NEUROSCIENCE IN HUNGARY

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Neuroscience is one of the leading fields of the fast developing biological sciences. It comprises the study of the brain, the nervous system as a whole, and relationships of the brain to behaviour. The unique position of neuroscience lies in the fact that it is at the intersection of biology, the humanities, sociology, and computer sciences. "Basic" neuroscience includes research into the enigma of learning, memory, perception(s), emotions, and in the case of humans the neuronal basis of self-conscious behaviour, intellectual capabilities, creativity, thinking, creating and/or solving problems.

In fact one of the most intriguing questions since the beginning of self-consciousness, and certainly present already in Hellenistic times, is the origin of human cognition, consciousness, and its (at that time hypothetical) connection to the human brain, which is – according to the Nobel prize winner Sir J.C. Eccles – the most complicated, highly developed production of the universe. It is now generally accepted that the understanding of the functions and the mysteries of the brain represents the greatest conceivable intellectual and scientific challenge to mankind. An understanding of the unique nature of man bestowed by the brain is therefore a goal in itself. At the same time far-reaching applications can be expected also from research to solve major brain-related medical and psychosocial problems.

The utmost importance of neuroscience and related technologies in the treatment or prevention of brain-related health problems might be best illustrated by some data from the National Foundation of Brain Research, which reveals direct and indirect costs caused by disorders of the brain in 1992 in the U.S. (Unfortunately similar data are not available in Hungary.) Accordingly, direct and indirect costs for (1) psychiatric disorders were 136.1 billion dollars, (2) neurological disorders: 103.7 billion dollars, (3) alcohol abuse: 90.1 billion dollars, (4) drug abuse: 71.2 billion dollars, altogether 401.1 billion dollars, equivalent to 7.3 % of the GDP!

The magnitude of these costs – both economic and non-economic – illustrates the scope of the problem of brain disorders as well as their social relevance. Furthermore it indicates that, in addition to broadening our general knowledge of the "thinking centre," neuroscience and its clinical applications deserve high priority. Indeed, considerable increase in the investment to neuro-

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science has been taking place almost globally in the last twenty years. This trend seems to continue steadily in the United States, Japan and in most West-European countries – particularly since the announcement of the "Decade of the Brain" in 1989 by President Bush. What is the contribution of Hungary, or more precisely Hungarian researchers, to the "global" neuroscience?

1. History of Neuroscience in Hungary

Historically Hungary' s tradition in neuroscience has very deep roots. In the early decades of the twentieth century a number of excellent, internationally recognized research schools were founded in Hungary. They included in neuroanatomy the schools of István Apáthy, or Mihály Lenhossék (the latter together with Ramon y Cajal and others was one of the founding fathers of the schools of neurone concept); in neuropathology Károly Schaffer, who first described the Tay-Sachs disease and discovered the "Schaffer-axon collaterals" in the hippocampus, important elements in memory consolidation; the schools of the neurologists Robert Bárány (Nobel prize) and Endre Hőgyes (works on the labyrinthine reflexes), or George Békéssy (Nobel prize) with basic discoveries on the physiology of hearing. Béla Issekutz, a pharmacology professor in the thirties, contributed with his research to the establishment of a modern pharmaceutical industry in Hungary.

In the second half of this century Kálmán Lissák, (physiology) and Endre Grastyán (psycho-physiology) founded excellent research schools in Pécs. Grastyán' s work on the connection between orientation and learning and on the role of play in the normal neurobiological status of individuals influenced several researchers in the field of psychophysiology and psychology.

A special place in Hungarian neuroscience is reserved for János Szentágothai, a neuroanatomist and a student of Mihály Lenhossék in Budapest. He started his scientific carrier in the thirties and worked until his death in 1994. Szentágothai modernized his main field, neuroanatomy, by giving to his morphological discoveries, whenever it was possible, functional meaning. His main textbook for medical students was entitled *Functional Anatomy*. In addition to the morphological investigation of the central nervous system (functional anatomy of the spinal cord, cerebellar cortex, visual system, cerebral cortex, among others), he had a keen interest in the development of the nervous system, as well as in neuroendocrine regulation. His most cited papers, however, deal with the modular structure of brain stem (reticular formation, actually described earlier by Mihály Lenhossék), cerebellar cortex, and particularly the precise mapping of the main functional cortical network-elements, the cortical modules. He correctly recognized not only that these modules (each consisting of 5000–10000 nerve cells) are the main building blocks of the neocortex, but described also the inner

structure of these elements ("submodules"), including the connectivity between the inhibitory and excitatory neurones. It is only very recently that his functional interpretation of the working modules was fully verified by the use of modern, non-invasive imaging techniques. In his latest works (1988–1994) Szentágothai considered the hierarchically organised interconnected network of approximately two million cortical modules in human cortex as having the capacity of self-organisation and features essential for complex cognitive functions. Though logical, this concept needs further experimental and theoretical verification before a final conclusion of its validity can be drawn. However, this shows clearly the road of this productive scientist as he moved from minute analysis of the details toward a synthesis.

The schools established around these outstanding scientist-teachers helped to educate a large number of disciples and to establish functioning neuroscience research laboratories both within and outside the Hungarian universities.

