 71.2%.

TABLE 2. Number of funding organizations and response rate

Funding organization	Number identified	Number of replies	Response rate (%)
Charity	161	113	70.2
Government agency	65	48	73.8
Total	226	161	71.2

The number of organizations identified in each country varied between 0 and 34 (Malta and the UK, respectively), and the response rate between 0% (Poland and Slovenia) and 100% (Hungary, Ireland, Luxembourg and Switzerland).

Industry funding data

Data were collected using three previously published approaches for evaluating industry funding of cancer research (Wilking & Jönsson, 2005).

The first approach to assessing industry spending on brain research was based on the Centre for Medicines Research (CMR) International 2005/2006 Pharmaceutical R&D Factbook (CMR, 2006). This provides a clear picture of evolving trends in worldwide pharmaceutical R&D. Data were derived solely from primary sources that included all major pharmaceutical companies, which account for some 80% of the industry's global R&D spending (CMR, 2006).

In 2002, the European Federation of Pharmaceutical Industries and Associations (EFPIA) highlighted the increasing costs of developing a new drug or NCE over time (DiMasi *et al.*, 2003). In this approach to determining pharmaceutical industry funding for brain research, total spending for each year was obtained by multiplying the number of brain NCEs by the cost of a single NCE in that same year.

The total research investment by pharmaceutical companies in Europe has risen more than seven-fold over the past 20 years, and doubled over the past 10 years, to reach €18 800 million in 2001 as compared to €7800 million in 1990 (EFPIA, 2002). In 2004, research expenditures had increased to €21 100 (EFPIA, 2006). Between 1985 and 2004, 9.54% of all the NCEs that entered the market were drugs for brain diseases. Assuming that this proportion of brain drugs to total NCEs reflects the R&D spending on brain research in Europe, a third measure can be constructed.

Comparative data

Data from the US were mainly obtained from NIH [National Institutes of Health (NIH), 2005], but also from the published literature (Hamilton *et al.*, 2005) and electronic sources [Federal Reserve Bank of New York (Federal Reserve), 2004; Inflation Data, 2005]. Data on the funding of cancer research were taken from the ECRM study (European Commission, 2005a) and the oncology report by Wilking & Jönsson (2005).

Data on burden of disorders

The data on burden of disorders were taken from the published literature written in English. This included disorder-specific QoL estimates (Essink-Bot *et al.*, 1995; Messori *et al.*, 1998; Schrag *et al.*, 2000; Foster *et al.*, 2002; Stein *et al.*, 2002; Prieto *et al.*, 2003; Ravasco *et al.*, 2003; Tengs & Lin, 2003; Andersen *et al.*, 2004; Vles *et al.*, 2005; Kobelt *et al.*, 2006; Sobocki *et al.*, 2006b) as well as prevalence (Andlin-Sobocki *et al.*, 2005) and cost estimates (Andlin-Sobocki *et al.*, 2005; Wilking & Jönsson, 2005) for different disorders. Data for the burden of brain disorders (i.e. cost-of-illness and prevalence) were taken from the final results of the 'Cost of Disorders of the Brain in Europe' study (Andlin-Sobocki *et al.*, 2005). Statistical data were mainly taken from Eurostat (Eurostat, 2005a,c,d,e,f, 2006a,b), but also from NIH (NIH, 2005), the Organization for Economic Co-operation and Development (OECD, 2005), the WHO (WHO, 2004, 2006) and the Federal Reserve Bank (Federal Reserve, 2004).

Method for estimating the size of investments

Public funding

The method used in the ECRM survey (European Commission, 2005a) was used for estimating public brain research spending, i.e. funding agencies were contacted directly and asked to provide data on their research spending. Using this method, research spending from European funding institutions was estimated, rather than total research spending at European research institutions (which might also receive funding from foreign research funding agencies such as NIH). There is no certainty that research spending is spent in Europe, only that it is spent by European institutions. There is no data on the net effect of research funding and research production for Europe, but it is reasonable to assume that it will not significantly affect the estimates. Research funding by European agencies and actual resources used for research will be very closely linked. There are two major reasons for measuring funding and not actual research resources. The first is that it is easier to identify funders and their allocation of expenditures than it is to identify research institutions and their resource allocation. The second is that research funding is more relevant from a public policy perspective, as funding determines the magnitude and direction of research activity.

The results from the funding survey have been corrected for purchasing power by using Eurostat's comparative price level (CPL) index (Eurostat, 2006a), to enable a comparison across European countries. Nevertheless, the data received were rather scarce for some countries due to the poor response rate. To cope with this and to assess a probably more reasonable estimate for the whole of Europe, imputations were made based on the countries whose major funding agencies provided the most comprehensive responses. These were: Austria, Belgium, Denmark, Estonia, Finland, Germany, Hungary, Iceland, Ireland, Luxembourg, Netherlands, Norway, Sweden, Switzerland and the UK. An average of these countries' brain research expenditure per capita was used as a base case for imputing values to the other countries. The imputation index used for the base case was based on the countries' R&D expenditure per capita (Eurostat, 2005c,d,f).

The original indices used in base cases were both altered to have the 15 countries with the most comprehensive responses as references. Sensitivity analyses were made on different types of indices as the basis for the imputations. These include indices based on spending as a percentage of GDP, health expenditure (Eurostat, 2006b; OECD, 2005) and CPL (Eurostat, 2006a) for all countries, as well as for reference countries as bases for indices, with and without outliers.

All results presented over different organizational types and disorders were based on data received from funding agencies. These data were then altered to relate to the total estimate from the imputed values.

Industry funding

The pharmaceutical industry accounts for the overwhelming majority of all industry research funding (CMR, 2006). However, due to lack of data, the exact contribution to brain research funding of industry organizations other than pharmaceutical companies cannot be determined.

The first attempt to assess the spending in Europe on brain research was based on a worldwide survey of pharmaceutical expenditure by disease area (CMR, 2006), assuming the share spent on brain research to be the same in Europe as in the rest of the world. This assessment was used as the comparative estimate to public spending on brain research, because it provides a complete overview of emerging trends in worldwide pharmaceutical R&D. From this estimate, it was possible to narrow down the funding allocated to each brain disorder using the

number of NCEs that have entered the market between 1985 and 2004. [Personal communication with Läkemedelsverket provided the list of all human NCEs that entered the European market over 20 years. The complete list can be provided upon request. See appendix to present study at <http://www.europeanbraincouncil.org/publications> for details on R&D calculations and NCEs.] Data provided by the CMR Factbook were, however, expressed in US\$ for 2004; using the Federal Reserve (2004) data; we therefore obtained the mean of the foreign exchange rate between the US dollar and the Euro in 2004 [an exchange rate of 1.24 US\$/€ was used] and inflated to 2005 values (Inflation Data, 2005). Country-specific estimates of industry funding were calculated using the estimate for industry funding and the distribution of industry R&D spending provided by EFPIA (2006), using the assumption that brain research spending is distributed in the same way as total R&D and that countries for which there are no data have no private R&D.

We then considered the cost of developing a new drug and the number of NCEs that entered the European market, giving an estimate of the industry spending supporting the new drugs entering the European market, regardless of where this money was spent. The NCEs included in this study were those that were specific to a disorder and that had been verified by a panel of experts.

The third method used to assess industry funding of brain research was to estimate total R&D expenditure by pharmaceutical companies in Europe on brain research as a proportion of total research expenditure. This approach highlighted research spending by the European pharmaceutical industry, regardless of whether the spending resulted in products marketed in or beyond the EU.

In the study of industry funding, it was assumed that all drugs listed as brain drugs [see appendix to present study <http://www.europeanbraincouncil.org/publications> for list of NCEs] were used exclusively to treat a specific brain disorder. According to this definition, TBI, also known as closed head injury, did not have any drug.

Method for drawing comparisons with US brain research funding and cancer research funding

The estimate of total funding of brain research in the US was based on a publication by Hamilton *et al.* (2005) and data from NIH (2005). Total US spending on biomedical research and the proportion of spending on biomedical research by NIH and other sectors were analysed (Hamilton *et al.*, 2005). For the present study, it was assumed that the same proportion of spending on research by different sectors was applicable to the brain sector. Based on NIH data for 2004 (NIH, 2005), it was possible to estimate total funding of brain research in the US, inflate it to 2005 values (Inflation Data, 2005) and convert it to Euros (Federal Reserve, 2004). As the US and Europe differ in size of population and GDP, a comparison of spending was made also in relation to these parameters.

The ECRM study (European Commission, 2005a) and the oncology report by Wilking & Jönsson (2005) used very similar methods, which were found to be suitable for supplying comparative data on cancer research spending. Total funding and the relative contribution from different funding bodies to the total were compared for cancer and brain research. The data obtained from the two previous cancer studies (European Commission, 2005a; Wilking & Jönsson, 2005) were for 2003 and were hence inflated to 2005 values using the EU-25 annual average rate of change as provided by Eurostat in the harmonized indices of consumer prices (HICP) (Eurostat, 2005e). To provide a perspective on the relative size of investments in the brain and cancer fields, selected data on the burden of the two groups of disorders

(Olesen & Leonardi, 2003; WHO, 2004, 2006; Andlin-Sobocki *et al.*, 2005; Wilking & Jönsson, 2005) were presented.

Comparison with cost of brain disorders

In the late 1990s the Institute of Medicine was appointed to 'do a comprehensive study of the policies and processes used by NIH to determine funding allocations for biomedical research' (Institute of Medicine, 1998). In the recommendations the Institute of Medicine made to the 'Priority Setting Document' for research funded by NIH, it stressed the importance of considering public health needs. It was stated in the study that NIH should pay greater attention to the burden of illness in assessing priorities for research to meet public health needs.

This type of method is not a full economic evaluation in the strict sense described by Drummond *et al.* (1997); rather, it gives an idea of whether the amount spent on research could be returned through a reduction in the economic cost of brain diseases. In the present study, the burden of brain disorders was compared to funding of research. To illustrate this relationship, calculations were made on disorder-specific research funding as a percentage of the cost of the disorder. The results from the public funding survey of research spending on different groups of disorders were also compared to the equivalent costs.

Assessment of benefits from brain research

Medical improvements and discoveries are generated by investments in medical research. However, it is difficult to identify, measure and value the benefits gained from medical innovations. Several methods were therefore applied to assess the benefit of investments in brain research: (1) by presenting case studies from the published literature in order to illustrate how medical interventions can lead to improvements for different disorders; (2) by illustrating future trends in brain research; and (3) by assessing the equivalent research investment value of the potential QoL increase due to medical innovation.

Individual brain diseases were studied to illustrate the benefits of medical research and development. Medical innovations offer new and hopefully better treatments, increasing QoL and leading to a reduction in the cost of diseases to society. Medical innovations include new technologies for diagnosis, surgical techniques, radiotherapy, psychotherapies, physical therapies and drugs. Drugs constitute the majority of such innovations. New medicines have been shown to improve health and QoL, and to prevent or reduce the risk of illness (e.g. vaccines) (Pharmaceutical Research & Manufacturers of America, 2006). The case studies presented here were therefore chosen to illustrate the effects of new drugs. Data for the different cases were retrieved from the published literature and the cases were selected according to how representative a picture they provided of the effects of medical innovations. Four different disorders were chosen, to illustrate major disease-specific changes due to improved treatments. The present study then expanded on the benefits seen in those specific cases to emphasize the need for further improvements in the future.

