Questionnaire

Summary of the main activities of a scientific Organisation of the Slovak Academy of Sciences

Period: January 1, 2003 - December 31, 2006

I. Formal information on the assessed Organisation:

1. Legal name and address

Institute of Neurobiology,
Centre of Excellence
Slovak Academy of Sciences
Šoltésovej 4-6,
040 01 Košice
Slovakia

2. Executive body of the Organisation and its composition

Directoriat	name	age	years in the position
director	Ivo Vanický, D.V.M., Ph.D.	44	8
deputy director	Jozef Burda, D.V.M., D.Sc.,Judita Orendáčová, M.D., Ph.D.	62,59	12,6
scientific secretary	Viera Danielisová, D.V.M., Ph.D.	54	14

3. Head of the Scientific Board

Prof. Jozef Maršala, M.D., D.Sc.

4. Basic information about the research personnel

i. **Number of employees with a university degree (PhD students excluded) engaged in research and development and their full time equivalent work capacity (FTE) in 2003, 2004, 2005, 2006 and average number during the assessment period**

ii. Organisation units/departments and their FTE employees with the university degree engaged in research and development

Research staff	2003		2004		2005		2006		average	
	No.	FTE	No.	FTE	No.	FTE	No.	FTE	No.	FTE
organisation in whole	12	11,74	14	14,09	13	12,9	15	14,16	13,5	13,22

Informally, Institute consists of four Laboratories: Laboratory of Neuromorphology, Laboratory of Neurobiochemistry, Laboratory of Neurophysiology, and Tissue Cultivation Laboratory.
Formal organizational structure of the Institute is derived from research projects

5. Basic information on the funding

i. Total salary budget[1] of the Organisation allocated from the institutional resources of the Slovak Academy of Sciences (SAS) in 2003, 2004, 2005, 2006, and average amount for the assessment period

Salary budget	2003	2004	2005	2006	average
total salary budget (millions of SKK)	6,002	6,229	6,586	6,842	6,415

6. URL of the Organisation's web site http://inb.saske.sk/

II. General information on the research and development activity of the Organisation:

1. Mission Statement of the Organisation as presented in its Foundation Charter

A) Research activities of the institute are dealing with basic research of events in the central nervous system, taking place under normal and pathological conditions. Studies are focused on understanding basic patterns of relationships between circulation and nervous system, especially during circulation and metabolic disorders. Research is related to major neurological disorders that occur in the spinal cord and brain and circulation.

[1] Sum of the brutto salaries without the fund contributions.

B) Institute provides for consultant service and expertises, related to the main activities of the institute.
C) Institute accomplishes postgraduate studies in neurobiology according to current legislation.
D) Results of the research are being published in periodical and nonperiodical printed media. Publishing of periodical and nonperiodical printed media is regulated by the resolutions of Presidency of Slovak Academy of Sciences.

2. Summary of R&D activity pursued by the Organisation during the assessed period, from both national and international aspects and its incorporation in the European Research Area (max. 10 pages)

Research focused on hot topics in neurosciences :

During 2003-2006, the research program at the Institute of Neurobiology has closely followed the mission statement of the Institute, as defined in its Foundation chapter. All research activities have been focused on studying the events associated with circulatory, traumatic and metabolic disorders of the central nervous system. Selective degeneration of individual structures in the central nervous system in response to injury is strikingly specific, and understanding the molecular mechanisms of neurodegeneration is a prerequiste for developing any effective therapeutical interventions.

The regeneration in the damaged CNS is minimal, as compared with other tissues and organs in the body. However, it seems that neural cells do possess inherent capacity to regenerate, and in specific areas of the brain, neurogenesis has been observed in adult CNS, as well. These topics are highly motivating for neuroscientists all around the world.

Scientists at our Institute have been incorporated in more than 30 national and international projects, of which more than 20 have been allocated directly to the Institute. These projects have studied various aspects associated with neural regeneration and plasticity after various models of ischemic and traumatic injury in the brain and spinal cord.

