The impact of economic change on clinical neurology and research: a window into the European situation¹

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INTRODUCTION WITH A VIEW OF EUROPEAN HISTORY

The last decade brought a significant number of profound political and economic changes in Europe. The collapse of the Iron Curtain and the removal of the Eastern and Western European blocks as well as the formation of the European community caused a revolution of the health care system and medical research in Europe.

A superficial view could suggest that Europe is characterized by its diversity; major linguistic, ethnic and ideological differences appear to separate and even divide its constituent countries. In the Middle Ages however, scholars of these countries were united by a common language (Latin) and shared a common culture. These factors provided the basis for the development of our universities and a framework for scholarly communication and collaboration. This framework survived the fragmentation of European society in the early modern period and, in science and medicine, it not only survived but grew progressively stronger. Science was one of the threads which held the fabric of international society together during the 17th and 18th centuries. The European tours undertaken by scholars both previous to and throughout that time, created a network of personal contacts and established the tradition (maintained by correspondence) of a regular exchange of ideas and information among those interested in the natural sciences.

These private communications between individuals were subsequently reinforced by the founding of learned societies and the publication of periodicals. Today, there are over 100 European societies in the biomedical sciences. A review of the major journals reveals that the

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proportion of international collaborative studies has increased 12-fold since 1950. These are secure foundations, since they are based not upon direction or dogma but upon the most durable and cohesive of forces—consensus.

The purpose of this background is to emphasize that many effective European collaborations are established "from the ground up" and are science-led. The role of international agencies, in these cases, is primarily a facilitatory one. There are, however, good reasons for seeking to promote further collaboration in Europe. The most obvious are that the continent, as a whole, has a range of financial and human resources which are not all available within one country, and that there are some research studies which can derive unique benefits from an international approach. The principal founding mode is through cooperation, thus enhancing and extending interactions between scientists in the European Community countries (Evered, 1992).

MENTAL AND NEUROLOGICAL ILLNESSES IN EUROPE

Mental and neurological diseases are one of the biggest public health problems in Europe. Tens of millions are affected, representing more than 15% of the population. Because of the increasing life expectancy in most European countries, the neurological and psychological disorders linked to the ageing brain are becoming a serious problem.

Epidemiological figures of the most relevant neurological and psychiatric disorders in European countries are reported in Table I. Dementia today afflicts between 820 and 1300 people per 100 000, so that 3.5 million people



Disorder	Country	Authors	Yearly minimal cost in ECU	
			Social costs	Health care costs
Dementia	UK	Broe et al. (1976)	20 461 123 200	30 753 068 200
	Italy	Rocca et al. (1990)		
Cerebrovascular	Greece	Paschalis et al. (1983)	17 469 166 000	26 256 156 700
diseases	Finland	Abo et al. (1986)		
Epilepsy	UK	Brewis et al. (1966)	11 581 769 000	17 407 398 800
	Denmark	Juul-Jensen and Ipsen (1975)		
Parkinson's	Spain	Gutierrez del Olmo		
disease		et al. (1989)	2576943600	3873146200
	UK	Mutch et al. (1986)		
Multiple	Italy	Diodato et al. (1988)	1959246800	2944747940
sclerosis	UK	Poskanzer et al. (1980)		
Myasthenia	UK	Pensington and Wilson (1961)	76 246 800	114 598 940
gravis	NL	Oosternis (1977)		
Muscular dystrophy	Italy	Danieli and Mostacciulo (1979)	79142000	118 950 426
ALS	Denmark	Hojer et al. (1989)	100 374 400	150 862 723
	France	Chazot et al. (1986)		
Schizophrenia	UK	Wing et al. (1976)	4 344 664 800	6530031200
	Germany	Hafner et al. (1980)		
Affective	Germany	Dilling et al. (1989)	6611259200	9936722600
psychoses	Greece	Madianos et al. (1987)		
		1000-0-0-0-0-0-0-0-0-0-0-0-0-0-0-0-0-0-	65 259 935 800	98 085 683 729

TABLE I. Costs of selected disorders of the nervous system in European countries (CEE, EFTA, COST)

are affected in Europe. Four million become victims of cerebral strokes. More than 2 million people are subject to accidental brain injury, which affects the working of their brains. Parkinson's disease affects more than 1 million European citizens. In a country like Germany, it is estimated that 14% of inhabitants (11.5 million people) suffer from psychiatric problems at some time during their lives (Mendlewicz, 1993).