In this study, the burden of disorders was expressed in DALY. However, when estimating the value of a potential future benefit, quality-adjusted life years (QALY) were used instead. In DALY, disability and mortality measures are combined whereas, in QALY, QoL measures are combined with mortality measures. The advantage of measuring the benefits of brain research in QALY is that it can easily be compared with all diseases, regardless of their nature (i.e. irrespective of whether the major impact of the disease is on longevity or QoL). Calculations were hence needed to estimate the impact of

brain disorders on QALY. Subsequently, calculations were made to evaluate the equivalent of an increase in QoL and QALY in terms of investment.

The QoL estimates retrieved from the published literature in the English language had to have been obtained using EuroQol in five dimensions (EQ-5D; Richards & de Wit, 2004) for coherence and comparability. [EQ-5D is a short self-report questionnaire designed to measure generic health-related QoL; the five dimensions are: mobility, self-care, usual activity, pain/discomfort and anxiety/depression. Each dimension is measured by one item and scored between 0 and 1 (where 0 equals death and 1 perfect health). It also includes a 0–100 graphic rating scale to measure overall health status, called Visual Analog Scale (EQ-5D VAS).] The disorder-specific estimates were assumed to be representative for the whole European population, even though data were only estimated based on one country. If a mean EQ-5D estimate was not available, the EQ-5D visual analog scale (VAS) was used as a proxy. A potential QoL increase was simply assumed and the QoL value of the increase was multiplied by the prevalence to give the total value of the QoL increase for the whole affected population. As the timeframe was set at 1 year, this estimate would equal the total amount of QALY gained.

To evaluate the QoL increase in monetary terms, we used an estimate of willingness to pay (WTP) for a QALY. According to standard economic principles, WTP for gains in health and longevity is determined by how much changes in life expectancy and QoL affect the discounted present value of lifetime utility, among other factors. Given the life cycle pattern of health, and the survivor function, the expected lifetime utility for a representative individual can then be estimated. Point estimates of the WTP for a QALY range from \$50 000 to \$100 000 in the literature (Goldman *et al.*, 1992), but results from Murphy & Topel (2003) and Johnston *et al.* (2006) show that the value of health benefits for many diseases greatly exceed the investments made, when testing for lower WTP ranges for a QALY. In this study, we assessed the threshold discussion initiated by WHO. The WHO Commission on Macroeconomics and Health (WHO, 2001a) suggested that interventions in undeveloped countries should be considered good value for money if the cost-effectiveness ratio is lower than three times the GDP per capita. The present study uses somewhat different guidelines because it is European and uses QALY as an outcome measure (rather than DALY as in the WHO report). Nevertheless, as discussed by Borgström *et al.* (2006), this should not significantly alter the results and a reasonable level for the WTP could be two times the GDP per capita, or almost €46 000 for Europe.

Results

Total funding of brain research

The total funding of brain research in Europe was estimated at €4.1 billion in 2005, of which the public sector contributes €855 million. Industry therefore invests €3.25 billion in brain research, or 79% of the total funding. The range of industry funding estimates is €2.7 to €3.9 billion. The estimate provided by the CMR, €3.25 billion, was used as the primary comparative estimate (CMR, 2006).

Figure 2 shows the distribution of research spending over groups of brain disorders, plus the investment made in basic research and research on other brain disorders.

Public funding

The results of the public funding survey indicate that total spending by public institutions and charities in Europe in 2005 amounts to an

estimated €855 million, of which the EC contributes €94 million (Fig. 3). The EU-15 countries (the members of the European Union prior to 2005) account for 91% of total spending. Average spending per country was €27 million, with a median of €6.6 million (the EC excluded). However, the absolute spending estimates on brain research varied greatly across countries, from €60 000 to €312 million (Malta and the UK, respectively).

The results of the sensitivity analysis produce a range of estimates between €743 million and €1063 million, depending on which indices were used for imputation and price adjustments.

Spending per capita in Europe was €1.82. The average spending per capita included in the study was €1.28 in all European countries and €1.70 in the EU-15. Figure 4 illustrates European country-specific public brain research spending per capita in 2004. The highest spending per capita was in Ireland, with €6.73 per capita, and the lowest in Latvia, with €0.14 per capita.

Total spending in Europe as a percentage of GDP was 0.008%. The highest spending on brain research as a percentage of GDP was in Hungary, with 0.0215% of GDP, and the lowest in Malta, with 0.0009% of GDP. Average public spending as a percentage of GDP, which was included in the study, was 0.0055% in all European countries and 0.0067% in the EU-15.

Charities accounted for 22% of the total spending reported on brain research in Europe in 2005. It should be noted that the UK's Wellcome Trust spent over €80 million, which is 52.5% of the total reported spending by charities in all of Europe. Table 3 illustrates the top five brain research funding charities. The average reported spending by charities is €688 369 (excluding the Wellcome Trust), and 78% of the charities reported a research spending below €1 million.

The funding body which contributes the most by far, among government agencies, is the group of UK Research Councils [Medical Research Council, 62%; Biotechnology and Biological Sciences Research Council, 26%; Engineering and Physical Sciences Research Council, 9.5%; Economic and Social Research Council, 2.5%], which accounts for €191 million (41.4% of the total reported government funding). Table 4 illustrates the top five brain research funding government agencies. The average reported spending by government agencies was €5.7 million (excluding UK Research Councils), and 40% of the government agencies reported a research spending below €1 million.

Basic research not related to specific disorders accounts for 47% of total spending. Together, the 12 most prevalent brain disorders account for some 39.4% of the total public funding of brain research (Fig. 5). The category 'Other brain disorders' accounts for 13.6% of total spending. By specific disorder, the total public spending ranges from €7 million for migraine to €57 million for dementia, with an average of €28 million per disorder.

Eighty-seven per cent of the funding of basic research not related to specific disorders comes from government agencies.

Mental disorders accounted for 32% of total public spending on disorder-specific research and neurological disorders accounted for 58%. Neurosurgical disorders accounted for 10% of public research spending.

Universities are not included in our analysis because it turned out to be hard for them to account for which resources are invested in brain research. Hence their inclusion would have brought with it a high risk of double-counting the financial resources used for research. Uppsala University in Sweden serves as an example of what research funding at a university looks like. In the university's neuroscience department, about one-third of the research funding comes from external sources such as the Swedish Research Council and various charities. The rest

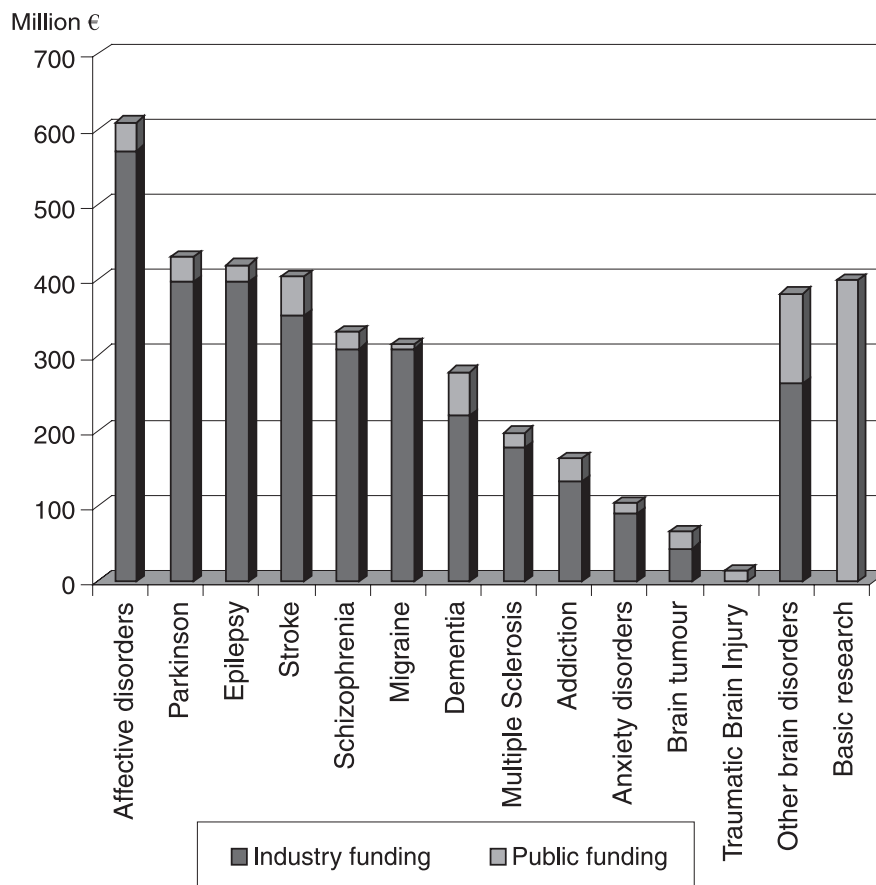


FIG. 2. Distribution of total funding by group of brain disorders in Europe (€ 2005). Note 1: the category 'Other brain disorders' includes all brain disorders that have not specifically been named, such as amyotrophic lateral sclerosis, attention-deficit hyperactivity disorder, neurodegenerative disorders, autism, eating disorders, dyslexia, cerebral palsy and Huntington's disease. Note 2: the disorder-specific categories include both clinical and basic research. The data set does not make it possible to distinguish between the two. The category 'Basic research' includes all basic brain research which is not attributable to specific disorders.

comes from a base grant from the government and from small foundations belonging to the university itself. The total budget for the neuroscience department at Uppsala University is €10 million, €4 million of which come from the base grant and in-house foundations (about half each) for research. According to an internet-based directory of universities (Braintrack, 2006), there are almost 700 universities in Europe today. Many of these are not involved in the medical sciences and not all are funded in the same way or to the same extent as Uppsala University. Nevertheless, if 200 is a fair guess of the number of universities involved in brain research, and if Uppsala University's spending is representative in Western Europe, while Eastern European countries spend half of that, then an additional €700–800 million should be added to the total research spending estimate. However, as we do not know how large the overlap is between university spending on research and the total research spending estimate excluding universities, we have chosen not to include this figure in the base case comparisons.

Industry funding

The three different estimates of industry funding gave a range of €2.7–3.9 billion being invested in brain research per year by the pharmaceutical sector of industry.

In 2004, global pharmaceutical R&D expenditures reached US\$56 billion worldwide, and brain disorders accounted for 15.4%

of total R&D expenditures, or US\$8.6 billion. Europe accounted for about 45.9% of total R&D expenditures in 2004 (CMR, 2006). According to this estimate therefore approximately US\$3.96 billion (€3.2 billion; Federal Reserve, 2004) were spent on brain research in Europe in 2004. We inflated the values to 2005 (Eurostat, 2005e), resulting in a total estimate of €3.3 billion.

Country-specific estimates of industry funding (Fig. 6) were calculated by using the estimate for industry funding and the distribution of industry spending provided by the EFPIA (EFPIA, 2006). As with public funding, there is a big difference in industry funding between the highest and lowest funding countries, ranging from the UK with €737 million to Greece with €5.5 million (note that some countries included in this study have no industry funding registered in the EFPIA report, and hence are assumed not to have any industry funding in brain research either).

Using the next estimate, in which we considered the cost of developing new drugs and the number of NCEs on the European market, we were able to estimate industry spending on brain disorders in a disease-specific way (Table 5 and Fig. 7). [See appendix to the present study at <http://www.europeanbraincouncil.org/publications> for details on NCE calculations.]

Figure 8 shows how industry funding of brain research has varied over the past 10 years.