One of the major topics in our laboratory is focused on studying the distribution and role of nitrergic structures in the spinal cord, and understanding of their participation on pathological processes. Both neuroprotective and neurodestructive role of nitric oxide in CNS have been suggested. Distribution and activities of enzymes producing nitric oxide in the spinal cord have been visualized and quantitated by using complex analyses involving histochemical, immunohistochemical and biochemical methods. Role of nitric oxide has been analysed in secondary degeneration processes associated with inflammation and chronic pain, as well as its participation on nociceptive and proprioceptive afferentation of the spinal cord. Our “nitric oxide” groups are closely collaborating with Medical Research Center of Polish Academy of Sciences in Warsaw, Poland.

Another important topic traditionally studied in our laboratory is the role of protein synthesis disturbances on pathophysiology of ischemic injury. Protein synthesis regulation, its association with the phenomenon of ischemic tolerance and regulatory mechanisms of initiation factors, together with the role of extracellular glutamate concentration are studied at molecular level. Long-term collaboration in this area exists between the Hospital of Ramon y Cajal in Madrid, Spain, and our Institute.

Pathomechanisms of spinal cord injury (both ischemic and traumatic) have been traditionally studied in our laboratory, using various animal models. Based on collaboration with laboratories in the US, this research has recently included transplantation experiments

stimulated by recent progress in stem cells research. We have been participating on transplantation projects studying the effect of local microtransplantations of neural precursors into ischemically damaged spinal cord. After traumatic injury, systemic applications of bone marrow stem cells and spinal neural precursors have been studied. With advanced molecular techniques, we are studying neurogenesis in adult CNS, as a potential inherent source for neuroregeneration. In stem cells research, extensive collaboration exists between our researchers and Anesthesiology research group from University of California, San Diego, USA.
In general, in the last 4 years, the main reserarch topics, i.e. mechanisms of neurodegeneration and neuroregeneration associated with ischemic and traumatic injury in the CNS remained unchanged. However, new methods allowed us to start studying these processes at molecular level. These research topics, closely associated with regeneration medicine and transplantation experiments are stimulated by recent progress in stem cells research.
We have succeeded in obtaining funds for building a tissue culture laboratory for *in vitro* cultivation of cells and tissues. Our new laboratory has been working from 2005 in close collaboration with clinical Tissue bank laboratory in Košice.

Priority results achieved:
1, We have published new findings on the role of protein synthesis in the mechanism of ischemic tolerance in the brain. Our studies on mechanisms of ischemic tolerance have brought two new findings that might be of importance in clinical practice. The first finding was that protection against ischemia-induced delayed neuronal death in selectively vulnerable hippocampal pyramidal cells is activated by the second ischemia that seems to represent the end-effector of the protective mechanisms. The activation of this robust protective mechanism thus requires combination of two metabolic stresses used in appropriate timing (postconditioning). The second stress seems to trigger protective mechanism additive to ischemic tolerance, if used two days after lethal ischemia (delayed postconditioning), which seems to prevent neuronal death in selectively vulnerable brain regions. This arrangement of experiments allows extension of "safe" ischemic interval at least two times compared to that after single transient ischemia. The second finding is that postconditioning does not induce accumulation of injuries produced by the first and the second stress. This is a novel protective mechanism, capable of protecting selectively vulnerable neurons in the brain from delayed injury.
2, We have described a new nitrergic pathway in the spinal cord. The pathway originates from neurons located in the grey matter structers in lumbar intumescence of the spinal cord. These neurons project their axons ipsilaterally in the ventrolateral funiculus and in the lateral and medial portions of the ventral column. These projections terminate mostly in the ventral motor nucleus located in C7-Th1 segments. This pathway has been revealed by using immunohistochemical analyses in combination with retrograde fluorescent tracer (Fluorogold). In addition, its ascending projections have been confirmed by observing degeneration changes after unilateral hemisection at thoracic level.

3, Our results have disclosed an important role of nitric oxide in the cauda equina syndrome, which develops as a consequence of multiple lumbar and sacral root constriction. Spinal mechanisms involved in the development of this syndrome are not completely understood. In these experiments we sought to clarify the role of nitrergic spinal cord structures in this process. The dynamics of changes in enzymes producing nitric oxide in lumbosacral spinal cord have been documented immunohistochemically during the first 2-5 days after root constriction in experimental animals.