THE COSTS OF BRAIN DISEASES

Mental and neurological illnesses create huge costs for society. The total cost is estimated to be about 20% of the total expenditure on health in Europe: that is five times more than cancer and 1.5 times more than cardiovascular illnesses. To the direct costs of treatment (days of hospitalization) should be added the enormous indirect costs related to productivity losses, compensation for loss of revenue, preventive efforts and psychosocial assistance. The figures for Europe are rather hard to gauge, because of differences in the social security systems in each country. However, using available data the following totals are extrapolated (Seligman, 1992; Mendlewicz, 1993):

Costs of treating brain diseases	43 billion ECU
Indirect costs	54 billion ECU
Total amount/year	97 billion ECU

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The magnitude of these costs, both economic and noneconomic, gives an idea of the social relevance of the CNS disorders and indicates that research in this field must be intensified. The main goals of such research should be more effective treatment, improved rehabilitation programmes and prevention of relapses in periodically recurring diseases.

The yearly minimal costs are calculated according to epidemiological data and an EU estimation (Table I).

Health-care costs of different European countries compared with the USA are presented in Fig. 1, calculated as percentage of the gross domestic product (Zeit, 1993). For Germany, direct and indirect costs increased from 23% of the gross domestic product in 1961 to 29.3% in 1991. The biggest part of these expenses is attributed to the elderly population and survivors. On the second range one can find health care costs. These costs are the totals of hospital expenses, physicians, dentists, drugs and care. Figure 2 shows the high percentage of acute beds in Germany and in Austria in comparison with the lowest percentages in the USA and Great Britain (Pharmig, 1994).

BRAIN RESEARCH IN EUROPE

The neurosciences are located at the crossroads between neurobiology, neuroanatomy, biochemistry, biophysics,

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pharmacology and psychology. This field of research has existed as a self-sufficient entity since the 1970s. It has expanded without parallel in the history of science. In 1971 the first International Neuroscience Congress brought together 400 researchers, whereas in 1992 more than 20 000 neuroscientists attended the Neuroscience Meeting. Table II shows the distribution of members of the International Brain Research Organization. Neuroscience is a field in which European research has solid resources and strong traditions. It is estimated that in Europe there are between 8000 and 10 000 researchers in the neurosciences compared with 15 000–18 000 in the USA. Not all neuroscientists are registered in the International Brain Research Organization. There are about 250 neuroscience journals and in 1991, 100 000 publications came out under the keyword "brain". In neurophysiology, clinical neurobiology and neuropharmacology many breakthroughs have been achieved. In most of the fields involved, many of the centres of excellence are to be found in Europe: the Max Planck Institute for Brain Research in Frankfurt, the Karolinska Institute in Stockholm, the Obersteiner Institute in Vienna, and the University of Oxford brings together the largest number of researchers in cognitive science in the whole world.

In many other fields, Eastern European research suffered from the previous communist system. Before the fall of the Iron Curtain, East European countries contributed less to the development and application of medical technology, in both clinical and research areas. The phar-

TABLE II.	International Brain Research Organiza-
tion: 1991	graphical listing of members

	No. of members
Africa	170
Asia,	1370
including	
China,	117
Japan	865
Australia,	430
including	
New Zealand	33
Canada	1370
Central and	411
South America	
Middle East	193
Europe	8060
Israel	149
USA	14707
Russia	209

maceutical industry of the former USSR produced only 30% of their own requirements. Few new drugs were produced from the Eastern European countries. The communist political system caused profound restrictions to basic and clinical neuroscience, however, some joint events and more or less private initiatives tried to overcome the political restrictions in the past. Austrian neurology was associated with some groups: the Danube Symposium and the South East European Society for Neurology and Psychiatry offered a scientific Eastern– Western exchange; Austrian neurology was involved in the Austrian–Russian space project; the Department of Neurology in Innsbruck collaborated actively with the universities in Praha and Zagreb resulting in scientific publications and books.

European research suffers from the effects of dispersal and fragmentation of effort, a lack of coordination between the work of different teams, and difficulties in reaching the critical mass, in both human and financial terms, needed to undertake large-scale epidemiological studies. In many countries initiatives have been taken at the national level, for example the launch in Germany of 10 groups of projects in neurobiology, to be undertaken at the Max Planck Institute and the universities.

In the future these activities should be undertaken in the framework of European research networks by means of shared cost research projects and thereby making use of a number of institutions, centralized at European level, which will act as resource centres for the different laboratories.

Some neuroscience projects financed by the EC in the period 1987–1991 are listed in Table III. The medical and health research programme of the EU (1987–1991) contained a section dealing with age-related health problems. In this context several projects dealing with brain pathology have been undertaken, such as the EURAGE project on diseases of ageing, the concerted action on the epidemiology and prevention of dementia (EURODEM) and a study of the risk factors in Parkinson's disease (Seligman, 1992).