As shown in Fig. 8, not all brain diseases have seen their research spending increase over time. Indeed, research spending on MS, PD

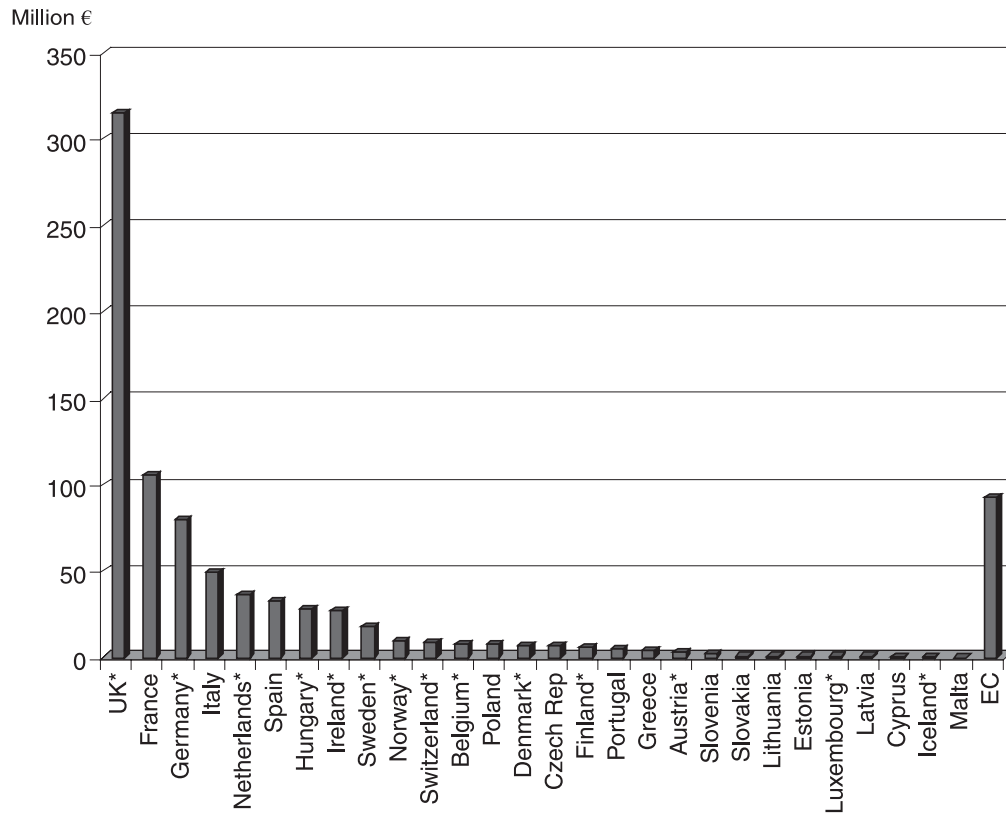


FIG. 3. Public brain research spending by country, including the EC (€ 2005). *Reference countries for imputations.

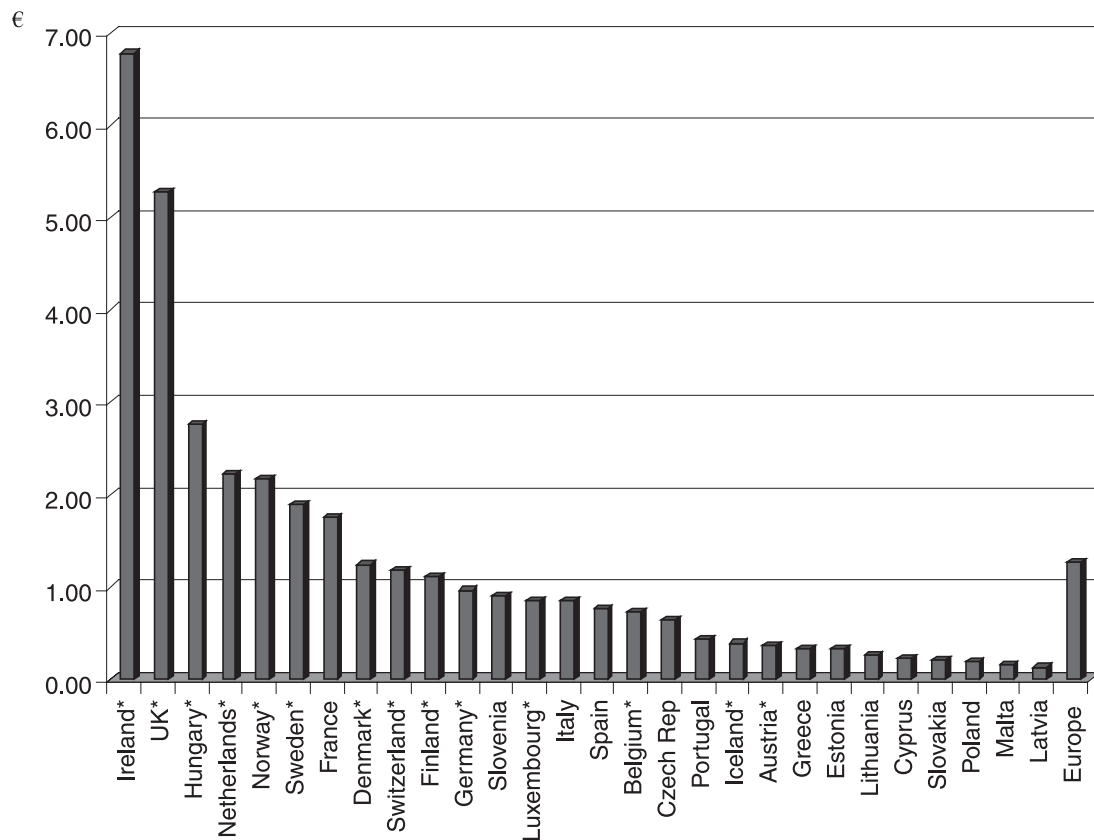


FIG. 4. Country-specific public brain research spending per capita (€ 2005). *Reference countries for imputation. See the appendix to present study for details on spending in reference countries by organization type [<http://www.europeanbraincouncil.org/publications>].

TABLE 3. Top five charities by spending on brain research (2005)

Charity	Spending in €
Wellcome Trust (UK)	80 746 302
The Hertie Foundation (DE)	6 359 860
Volkswagen Stiftung (DE)	4 027 911
Deutsche Krebshilfe (DE)	4 007 560
Parkinson's Disease Society (UK)	3 668 184

TABLE 4. Top five government agencies by spending on brain research (2005)

Government agency	Spending in €
UK Research Councils (UK)	191 100 683
Deutsche Forschungsgemeinschaft (DE)	39 243 442
National Office of Research and Technology (HU)	27 627 787
Ministero della Salute (IT)	26 594 685
Bundesministerium für Bildung und Forschung (DE)	24 876 107

Note: Other agencies which were expected to have a large research spending either reported lower spending than those named, declined to answer the questionnaire or did not respond at all. See the appendix for details on participants and their status in replying at <http://www.europeanbraincouncil.org/publications>.

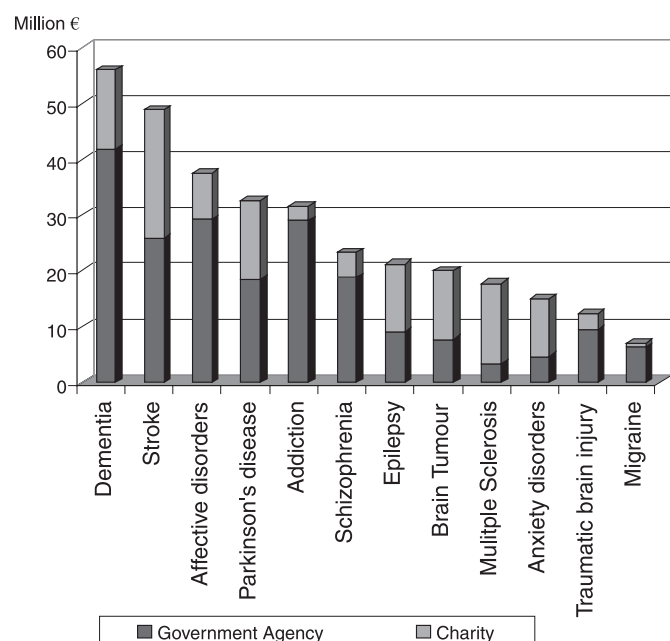


FIG. 5. Public brain research spending by disorder in Europe in (€, 2005).

and stroke has been significantly reduced over the past five years. No funding at all was reported for research on anxiety disorders or TBI.

One potential reason for these discrepancies is the chosen method of estimation, which depends on acceptance of NCEs that have entered the European market during these periods, rather than actual input for research. [See appendix to the present study at <http://www.european-braincouncil.org/publications> for details on calculations of industry funding.] The distribution across disorders also represents previous research investments rather than investments for the year of the NCE's market entrance. As noted earlier, only drugs specific to each brain disorder were used in the present study, and other NCEs related to brain diseases were not taken into account.

Million €

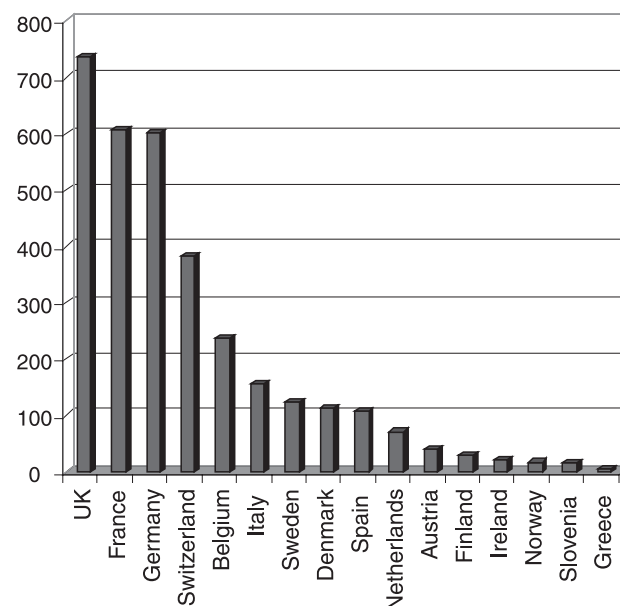


FIG. 6. Industry brain research funding per country (€, 2005). Note: Figures are based on estimates by the EFPIA (EFPIA, 2006) of pharmaceutical industry R&D, assuming that brain research spending is distributed in the same way as total R&D, and that countries for which there are no data have no private R&D.

TABLE 5. Industry funding by disease area in Europe (2005)

Disease area	NCEs (n)	Share (%)	Funding in €
Addiction disorders	3	4.05	131 857 664
Affective disorders	13	17.57	571 383 209
Anxiety disorders	2	2.70	87 905 109
Brain tumour	1	1.35	43 952 555
Dementia (including AD)	5	6.76	219 762 773
Epilepsy	9	12.16	395 572 991
Migraine and other headaches	7	9.46	307 667 882
MS	4	5.41	175 810 218
PD	9	12.16	395 572 991
Stroke	8	10.81	351 620 436
TBI	0	0.00	0
Schizophrenia	7	9.46	307 667 882
Other brain disorders	6	8.11	263 715 327
Total	74		3252 489 033

AD, Alzheimer's disease. Note: the category 'Other brain disorders' includes all brain disorders that have not specifically been named, such as amyotrophic lateral sclerosis, attention-deficit hyperactivity disorder, neurodegenerative disorders, autism, eating disorders, dyslexia, cerebral palsy and Huntington's disease.

In 2002, EFPIA highlighted the increasing costs over time of developing new drugs (EFPIA, 2002). The cost of developing a new drug has been estimated in 1993, 1997 and 2003 at €307 million, €378 million and €895 million, respectively (EFPIA, 2002). This results in a cumulative investment of approximately €37 billion total spending over 19 years (1985–2004) to develop all new brain drugs, an average of almost €2 billion per year. Over the last five years, the estimated average annual spending on brain research by the pharmaceutical industry is about €3.8 billion, or €3.9 billion at 2005 prices (Eurostat, 2005e).