2. Results and Productivity of Neuroscience in Hungary

Presently in Hungary more than 700 researchers are engaged in more than thirty-five laboratories of basic and clinical neuroscience research. These include subfields such as molecular neurobiology, neurochemistry, neuropsychology, and clinical neurosciences. This research is supported, in addition to Hungarian grants, by international cooperation, which also has a long tradition in Hungary. Characteristically, already in the 1970s, more Hungarian researchers from all generations were participating in European and/or American neuroscience meetings, than from all the neighbouring countries put together. Furthermore during the last two decades of the communist era many Hungarian neurobiologists spent shorter or longer periods in West-European, American, and Japanese laboratories, returning home with modern techniques and attitudes. Of course, a significant number of these generally younger scientists settled down at the host institutions and continued their work there. Fortunately, most of them maintain continuous, fruitful connections with parent institutions in Hungary, visiting and inviting young Hungarian trainees to their laboratories. Beside "Hungarian-Hungarian" cooperation other international scientific collaborations also exhibit a growing trend. While in 1980–85 only 15% of all neuroscience publications were the results of international cooperation, by 1995 50% of all papers with Hungarian authorship resulted from international cooperative research. Furthermore Hungary was the first country in Europe that joined by official governmental decree the "Decade of the Brain" initiative of President Bush and the United States Congress.

Internationally recognised scientific results by Hungarian neuroscientists include (among others):

(1). Discovery and description of the internal structure of cerebellar and cerebral modules, the basis of cognitive and subcognitive functions of the brain.

(2). The development of a new, efficient anti-Parkinsonian drug, Deprenyl (Eldepryl in the United States).

(3). Discovery of a new cortical inhibitory structure (the axo-axonal inhibition) essential for the normal functioning of the cortex.

(4). Connectivity and role of inhibitory elements in the functioning of hippocampus, the main archicortical region responsible for memory processing and retrieval.

(5). Description and pharmaco-kinetics of a new, interneuronal, but non-synaptic signal transduction.

(6). Experimental proof for morphological plasticity of nerve cells and neuronal networks of the adult brain.

(7). Experimental demonstration (via destruction of nerve cells by Capsaicin) of the role of the neuropeptide P-substance in pain perception.

Scientometric data provide also evidence for the relative strength of Hungarian neuroscience. According to international surveys (*Scientometrics,* 16 (1989): 257) Hungary's contribution to the world's scientific production in the eighties was 0.49% of the world production for neuroscience publication in internationally recognized journals and even more, 0.55%, for the citations in the same journals. Hungary occupied the twentieth and the fourteenth place among the world's countries in the number of publications and citations respectively. In that period, moreover, Hungarian neuroscience publications had the highest expected citation rate (ECR) in the world (4.81 per paper). (ECR indicates the visibility of the publication channels used and informs about the publication strategy of the country). It is also remarkable that Hungary's attractivity index (AI) in neuroscience was also the highest in the world (2.03) indicating the enormously high role and prestige of neuroscience in Hungary. (AI: country's share in citation in neuroscience divided by that in all sciences). If we are calculating Hungary's "per capita" production (number of publications) in neuroscience as a function of GDP, it was the highest in the world (USA: 100%, Hungary: 189%). It is not surprising therefore that the Second World Congress of Neurosciences in 1987 was held in Budapest.

3. Present State – and the Future

Although Hungary' s contribution to global neuroscience is relatively well-recognized, its place and participation in the country' s cultural and academic life is equally important. Here, however, a note of warning is necessary. This "success"-story, the high level of neuroscience research in the 1980s could be maintained only through (1) continous education of a new generation of neuro-

scientists, (2) proper material support for research and researchers, (3) introduction of new, modern techniques such as neuromolecular and neuroimaging methods, (4) further strengthening of international cooperation.

The introduction of up-dated Ph.D. programmes to Hungarian universities in the early 1990s seems to ensure the necessary number and quality of the new generation. Altogether eight neuroscience Ph.D. programmes with more than eighty students are presently in operation. There are, however, problems with finding positions for the fresh Ph.D.s after graduation. Extramural institutions (pharmaceutical industry, biotechnology, etc.) for reasons I do not have the time to discuss here, have only very limited possibility to employ fresh Ph.D.s. Although the so-called postdoctoral positions, planned to be introduced beginning in 1997 might partially help to perpetuate research by Ph.D.s in the universities, this is, considering the present economic situation of the universities, clearly only a temporary solution. This helps to explain the rapidly increasing number of Ph.D.s leaving the country and working permanently in other (mostly West-European) laboratories. The necessary increase or at least the maintenance of material support for neuroscience and science in general has became seriously handicapped in the last several years. As an illustration, the steadily decreasing share of research and development expenditures as expressed as a percentage of the decreasing GDP should be mentioned. While in 1989 it was close to 2%, and even in 1992 it was 1.2%, by 1995 it had declined to 0.77% of the GDP! In a country, which would like to join the European Union (where research, testing and development expenditures are well above 2%), this dramatic decline in the support of research might cause serious structural and functional, in some respects irreversible problems for future generations. International cooperation might partially compensate for the decline of domestic support, but only if it does not lead to the mass-emigration of those talented young scientists, who under normal circumstances should become the leaders and teachers of the next generation of Hungarian neuroscientists.

I want to conclude this presentation, however, by expressing the optimistic hope that the declining trends can be stopped in the not distant future and science, as well as neuroscience will continue to be succesful in Hungary during the twenty-first century.