A number of initiatives in the medical technology area similarly cover work which is directly related to new diagnostic methods in neurology, like PET and NMR. It is a sign of the growing importance being given to this field that a complete section of the new biomedical

	1987–1991		
	Evaluation of the Efficacy of Technology in the Assessment and Rehabilitation of Brain Damaged Patients	•	
	Tissue Characterization by Magnetic Resonance Spectroscopy (MRS) and Imaging (MRI)	Ð	
	Mobility Restoration for Paralyzed Persons	1	
	Comprehensive Community Care of the Mentally III		
	European Coordination of Research in the Field of Head Injury		
	European Research of Incapacitating Diseases and Social Support		
	Brain (Basic Research in Adoptive Intelligent Networks)		
	European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS)		
	Aging and Diseases (EURAGE)		
	Concerted Action on the Epidemiology and Prevention of Dementia (EURODEM)		
	Study of Risk Factors on Parkinson Disease		
	Neuropathology of AIDS		
	Aging-like Acquirement CNS Impairment from Long-term Exposure to Industrial Chemicals, with Special Reference to		
	Organic Solvent Neurotoxicity		
	Methodology for the Analysis of the Sleep-wakefulness Continuum		
	Technology and Blindness		

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and health research programme (1990–1994) is devoted to mental illnesses and neurological problems, molecular and developmental neurobiology, neuropsychopharmacology, neuroendocrinology, neuroimaging and clinical research (Mendlewicz *et al.*, 1993).

In the area of more basic research, several projects in the SCIENCE programme dealt with neurological problems: study of the visual cortex, information-processing in the brains of mammals and others. Ten of them, dealing with various aspects of neurocomputing, were grouped in the BRAIN initiative. In the related section of cognitive science a series of studies have been carried out in the framework of the FAST programme: cognitive psychology, logic and linguistics, human/computer interface and cognitive neuroscience.

THE EUROPEAN DECADE OF BRAIN RESEARCH



Europe is a major world force and experiences an intense drive for integration between various nations and organizations. Both because of the strong research traditions in European institutions of learning, and the long standing of Europe as a dominating cultural force, it appears selfevident that this continent should play a major role in the world-wide research attack on the problems associated with the brain and its diseases. However, beyond a great industrial high technology, advances can now be made in this field from which the European Community must not find itself excluded. The stimulus to concerted community-wide action is needed to avoid such an exclusion from this technological revolution.

Neuroscience is creating its own new high technology. A range of diagnostic tests and medical instrumentation will emerge with considerable potential in manufacturing and design. Small-scale, highly skilled technological entities can be developed in this field, even in small communities, and without requiring a base in heavy industry. The pharmaceutical industry world-wide is already becoming increasingly dependent upon new drugs acting on the nervous system. The application of new methodologies will involve large teams of scientists and supporting staff, major equipment and new physical installations. Only Europe as an entity can compete with the major efforts being mounted in the United States and in Japan: the USA proclaimed the US decade of the brain, and Japan created the "Human Frontier Science Program".

Programmes in the neurosciences are conducted separately in each EC member state by the national research organizations. These are valuable in their own context, but by their nature they will be unable to expand in this field disproportionally to the other field which they have to serve. They constitute a base from which to start a community-wide programme of new research initiatives in neuroscience, of new training programmes and of shared research facilities and clinical resources.

The European decade of brain research is an extension and a complement to the US decade of the brain and is intended to stimulate the development of research into neurobiology, neurology and psychiatry in Europe. The European decade should make it possible to combine all these efforts, and keep in Europe those researchers who might today be tempted to pursue their work in American laboratories. At the same time, the objective is to organize these activities into a coherent framework, thereby achieving the critical mass which is essential for largescale studies.

In July 1992 the European Parliament gave its support to a resolution on brain research. In February 1992 the Commission of the European Communities set up a task force on European brain research which has the task of studying the whole range of existing problems and setting out guidelines for a programme of action in the field. Among the actions to be undertaken in the framework of the decade, the task force identified the establishment of harmonized epidemiological data about neurological illnesses in Europe; the stimulation of work leading to better understanding at molecular and cellular level of degenerative brain disease and mental illnesses; and the harmonization and standardization of clinical testing protocols for new medicines.

The required European effort must be transnational, multidisciplinary, industrially pre-competitive and science-led. For these reasons, only an initiative at the Community level can be effective in creating the resources needed. The USA and Japan have fully appreciated the implications of the advance of neuroscience. However Europe, despite a strong tradition in neuroscience, is being left behind by the lack of comparable investment.

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Sleep spindles in the initial stages of the vegetative state.

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Abstract

The aim of this study was to look for the presence of spindling in the different stages of remission of the vegetative state to underline all possible correlations with lesional sites, severity of coma and final outcome. The nocturnal polygraphic recordings from 30 patients were examined: 20 (15M, 5F, mean age 31.7 years, range 16-41) had originally suffered a traumatic brain injury, 10 (4M, 6F, mean age 40.5 years, range 24-48) had hypoxic brain lesions. Evidence of spindling, always reduced in density and duration, was found in 44% of these patients, prevalently in the traumatic patients (53.3% versus 30% of hypoxic patients). No subjects in the full stage 0, 0-1 of the vegetative state (apallic syndrome) presented spindling. No significant correlation was found between spindling and the following parameters: gender, the time between the onset of coma and the polygraphic recording, or the site of the lesion.

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