R&D investments by pharmaceutical companies in Europe have doubled over the last 10 years from €7800 million in 1990 to €18 800 million in 2001. Over the last 20 years (see Fig. 9), R&D

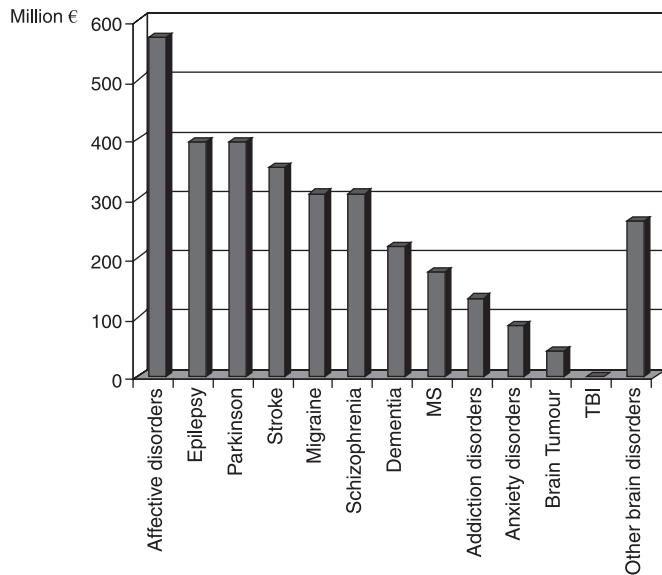


FIG. 7. Industry funding of brain research by disease area in Europe (€, 2005).

spending by pharmaceutical companies in Europe has risen more than seven-fold (EFPIA, 2002). Between 1985 and 2004, 9.54% of all NCEs that entered the market were drugs for brain disorders (74 of 776 NCEs were classified as brain drugs). This means that the R&D expenditure for brain research over 19 years (1985–2004) can be estimated at €28.1 billion, or €2.6 billion per year over the last five years, which is €2.7 billion at 2005 prices (Eurostat, 2005e).

Comparative data

Comparison with the US

In 2003, NIH contributed 67.2% of the total public investments in biomedical research in the US (Hamilton *et al.*, 2005). Total spending

by NIH on brain research in 2004 was US\$4.9 billion (NIH, 2005) or €3.95 billion [Exchange rate 1.2439 US\$/€ (Federal Reserve)]. Total public spending on brain research therefore amounted to almost €5.9 billion for 2004, assuming that the share for brain research of biomedical research outside NIH is the same as it is within NIH. With an inflation rate of 3.39%, spending in 2005 will be €6.1 billion, which should be compared to the public spending in Europe of €855 million. US public funding of brain research is therefore more than seven times European funding (Fig. 10). It should be noted that the US also dominates other medical fields. For example, US public spending on cancer research (NIH, 2005; Hamilton *et al.*, 2005) is more than four times European spending (European Commission, 2005a). In diabetes, US public spending is more than 13 times European public spending (Halban *et al.*, 2006).

We have estimated the European industry funding going to brain research at €3.25 billion, or 79% of the total funding. The corresponding figure for the US is \$8.1 billion, or 58% of the total funding (NIH, 2005; Hamilton *et al.*, 2005). Charities only constitute 6.5% of the total funding from US public institutions, and NIH is the single largest contributor to research, with 28.3% of total funding (67.2% of the funding from public institutions). In Europe, on the other hand, charities contribute 22% of the total funding from public institutions even though, in absolute terms, European charity funding is substantially smaller than charity funding in the US.

When research investments are expressed in relative terms, the US still dominates Europe. In 2004, total spending on brain research as a percentage of GDP was 0.153% in the US, four times the equivalent European estimate of 0.037%. Public spending on brain research per capita was €1.8 in Europe and €20.8 in the US (Eurostat, 2005f; NIH, 2005). When looking at these estimates, the gap between the US and Europe appears larger than when looking at absolute values.

In terms of government spending, NIH outspends Europe in all brain disorder categories by at least four times, except in migraine and anxiety disorders. Total European government spending constitutes 12% of NIH spending on brain research. The largest difference in spending is in addiction and the smallest in epilepsy, although there is a significant difference across all disorders. European government

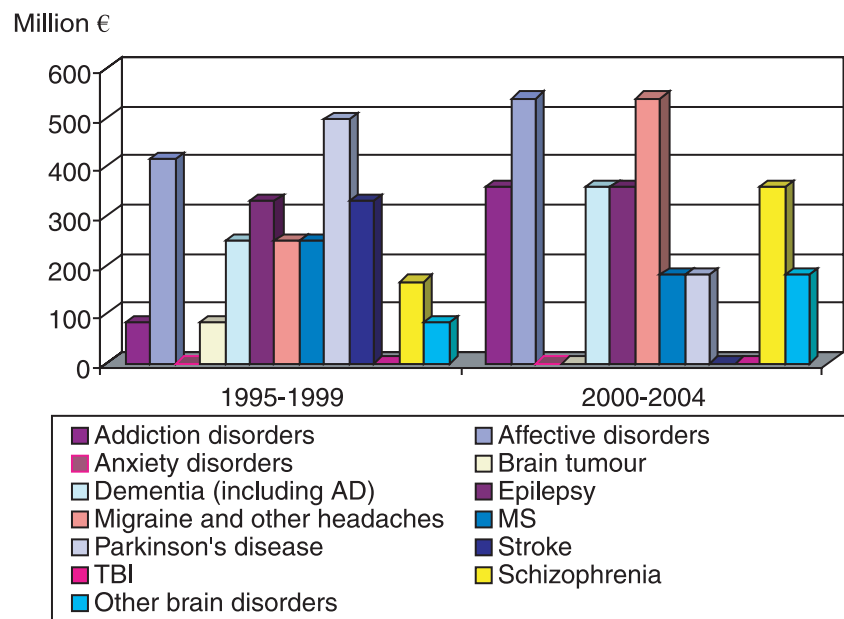


FIG. 8. Annual industry funding of brain research by disease area in € million in Europe with a five-year interval (1985–2004). The 2005 estimate from the CMR Factbook was used and deflated to previous years to obtain the most accurate assessment possible for 1995–99 and 2000–04.

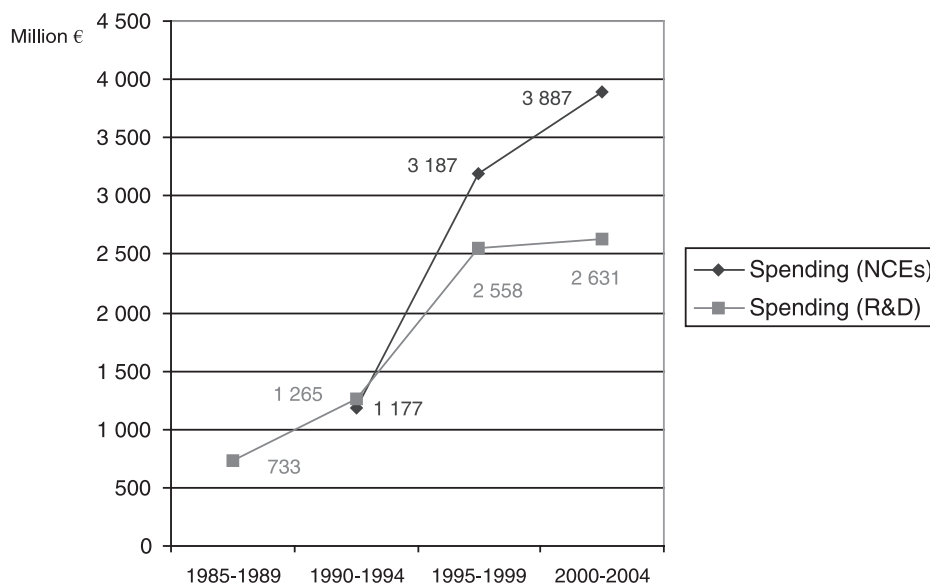


FIG. 9. Industry funding of brain research in Europe estimated by two different methods: (i) from the cost per NCE and number of NCEs for brain disorders introduced per year (blue diamonds); (ii) from the share of total research expenditure in 2004 used for 'brain drugs'.

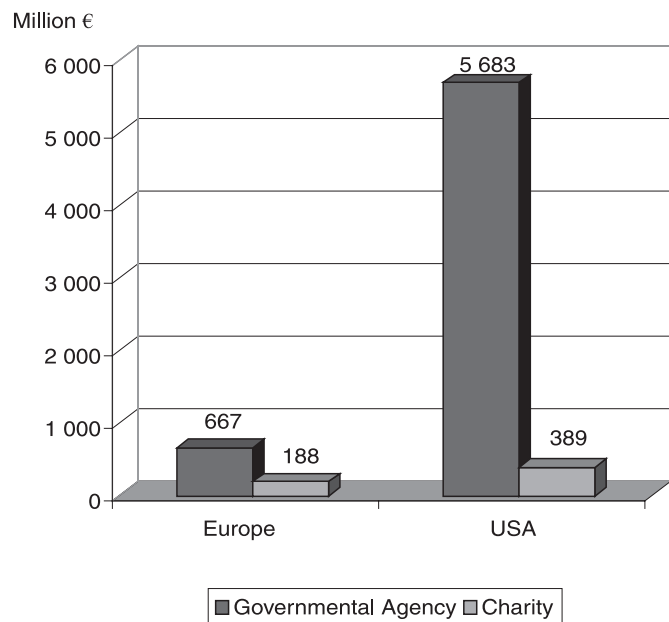


FIG. 10. Europe and the US: comparison of public brain research spending in million Euro (2005).

spending as a percentage of NIH spending by disorder is illustrated in Fig. 11. It should, however, be noted that data for NIH are not exclusive, and could therefore be partly overlapping. According to NIH data (NIH, 2005), research on drug abuse and alcoholism were accounted for separately and their sum exceeded NIH research spending on substance abuse. As there is a risk of overlap in these data, the estimate for substance abuse was used.

Comparison with cancer research

The estimated funding of cancer research and brain research in Europe are strikingly close to each other in terms of total funding (Table 6). However, in relation to total cost of disease and the burden of disease

as measured by DALY lost, funding for brain disease is significantly smaller. The research expenditure per death is significantly higher for brain disorders, as a large portion of the disease burden is attributable to morbidity and not mortality.

Industry funding of brain research (€3.25 billion) is larger than industry funding of cancer research (€2.5 billion; Wilking & Jönsson, 2005), but cancer research claims a higher total public investment. As illustrated in Fig. 12, investment in research by the government sector is almost the same for both. However, cancer charities contribute almost four times more to research than do brain research charities.

Research funding in relation to cost of different brain disorders

The total cost of brain disorders was estimated at €386 billion in 2004 (Andlin-Sobocki *et al.*, 2005). The majority of the costs of brain disorders were indirect costs due to morbidity. A big part of the costs, for example, were due to lost working ability (sick leave and early retirement), particularly in mental disorders such as depression. The costs of social services and informal care were also high, especially in dementia and MS. Mental disorders accounted for 67% of the total costs of brain disorders. The most costly brain disorders were depression, dementia and addiction.

The total funding for brain research estimated in the present study amounts to 1% of the total cost of brain disorders (Andlin-Sobocki *et al.*, 2005). Public funding makes up 0.2% of the total cost of brain disorders, and industry funding 0.8%. Figures 13 and 14 illustrate the relationship between public spending and the costs of brain disorders. For the specific disorders, the range is 0.02–0.5% of the costs (migraine and brain tumour, respectively). Brain tumour and TBI are relatively rare compared to other brain disorders, but very costly per case. Migraine and mental disorders (affective disorders, anxiety disorders, addiction and schizophrenia) are common and represent a heavy monetary burden on society, but receive less public funding relatively.