4, We have shown, that ischemic injury in the spinal cord is associated with development of spasticity. This specific neurological consequence of spinal ischemia results from the specific loss of small inhibitory neurons from the fifth to seventh laminae in the spinal grey matter. We have documented, that this spasticity is dependent on GABA-mediated transmission, as it could be completely reversed by spinal application of baclofen.
In addition, we have studied the role of nitric oxide synthase in the monosynaptic Ia-motoneuron pathway, which also seems to be involved in postischemic spasticity.

5, In our laboratory, we have developed a new model of compression spinal cord injury in the rat. This model have several advantages compared to currently used rat models, allows gradation of injury and quantitative assessment of the lesion. Our model has been adopted and used by other experimental groups abroad for various treatment experiments. One of them, performed in collaboration with the Tissue bank in Košice involved transplantation studies, using human mesenchymal stem cells. We have shown, that these cells survive after systemic application, migrate into the lesion site and seem to influence the regeneration processes, resulting in improved neurological outcome in the injured animals.

6, We have participated on experiments studying the effect of transplantation on experimental ischemic injury in the spinal cord. Specific populations of neural cells, cultivated *in vitro,* have been microtransplanted into the spinal cord of ischemically damaged animals. It has been found that transplanted human neuroteratoma cells, or rat neuronal precursors can survive for long time, integrate into the host tissue and eventually form long projections within the spinal cord. The host animals showed gradual alleviation of their spasticity and improved recovery of neurological functions. Histological analyses documented presence of transplanted cells, their differentiation into neurons (producing typical neuronal marker proteins) mostly of inhibitory phenotype (GABA-ergic neurons). These cells seem to replace the lost interneurons in the grey matter of the spinal cord. Our observations indicate that partially differentiated cells have a potential to differentiate into neuronal phenotype in the damaged CNS tissue.

National aspect of R&D activities of the Institute:
Institute of Neurobiology has existed under this name since 1977 and is historically the first institution in Slovakia, fully devoted to neuroscience research. Our long-term goal is to promote and integrate neuroscience research in Slovakia, which is atomized at different academic institutions, universities and hospitals. Scientists from our Institute have initiated foundation of Slovak Society for Neuroscience. This Society has been officially registered in 2005 and is organized as one of several scientific societies affiliated at the Slovak Academy of Sciences (http://www.neuroscience.sk/). Currently, the organization has more than 80 individual members. In 2006, the Slovak Society for Neuroscience has been incorporated as a regular member into IBRO (International Brain Research Organization) and FENS (Federation of European Neuroscience Societies).
Since 2004 Institute of Neurobiology has been a part of Center of excellence of Slovak Academy of Sciences (Center of excellence for Alzheimer disease and related neurodegeneration diseases), which integrates 7 academic institutions from Slovakia.
Historically, there are excellent relationships between the Faculty hospital in Košice and our Institute. We have close collaboration with the Neurosurgery Clinic, Surgery Clinic and Departments of Pharmacology at Medical Faculty of University of Pavol Jozef Šafárik in Košice. We regularly provide our expertise and access to the laboratories to the researchers from these institutions for their experimental work.

International aspect of R&D activities of the Institute:
Institute of Neurobiology has an active international collaboration with laboratories in Czech Republic, Poland, Hungary, Ukraine, Russian federation, The Netherlands, Spain, Israel, and the USA.
Our researchers are incorporated in the international programme Cost B30, entitled Neural Regeneration and Plasticity, involving more than 40 research groups from 21 European countries.
Mutual projects exist with laboratories in Poland (Warsaw), Hungary (Szeged) and Spain (Madrid, Bilbao).
Institute of Neurobiology organized an international meeting in 2005 with the title 5th International Symposium on Experimental and Clinical Neurobiology. The meeting took place in the congress center Academia in the High Tatras and it was our first international meeting after integration of Slovakia into EU. 125 participants from 18 countries from all over the world took part on the meeting. We received financial support from the most important international societies, including International Brain Research Organization, International Society for Neurochemistry, General Electrics – Healthcare Bio-Sciences and numerous sponsors from industry. We have invited leading scientists from the USA, Germany, Canada, Israel, Japan, and Russia presenting their latest advances in their fields of research. Thanks to our sponsors we could provide travel grants to more than 50 young scientists. Selected papers from the Symposium have been published as a special issue of an international journal Cellular and Molecular Neurobiology. We appreciate that due to the meeting, the number of international visitors at the Institute, both professors and young scientists for long-term fellowships, increases.