The range for industry funding is 0.2–3.6% of the costs (anxiety disorders and PD, respectively). [TBI is not included in these calculations as there is no industry funding attributable to this disorder.] Mental disorders and dementia are the least funded disorders

TABLE 6. Research funding, costs, deaths and burden of cancer compared to brain disorders in Europe (2005)

Disorder	Burden of disease				Funding relative to burden		
	Funding (million €)	Costs (million €)	Deaths due to disease (2002)	DALYs lost	Funding/cost (%)	Funding per death (€)	Funding per DALY (€)
Cancer	3 996 ^{a,f}	226 486 ^a	1190 295 ^c	9 839 035 ^d	2	3 357	406
Brain disorders	4 107	389 364 ^b	687 170 ^c	20 582 746 ^{d,e}	1	5 977	200

The cost estimates are based on 19 European countries as stated in Wilking & Jönsson (2005) for comparability. The cancer cost estimate assumes that indirect costs are three times the direct costs, giving a relatively high estimate (see Discussion in Wilking & Jönsson, 2005). The cost estimate is also inflated to 2005 year values. The death estimates exclude Cyprus. Source references: ^aWilking & Jönsson (2005); ^bAndlin-Sobocki *et al.*, 2005; ^cWorld Health Organization (2006); ^dWorld Health Organization (2004); ^eOlesen & Leonardi (2003); ^fEuropean Commission (2005).

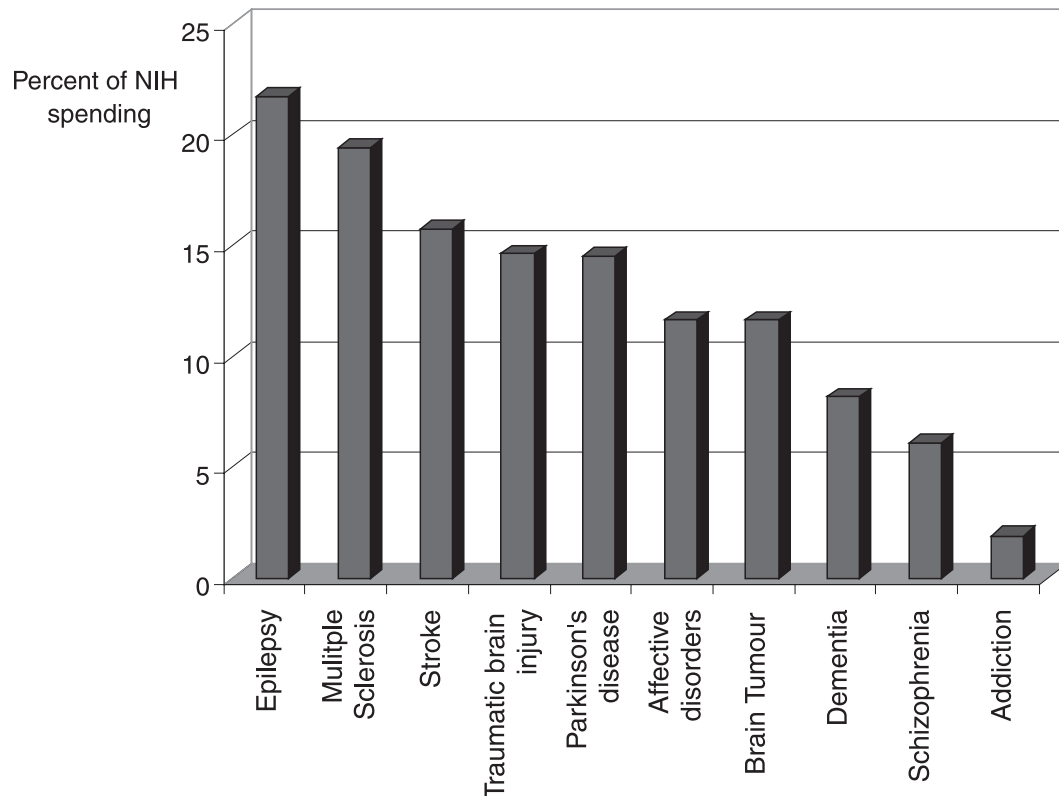


FIG. 11. European government brain research spending as a percentage of NIH spending (2005). Source: NIH (2005). NIH spending on migraine and anxiety disorders was not included in the dataset and, hence, left out of this comparison.

in terms of industry funding in relation to their societal cost. PD and epilepsy receive the most funding from industry, relative to their cost to society, followed by MS and stroke. In absolute terms, affective disorders is the group of disorders that receives most funding from industry in Europe, at €571 million. Epilepsy and PD both get almost €400 million. Least funding, in absolute terms, is dedicated to anxiety disorders and brain tumour.

Mental disorders account for 69% of the total cost of brain disorders in Europe, whereas the public spending on mental disorders accounts for 32% of the total (Fig. 14). For neurological diseases the pattern is the reverse: they account for 29% of the costs but receive almost 60% of the public funding. Neurosurgical diseases (brain tumour and TBI) account for 2% of the total cost of brain disorders and receive 10% of the total public funding. Industry funding shows a similar pattern, except for neurosurgical disorders which only account for 1% of the funding. Mental disorders receive 37% and neurological disorders 62% of total industrial funding, respectively.

Benefits from brain research

Benefits from medical innovation in the past

The following are examples of specific benefits obtained from medical innovation in the area of brain diseases. Four disease areas have been chosen to illustrate how, in the past, medical innovation has improved the situation both for the patient and for society.

Reduced burden on community and caregivers. Many people afflicted with a brain disease are dependent not only on formal healthcare, such as that provided by physicians and specialists, but also on community care and informal caregivers (e.g. partners, family and friends). Dementia is a good example of a brain disease where community and informal care are important components of the cost of the disease (Jonsson, 2003). These caregivers become increasingly important as dementia progresses to severe states (Jonsson, 2003). Andlin-Sobocki *et al.* (2005) showed that the majority of the total estimated costs of

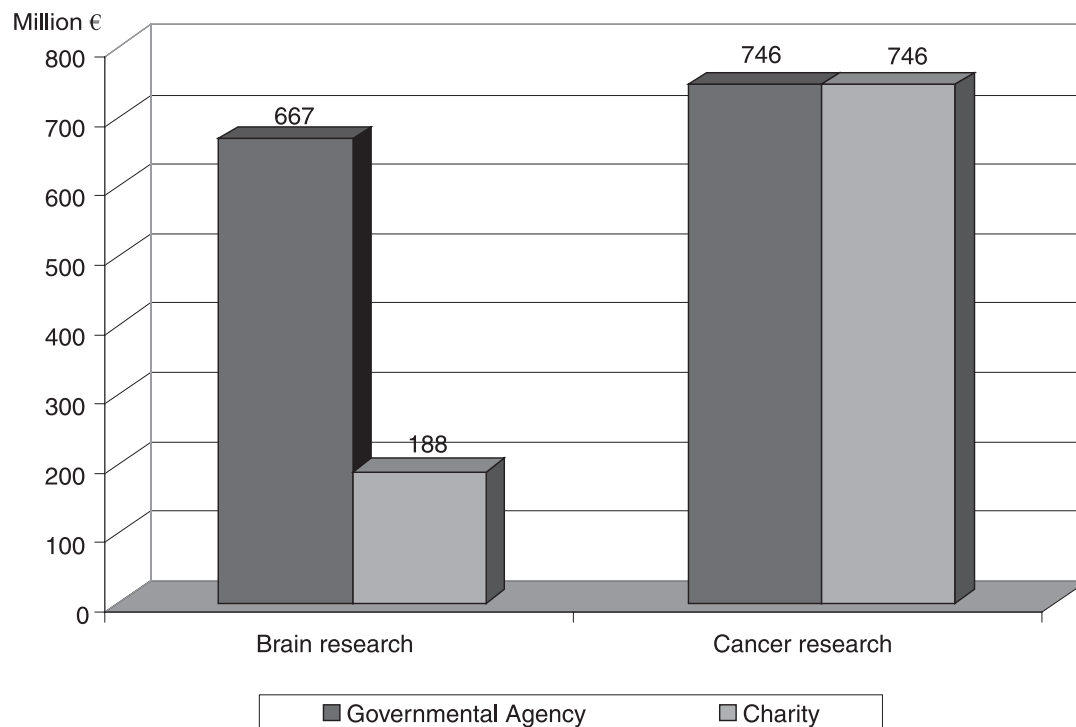


FIG. 12. Public funding of brain and cancer research in million Euro in Europe (2005). Source: Public cancer research funding figures (European Commission, 2005a); industry cancer research funding figures (European Commission, 2005a; Wilking & Jönsson, 2005). Cancer estimates were for 2003 and are hence inflated to 2005 values.

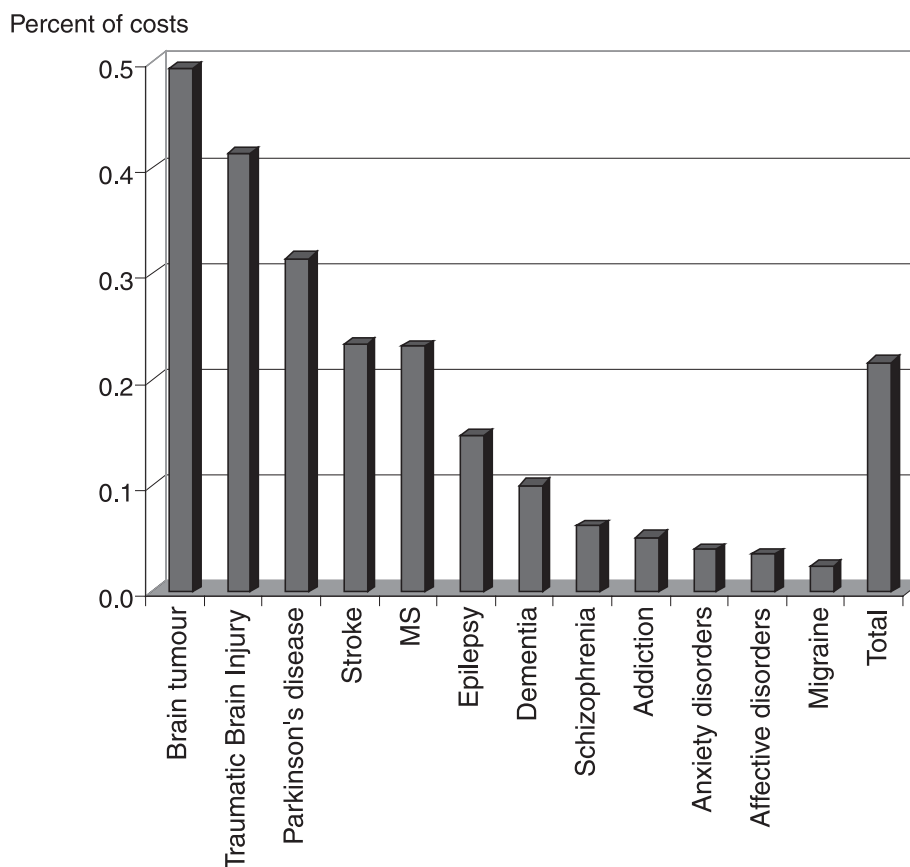


FIG. 13. Public brain research funding as a percentage of costs by brain disorder (2005). 'Total' represents the total estimate of public funding of brain research.

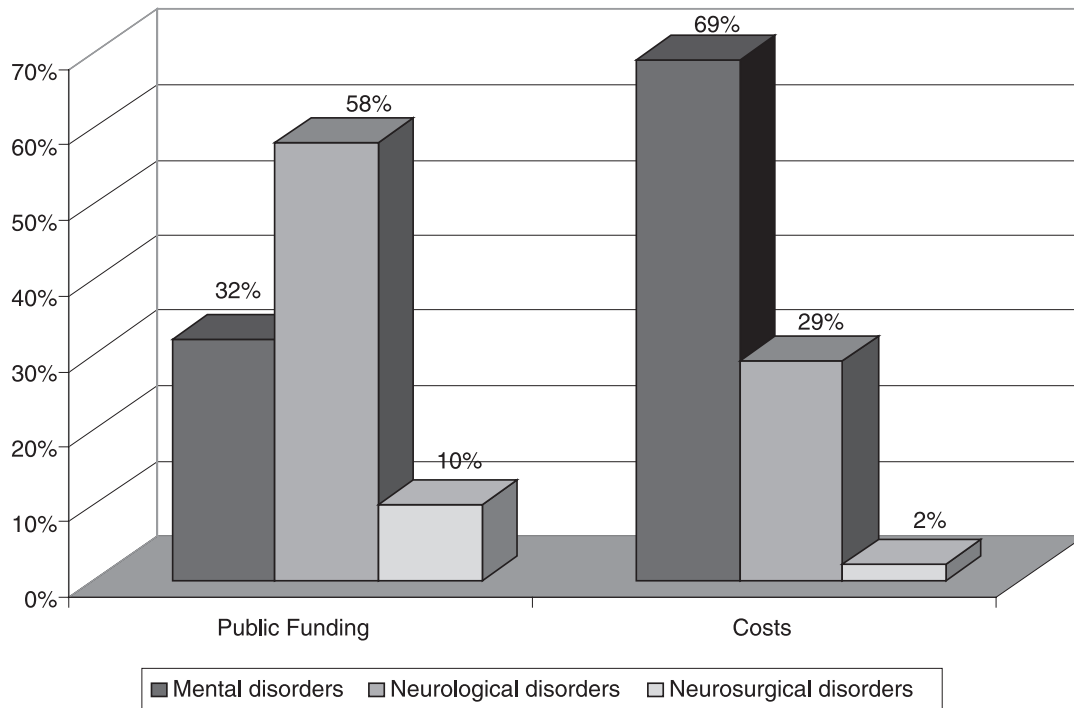


FIG. 14. Division of spending and costs by group of disorders (2005).

dementia in Europe, €55 billion, were due to community care and informal care. These accounted for 56 and 20% of the total cost, respectively, or €41 billion together (Fig. 15).

A number of new drugs have become available for the treatment of dementia. Cholinesterase inhibitors (donepezil, rivastigmine and galantamine) have entered the market in recent years. They can help improve the cognitive function and behaviour of patients, and may delay the progression of dementia (Jonsson, 2003). The most recent medical innovation is memantine, an NMDA receptor antagonist. Model assessments have indicated that cholinesterase inhibitors could decrease the cost for the community and informal care of demented persons (Jonsson, 2003, 2005; Wimo *et al.*, 2003), and also delay the costs relating to later stages of the disease (e.g. costs associated with

institutionalization). Moreover, a number of studies have shown that these new medical technologies are cost-effective if not even cost-saving compared to giving no treatment. Economic evaluations of these drugs indicate that there are potential offsets in terms of community care costs and reductions in caregiver time (Wimo *et al.*, 2003). At the present time, however, there is no treatment that stops the progression of dementia. In summary, there is a growing body of evidence suggesting that new treatments are often connected with substantial cost savings, especially in terms of community and informal care.

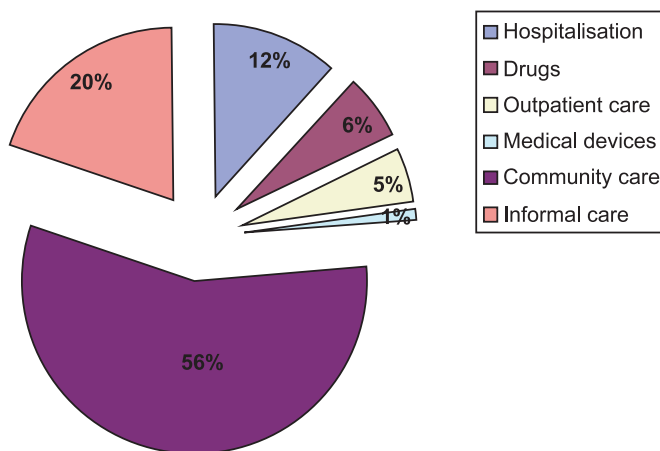


FIG. 15. Distribution of the cost of dementia in Europe. Source: Andlin-Sobocki *et al.* (2005).

Improved working ability. Most brain disorders start at an early age and have a significant impact on a person's ability to work. The cost of loss of productivity and mortality due to brain disorders has been estimated at almost €80 billion per year in Europe (Sobocki *et al.*, 2006c), or almost half the total cost of those disorders. Depression is a good example of a disease which disables the patient for long periods of time and makes it difficult for him or her to remain in the workforce (Paykel *et al.*, 2005). Moreover, depression has a lifelong recurrent or chronic course (Paykel *et al.*, 2005), which may lead to long-lasting absence from the workforce or even early retirement. Sobocki *et al.* (2006a) found that depressed patients have, on average, 1.5 months of sick leave during a depressive episode, which represents a six-monthly cost of almost €4000. There were statistically significant reductions in number of sick leave days and related costs for patients who had been successfully treated to remission (Sobocki *et al.*, 2006a).

In the last decade, a range of new antidepressants has become available which has changed the outlook for depressed patients. A convincing number of studies now suggests that antidepressants are cost-effective (particularly the selective serotonin re-uptake inhibitors and newer antidepressants) in reducing the burden of depression (Barrett *et al.*, 2005). Recent studies also indicate that these new

therapies are associated with substantial savings in terms of reduced productivity loss (Simon *et al.*, 2000; Peveler *et al.*, 2005; Sobocki *et al.*, 2006a). Sobocki *et al.* (2006a) have shown that more than half of patients achieve remission from a depressive episode through treatment with selective serotonin re-uptake inhibitors over a six-month period, and that statistically significant reductions in costs due to sick leave are observed. The same authors have estimated the cost saving to be in the range of €2000 per successfully treated patient. This finding is in line with previous findings in the literature (Simon *et al.*, 2000). Hence there are strong indications from the literature that medical innovations for treating depression have improved the chances that patients will return to employment faster, and so reduced the cost of the disease.

Improved health-related quality of life. Brain disorders have an enormous impact on health-related quality of life which is often neglected when the cost of the disease is estimated (Andlin-Sobocki *et al.*, 2005). MS is an example of a brain disease with a substantial impact on a patient's daily living and QoL (Kobelt, 2004). MS, which affects people early in life and often leads to severe functional disability, is the second most common cause of neurological disability in young adults (Kobelt, 2004).

Health-related quality of life is defined as the impact on an individual's well-being of his or her health, and it often encompasses physical, mental and psychological elements (Kobelt, 2002). Disability from MS reduces QoL (Kobelt *et al.*, 2006) as patients frequently have to endure health problems such as bodily pain as well as low vitality. This negative effect on patients' ability to perform normal daily activities leads to a significantly lower QoL (Kobelt, 2003). Measures with the generic EQ-5D instrument (EuroQol-Group, 1990) show that patients with severe MS (i.e. wheelchair-bound) rate their own QoL as reduced by more than half compared to a person with perfect health (Kobelt *et al.*, 2006), whereas QoL ratings of patients with the mildest forms of MS are closer to those of the general population. Hence, there are substantial gains to be made in terms of disability and QoL by slowing the progression of the disease, even if it cannot be stopped entirely.

In terms of medical innovation in MS treatment, there has been a breakthrough with the introduction of interferons. Interferon treatments are associated with significant delays in the time to confirmed progression of MS (Kappos *et al.*, 1998; Kobelt *et al.*, 2000, 2002). Although they are expensive, there is growing evidence that interferons are cost-effective in the management of MS patients (Kobelt *et al.*, 2000, 2002).

TABLE 7. Therapeutic area breakdown of active substances in development for first launch in Europe (2004)

Therapeutic area	Percentage (%)
Nervous system	22.5
Oncology and immunomodulators	18.3
Alimentary and metabolism	13.0
Cardiac	9.3
Musculoskeletal	8.8
Respiratory	8.1
Anti-infectives	7.8
Blood	3.9
Other*	8.3

Source: CMR Factbook (CMR, 2006), chapter 4, page 42. *Includes GU/sex hormones (4.8%), dermatological (1.3%), sensory (1.1%), antiparasitics (0.8%) and hormones (0.3%).

Future treatments and benefits of research investments

The CMR Factbook presented the proportion of all active substances in development by therapeutic area in 2004, for a total of 841 drugs (CMR, 2006). Drugs were allocated to therapeutic areas based on the indication under investigation, using the WHO's anatomical therapeutic chemical classification system (ATC codes). The analysis excluded drugs for which the mode of action was not provided. Table 7 illustrates the percentage of drugs in the developmental pipeline by therapeutic area.

The top five therapeutic areas in terms of the number of active substances in the pipeline are the central nervous system (CNS), oncology, alimentary and metabolism, CVD and musculoskeletal diseases. Together they account for 70% of all drugs in development (CMR, 2006), the leading therapeutic area being the CNS with 22.5%.

Figure 16 illustrates the number of brain drugs that entered a specified stage of development in a given year (CMR, 2006). The preclinical phase covers active substances between the 'first toxicity dose' and the 'first human dose', phase I between the 'first human dose' and the 'first patient dose', phase II between the 'first patient dose' and the 'first pivotal dose', phase III between the 'first pivotal dose' and the 'first submission', and finally the regulatory review between 'first submission' and 'first approval' (CMR, 2006).

The last three years have seen a considerable increase in the number of new brain drugs entering phase I, while the number of brain drugs entering phase II has remained relatively constant.

The data provided in this report demonstrate that more patients in Europe are being diagnosed with a brain disorder (WHO, 2004), but the mortality rates due to brain disorders are not as high (WHO, 2006). This indicates that more patients are living longer with the disease. In the light of this, it is clearly in a patient's best interests that innovative drug therapies should be made available as soon as possible after market authorization.

A number of treatments for brain disorders are under investigation. Clinical trials testing potential therapies are under way and other new treatments are being devised and tested. It is likely that many of these new brain drugs will be valuable tools for the medical treatment of brain diseases for many years after their patents have expired. We must remember that, for many of the drugs introduced just a decade or two ago, the patents will expire in the near future or generic versions are already available. According to the IMS LifeCycle Patent Focus (Class, 2004), for example, six major drugs are set to lose their US patent protection by 2007.

New therapies could save lives and improve the QoL of patients. However, it is hard to evaluate the benefits of medical innovation in general terms. Table 8 illustrates how much an increase in QoL for the European population affected by a brain disorder would equal in terms of research investment.

If we were able to improve the health status of all those affected by a brain disorder by 5% in a given year, this would amount to €180 billion in monetary terms. This value of increased QoL is only for one year and hence represents a minimum value of increased QoL (due to annuity being ignored in calculations). It is highly possible that the benefits of these improvements will prevail in the years to come. As the time for developing a new drug is approximately 10 years (EFPIA, 2002), the estimated value of the benefits would equal the yearly investments in brain research of €18 billion, which is to be compared to the total estimate of research funding in this present study of €4.1 billion. The results show that the value of this QoL increase exceeds the investment in research even at a lower WTP.

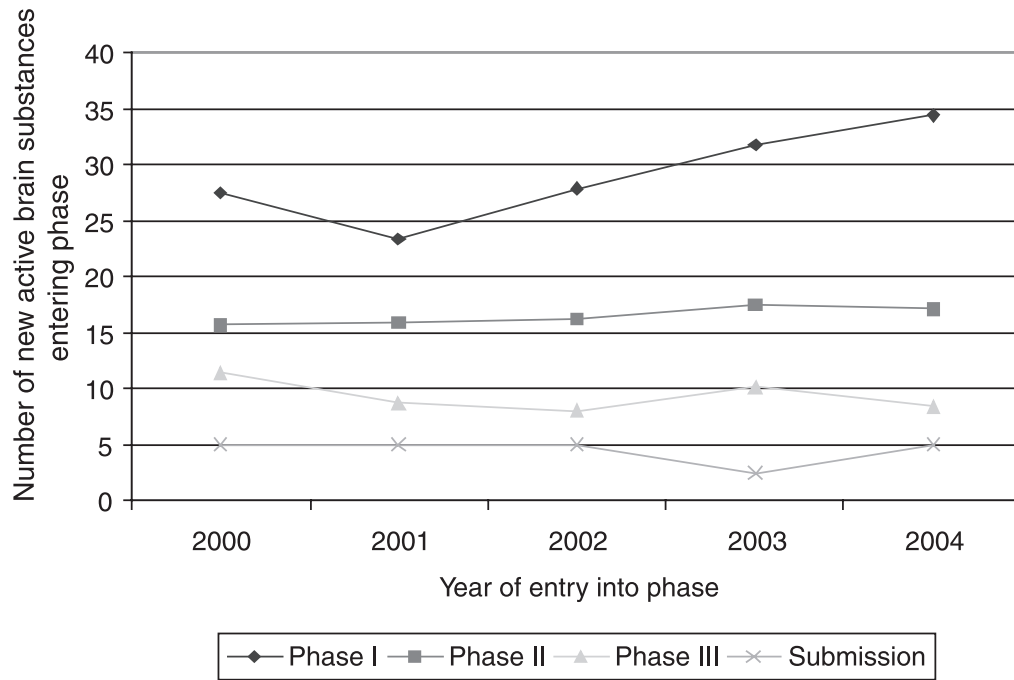


FIG. 16. Number of brain drugs entering each phase of development in Europe (2000–04). The number of brain drugs in each phase has been estimated from the total number of active substances entering each phase of development (2000–04), assuming that brain drugs constitute 22.5% of the total (CMR, 2006).

TABLE 8. QoL and QALY estimates per disorder in Europe

Disorder	QoL	Prevalence ^m	QALY gained at 5% improvement in QoL	WTP for 5% improvement in QoL
Addiction	0.43 ^a	9 194 244	197 676	9 021 797 054
Affective disorders	0.47 ^b	20 857 669	490 155	22 370 320 784
Anxiety disorders*	0.59 ^c	41 407 747	1 221 529	55 749 658 001
Brain tumour	0.66 ^d	135 251	4 463	203 700 812
Dementia	0.62 ^e	4 886 252	150 334	6 861 153 801
Epilepsy	0.78 ^f	2 690 608	104 934	4 789 097 033
Migraine*	0.77 ^g	40 777 009	1 569 915	71 649 750 770
MS	0.59 ^h	379 599	11 108	506 942 289
PD	0.54 ⁱ	1 158 990	31 293	1 428 177 415
Schizophrenia	0.52 ^j	3 687 173	95 867	4 375 276 323
Stroke	0.69 ^k	1 128 986	38 950	1 777 649 845
TBI	0.76 ^l	708 954	26 940	1 229 532 643
Total			3 943 163	179 963 056 771

*Estimated with EQ-5D visual analog scale, ^aFoster *et al.* (2002), ^bSobocki *et al.* (2006b), ^cStein *et al.* (2002), ^dRavasco *et al.* (2003), ^eAndersen *et al.* (2004), ^fMessori *et al.* (1998), ^gEssink-Bot *et al.* (1995), ^hKobelt *et al.* (2006), ⁱSchrag *et al.* (2000), ^jPrieto *et al.* (2003), ^kTengs & Lin (2003), ^lVles *et al.* (2005), ^mAndlin-Sobocki *et al.* (2005). Note: The QoL estimate is the value when affected by a brain disorder, i.e. the QoL is reduced to this specific estimate. The prevalence is for 2004 (Andlin-Sobocki *et al.*, 2005). Calculations are based on a 5% increase in the QoL estimates, which have been multiplied by the prevalence to obtain the amount of QALY gained from this QoL improvement. WTP for an additional QALY was set to almost €46 000, which gave a total value of the QoL improvement.

Discussion

Main findings

The estimate of the total spending on brain research in Europe in 2005 was €4.1 billion. Total public funding by government agencies and

charities was €855 million, of which charity funding accounted for 22%. Fifty-three per cent of the public investment went to disorder-specific research. Sensitivity analysis of the estimations of public funding gave a range between €743 million and €1063 million. These figures potentially excluded university funding; including university funding in public funding would result in estimates up to €1.8 billion (neglecting the risk of double counting). Industry funding constituted 79% of the total funding. For all industries and R&D fields, the industry contribution was 54%. Industry funding of brain research was estimated at €3.3 billion, with a range from €2.7 to €3.9 billion.

Our results indicate that research funding is differently distributed across the specific brain disorders. Research on TBI receives the least funding and affective disorders the most (50 times that of TBI). Much evidence supports the finding that brain disorders impose a great burden on society and that brain research funding is nowhere near the costs of these disorders. Public investment in brain research has been shown to be particularly low, constituting 0.2% of the total cost of brain disorders. It is also low compared to investment in cancer research, and extremely low compared to the brain research funding in the US.

Our assessments show that large benefits have been gained from brain research over recent decades, both for individual patients and for society as a whole. There are indications that further investment would produce even greater benefits.

Methodological aspects

Estimating public funding of brain research

The method of using a funding survey to estimate public funding of brain research has previously been used successfully (European Commission, 2005a) in the cancer field. The results from the cancer study were therefore directly comparable to the results of the present study. We chose to collect information on funding for brain research

directly from the primary sources of funding. There are two major reasons for measuring funding and not actual research resources. The first is that it is easier to identify funders and their allocation of expenditure than it is to identify research institutions and their resource allocation. The second is that research funding is more relevant from a public policy perspective, as funding determines the magnitude and direction of research activity.

The method employed imposed a challenge in coping with missing data. Values were imputed for countries whose major funding agencies yielded an unsatisfactory response rate, to produce the best possible estimate of total funding of brain research in Europe. Country-specific data are therefore uncertain for many countries and should be interpreted with caution. Nevertheless, the present study provides a unique insight into the public funding of brain research and highlights a need for further national investigations to more adequately account for national spending in this area.

The public estimate used in the comparative analysis is probably the most accurate one, as it takes into account the CPLs for the reference countries and the level of the respective countries' spending on R&D in general. The imputations might over-estimate countries' spending, but it is also possible that the estimates on which they are based have been underestimated, as some funding organizations may have been overlooked (see Discussion on missing data).

Funding data broken down by disorder should be treated with caution. Approximately 80% of the funding agencies were able to break down their spending by disorder, but the rest did not keep such records. Moreover, many charities and government agencies distribute their research grants by application competition, so that the spread across disorders and sciences is different each year. Many funding agencies also stated that their investments in brain research are to increase in coming years. For example, some of the organizations identified made their first investment in brain research later than 2004 and were therefore not included.

Estimating industry funding of brain research

Three different methods were used to assess industry funding of brain research, and to provide the best possible estimates. The second estimate of industry funding of brain research was based on new drugs coming onto the European market between 1985 and 2004, regardless of where this money was spent, and reflects earlier spending. The third approach highlighted research spending by the European pharmaceutical industry, regardless of whether this funding resulted in products marketed beyond the EU, and the comparative figure was taken from the CMR International Factbook 2005/2006 (CMR, 2006). The CMR data were derived from primary sources and give a clear picture of upcoming trends in worldwide pharmaceutical R&D.

The share of industry research devoted to the brain has increased over time (as has the share of all health economic publications devoted to brain disorders). This suggests that our estimates of industry brain research funding are too low. On the other hand, not all drug development costs are for research, suggesting that our estimates are too high.

Using data on NCEs entering the European market between 1985 and 2004, an estimate of funding of each of the 12 most prevalent brain disorders was obtained. It should be noted, however, that only NCEs whose main therapeutic application was for a specific brain disorder were selected, and not all new drugs registered during that period were included. The spread of industry funding over disorders is therefore an average based on previous years. It is also important to note that the amount of time and the cost involved in developing new drugs varies across therapeutic areas.

Measuring the gains of brain research funding

The funding of brain research in relation to the cost of brain disorders was investigated. Though research funding may have been underestimated, total research investment constitutes a small fraction of the total cost of brain disorders (1%).

There is a methodological challenge in fully assessing the benefits of medical research at a general population level, particularly in the field of brain research where the range of disorders is broad and patient-level benefits are measured in terms of morbidity rather than mortality. Earlier studies have investigated gains from medical research in terms of mortality and QALY gains (Murphy & Topel, 2003; Johnston *et al.*, 2006). For our purposes, different methods were chosen to illustrate historic gains from investments in brain research. First, illustrations were given of key benefits in specific brain disorders due to medical innovation. We chose substantial gains that have already been seen, to indicate that future innovations could potentially produce similar benefits. With an ageing population and people living longer, the importance of such innovations cannot be over-emphasized.

The WTP for increased QoL was also calculated, to see how much a given increase would represent in investment terms. Though the results from this assessment should be interpreted with caution, they indicate that current investments are substantially lower than the WTP for a 5% QoL increase.

Missing data on public and industry spending on brain research

Through the public funding survey, European funding agencies were directly contacted and asked to provide data on their research investments. There is, however, a possibility that organizations have been omitted, either because they have not been identified due to a lack of the necessary language skills (which is one potential explanation for the higher response rate in Western as opposed to Eastern European countries), and/or because of a failure to report data. These sources of error have been minimized with the help of national neuroscience societies. Imputations have been made for those countries whose major funding agencies produced an inadequate response rate. Moreover, the total estimate of brain research (and especially basic research not related to disorders) is probably underestimated. Universities are large and important research institutions, but it was hard to assess to which specific research areas their various funds were directed (internal and external funds). To minimize the potential for double-counting in funding, university funding was therefore excluded from our base case estimates. A rough estimate of university funding was reported, however, and it may be concluded that inclusion of university funding would not significantly alter the overall conclusions.

Stroke and brain tumour are listed under CVD and oncology, respectively, by the WHO. Research in these general fields may have had an impact on the understanding and treatment of brain tumour and stroke, though it is hard to assess how much. The contribution to brain research of 'basic research not related to specific disorders' cannot be included in the total estimate. However, this should not alter the comparison between disorders as 'basic research not related to specific disorders' is not divided between the brain disorders either.

Finally, during the assessment of drugs for specific brain disorders, carried out to estimate industry funding, it was concluded that there was no specific drug for TBI. It is regrettable that no drug development seems to target this serious and costly disorder that affects mainly young individuals.

Policy implications

Funding distribution within brain research

Individual brain disorders have sometimes been perceived as difficult to study because of their heterogeneity (Pendlebury *et al.*, 2004). This remains a challenge in studies of funding of all major brain disorders taken together (Olesen *et al.*, 2006). However, many brain disorders have important features in common. Although mental disorders account for two-thirds of the total cost of brain disorders (Andlin-Sobocki *et al.*, 2005) they only receive one-third of the total investment in brain research. The proportion spent on mental disorders is even less when public investment (especially investment by charities) is considered alone. A possible explanation is that mental disorders have long been stigmatized and hence 'invisible', receiving little acknowledgement from healthcare providers and society in general (WHO, 2001b). Moreover, those working in the field of mental disorders have had difficulty organizing patients and special interest groups to inform policymakers and public funders of the importance of increasing understanding of the field. The majority of the world's countries still lack data to support advocacy for mental health (WHO, 2001b), which could further explain the neglect of mental disorders on the public agenda. Indeed, many government agencies award research grants by selected themes (Editorial, 2004) and are influenced by lobbying forces. In the heterogeneous field of brain research, there has so far been little coordination of research efforts. Cancer is an example of a research field where successful coordination has been achieved. This has resulted in it receiving substantially more funds than brain research.

The industry sector is profit-driven and investments are therefore usually made where the expected profit is highest, i.e. where the cost of developing a new drug will give an anticipated profit (Vallance, 2001). Brain research is a field offering tremendous commercial opportunities, due to its high prevalence, chronicity and cost to the individual and to society [Invest in Sweden Agency (ISA), 2004].

Funding distribution by funding agencies

The results from the public funding survey on country-specific funding show large disparities between countries. Governments set their spending priorities according to tradition, political will, public influence, etc. According to Saraceno & Saxena (2004), in middle-income countries, mental health research has been constrained by such factors as resources, low research capacity and an unfavourable research environment (Saraceno & Saxena, 2004). In Eastern Europe, there has been a deterioration in health and social services since the collapse of Communism (Vlassov, 2005). Governments need strong public support if they are to invest in research, but this support is not present (European Commission, 2005b). Middle-income countries, especially, show low local support for research (Morris *et al.*, 2002), which further explains the low public research investments in Eastern European countries (with exceptions such as Hungary).

Public attitude is also critical for charities. Charities are usually dependent on private donations for their work, and on private personal involvement (European Commission, 2005b). How much the public contributes to charities is, in turn, dependent on national traditions of donating. The strength and size of a charity is also partly influenced by how well organized the charitable sector is. As many charities focus on one specific disorder, there is a lack of charitable effort in the more general field of brain disorders (with exceptions such as the Brain Fund in Sweden), compared to the cancer field. Cooperation between funding agencies has been scarce, and it has been hard to find any coherence or efforts to reach a higher common goal (by lobbying or

through better coordination). A well-organized charity sector has higher credibility among the public, encourages more charities to develop and promotes increased collaboration with other organizations, so that investments can be enlarged (European Commission, 2005b). Increased collaboration benefits all.

The largest charitable sector (in number and in spending) is in the UK. It is influential and well-organized through the government's Charity Commission. All charities in the UK are registered by the Charity Commission, from which information about them (such as contact details, mission and annual reports) can easily be obtained (Charity Commission, 2006). There is also a tradition of collaboration between charities and government entities in the UK; this has made the charity sector more powerful in setting the national research agenda (European Commission, 2005b). One effect of collaboration is that there is a combined drive to map all mental health research funding from government agencies and charities, with the aim of improving knowledge about the funding situation and inspiring further collaboration (Mental Health Research Funders' Group, 2005).

The large disparity in charity funding between European countries can partly be explained by national differences in laws and tax regulations that directly affect charities. Laws which limit or encourage charitable organizations include regulations affecting state approval for establishing a charity, requirements on starting capital, permitted purposes of the charity and regulations associated with the economic activity allowed (European Commission, 2005b). Tax regulations affect charities twice over, by affecting the incentives for people to donate and by relieving the charity of tax obligations. In the first case, some countries have tax deductions for private and/or corporate donors, which increase the incentives to donate. In the second, in many countries charities are exempt from taxes such as gift tax, inheritance tax and investment income tax, which makes their work more profitable and easier to manage. Many countries also exempt tax on public-benefit trading income and some even exempt tax on nonpublic-benefit trading income up to a certain threshold (European Commission, 2005b). The countries with more favourable laws for charities, such as the UK and the Netherlands (European Commission, 2005b), have reported high spending and numerous charities in the public funding survey. Many EU accession countries do not have as favourable incentives for charities (European Commission, 2005b), which could further explain the low charitable contribution reported in these countries.

While industry contributes 54% of total R&D spending in Europe, it contributes 79% of brain research funding. The goals of the Lisbon Strategy state that industry should contribute one-third of R&D investments and that the public should contribute 1% of GDP for research. In most fields, it is industry investments that are lagging behind, but the present study shows that for brain research it is public spending that must be increased proportionally more than industry spending. The key message of the Lisbon Strategy is that European research should be enhanced and brought up to an internationally comparable level. Today, however, insufficient research funding and a disorganized European research market are two of the largest obstacles to European brain research regaining its competitive edge globally (Sautter *et al.*, 2003). Part of the problem can be solved by increasing public research funds.

The results of the present study indicate that there are differences in the amount of funding of disorder-specific research provided by the public and industry sectors. For example, industry has not invested in any research on TBI, most probably due to the limited number of drugs used specifically for the treatment of TBI, so the total research burden of TBI rests on the public. For brain tumour, in contrast, the division is more even, due to the large public interest in investing in this area. When setting its priorities for future research funding, it is

important that the public sector takes into account where both the gaps in funding and the largest health needs are (Institute of Medicine, 1998). The present results indicate that, taking public spending as a percentage of costs, brain tumour and TBI are the most highly funded brain disorders at 0.5% and 0.4%, respectively. The least funded brain disorders are mental disorders and migraine, which together receive less than 0.1% of the costs.

Growing gap between Europe and the US

Although the prevalence of brain disorders is similar in the US (National Institute of Neurological Disorders and Stroke, 2006) and Europe (Andlin-Sobocki *et al.*, 2005), the results of the present study show that European government funding is only 12% of the spending of NIH. European public funding is also low compared to US funding of other fields of research.

The charity sector is much smaller in Europe than in the US (European Commission, 2005b). Part of the explanation for this is that Europe comprises many different countries with their own traditions, laws and regulations. Generally, tax exemptions on donations and the activities of charities are limited to the home country, which has led to difficulties with cross-border donations (European Commission, 2005b). In addition to low mobility of research capital, there is a low mobility of researchers (especially professors) within Europe (Dillon, 2001; European Commission, 2005b). As the extended academic market for capital and researchers is open within the US, this gives the US a significant competitive advantage (Editorial, 2004; European Commission, 2005b). The US also attracts many European scientists because research funding is better in the US (Edwards & Bell, 1994; Moore, 2000). This leads to a shortage of highly competent scientists in Europe, which has a negative effect on growth in the European research sector (Moore, 2000; Dillon, 2001).

As shown in the present study, both government and charity sectors are stronger in the US than in Europe. The US has a long tradition of private donations, not only to charities investing in medical research (European Commission, 2005b; Philipson, 2005). There has also been successful political lobbying by scientists in the US and this has influenced American public science policy (Moore, 2000; Simons, 2001). For decades, the US government has acknowledged the importance of R&D and, hence, has invested a considerable amount of resources in it. It has also made the investment climate favourable to industry. The US has long been the world leader in R&D and has dominated the published literature, where English has become the dominant language. A study by Fassoulaki *et al.* (2001) has shown that the impact factor (the number of citations of a scientific journal divided by the number of articles published) of published material in Europe is important for attracting further funding. As most journals are in English, many European countries are disadvantaged by not being able to conduct and publish research in their own language. These countries also have problems in attracting foreign scientists (Dillon, 2001). All these factors have probably had a negative effect on the advancement of European brain research.

Benefits of brain research investment

Publicly funded research can generate various types of benefits. Basic research can potentially lead to an increasing stock of useful knowledge, training of skilled graduates, creating new scientific instrumentation and methodologies, forming networks and stimulating social interaction, increasing the capacity for scientific and technological problem-solving and creating new companies (Salter & Martin, 2001). These all contribute to economic growth. Of these categories, health research should primarily affect the patients' lives by increasing

knowledge and by the creation of new instruments and methods. Studies have shown that health research has led directly to cost savings and increases in healthy lifespan (Buxton *et al.*, 2004; Johnston *et al.*, 2006), mainly through more effective treatments (Buxton *et al.*, 2004).

In the present study, we provided examples of the benefits of medical innovation, and suggested that substantial benefits have been gained in several major brain disorders over recent decades. New drugs have delayed progression into severe states for patients affected by brain disorders, or eased the symptoms and thereby reduced the burden on society while increasing the patients' QoL. Even small effects of relief or delayed progression may provide large benefits to patients. Hence, there is a substantial potential for future medical innovations to provide even larger benefits than the drugs that are currently available. Our assessment of future benefits from further investments in brain research indicates that these are worthwhile, based on society's WTP for further health gains. Even at low levels of WTP for health gains, research was found to be highly cost-effective. By studying the development pipelines of medical innovations, we already note that drugs targeting diseases of the CNS account for most of these. However, in the public sector, brain research still seems to be under-prioritized.

Conclusions

Spending on brain research in Europe, particularly public spending, is low compared to other fields of research, such as cancer, and it is particularly low compared to the US. Increased public investment in brain research in Europe may be highly cost-effective and bring great benefits. The EC prioritization of brain research in the Seventh Framework Programme of Research is supported by the present data. Each European nation should follow the example of the EC and make brain research one of its research priorities for the years to come. It is important that both basic and clinical research receive adequate funding. Basic research is responsible for the most fundamental breakthroughs and often leads to subsequent paradigm shifts in drug development and patient treatment. Clinical research may direct basic research towards disease-related mechanisms and is instrumental in translating findings of basic research into new products and treatments.

Using the same methodologies as in the present study, further studies could be undertaken in each European country to assess more precisely the spending on brain research. To facilitate more accurate future studies, industry and public funding bodies should group funding for 'brain research' together, including stroke, brain tumour, developmental disorders, mental retardation, brain trauma and brain infections. This would enable future studies to establish the necessary priorities for investments in brain research.

Acknowledgement

This work was supported by a Specific Support Action grant (number 013043) from the European Commission under the Sixth Framework Programme.

Abbreviations

CMR, Centre for Medicines Research; CNS, central nervous system; CPL, comparative price level; CVD, cardiovascular diseases; DALY, disability-adjusted life years; EBC, European Brain Council; EC, European Commission; EU, European Union; ECRM, European Cancer Research Managers forum; EFPIA, European Federation of Pharmaceutical Industries and Associations; EQ-5D, EuroQol in five dimensions; GAD, generalized anxiety disorder; GDP, gross domestic product; MS, multiple sclerosis; NCE, new chemical entity; NIH, National Institutes of Health; OECD, Organization for Economic Co-operation and Development; PD, Parkinson's disease; QALY, quality-adjusted life years; QoL, quality of life; R&D, research and development; TBI, traumatic brain injury; WHO, World Health Organization; WTP, willingness to pay.

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Map transformations in the rat somatosensory system. Tactile information from the body surface is represented in a somatotopic map in the primary somatosensory cortex (left panel). This essentially 2-D cortical map is transformed into a more complex 3-D map in the pontine nuclei (middle), in which somatotopic relations are largely preserved among axonal terminal fields. In the granule cell layer of the cerebellar hemispheres (right), tactile representations are organized in a more complex and disrupted map, referred to as a fractured map, as here shown in folium crus IIa and the paramedian lobule. Body parts are color coded (red, upper lip; purple, whisker; green, trunk; yellow, forelimb; green, hindlimb). For details see T.B. Leergaard *et al.* (pp. 2801–2812).

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Typeset in India by Scientific Publishing Services (P) Ltd
Printed in Singapore by KHL Printing Co Pte Ltd
ISSN <0953-816X> (Print)
ISSN <1460-9568> (Online)
For submission instructions, subscription and all other information visit: www.blackwellpublishing.com/journals/ejn

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0953-816X(200611)24:10;1-M