Collaboration with Universities:
Institute of Neurobiology has been performing postgradual education in collaboration with the Medical Faculty of University of Pavol Jozef Šafárik in Košice in the subject field of General Biology. Since 2006 education is performed in the newly created postgradual subject field of Neurosciences. Institute of Neurobiology has initiated the creation of this field during the preparation of legislation process in 2003.
Since July 2006, Institute of Neurobiology is a member of university center of excellence (Center of Excellence for Individualization of Antitumoric Therapy at University of Pavol Jozef Šafárik in Košice) which integrates 4 academic and medical care institutions.
In collaboration with the Faculty of Science at University of Pavol Jozef Šafárik in Košice, our Institute has applied for accreditation for postgradual education in the subject field Physiology of Animals.
The Institute also collaborates with the University of Veterinary Medicine in Košice, based on agreement on participation on a EU project the 6th Framework Programme, project FOOD-CT-2003-506487.

3. Concept of R&D activity of the Organisation for the next four years (max. 5 pages)

i. Present state of knowledge and status of ongoing research related to the subject of the Concept, from both international and national perspective

Institute of Neurobiology is an academic institution and its mission is to perform basic neuroscience research that is relevant to major disorders of the central nervous system, such as CNS stroke and trauma. Our scientific program is closely associated with clinical research,

and we understand that our mission is a part of the multidisciplinary approach to these problems.

Brain diseases represent a major public health problem in Europe and beyond. Based on official numbers from WHO, brain diseases acount for 35% of the burden of all diseases in Europe. That impressive figure reflects the debilitating nature of brain diseases and the fact that peaople usually live with them for many years. The total cost of brain diseases amounts to €386 billion (the equivalent of more than 25 Channel Tunnel). In 2005, European Brain Council has published an analysis called Cost of Disorders of the Brain in Europe, measuring the impact of individual brain diseases. Stroke and trauma are listed among the 12 most costly brain diseases, and their annual costs in Europe are calculated as €22 billion and €3 billion, respectively.

Stroke

Acute cerebrovascular diseases occur with an incidence of 200 cases per 100 000 people per year and are the most frequent organic disorders of the central nervous system. Their incidence increases with age. In Europe, stroke is the third most frequent case of death and a leading cause of disability. In the past few decades, european stroke research centers have contributed to knowledge of the pathophysiology of stroke, especially to the understanding of the development and propagation of ischemic cell damage and the concept of the penumbra which is the basis for therapeutic strategies in acute ischemic stroke. However, the only effective treatment to have been approved for acute stroke to date is the lysis of the clot obstructing the artery that supplies the affected brain region.

Future research must focus on those pathophysiological mechanisms which can be influenced by therapeutic strategies in order to prevent or mitigate the development and propagation of ischemic damage. For that purpose, it is important to develop and implement models which represent the clinical setting and to apply investigative procedures which permit the direct comparison of pathophysiological changes in animal models and in stroke patients. These models can be used to evaluate therapeutic concepts and treatment effects. Further studies are needed to clarify whether stem cells that are injected after experimental occlusion of the middle crebral artery, and which have ben shown to migrate to an ischemic lesion, can form connections and enhance neuroplasticity for improved recovery. Additional experiments are needed to demonstrate the applicability of neurogenic stem cells for therapeutical purposes.

Spinal cord injury

In 2005, the number of spinal cord-injured patients in Europe was estimated over 500 000. About half of these patients are the result of traffic accidents, and more than half occur in the 16-30 age group, men being more frequently affected (80%). Spinal cord injury (SCI) leads most frequently to permanent paralysis and a range of serious dysfunctions affecting the bladder, bowel, and reproductive and cardiovascular systems. In SCI, the initial impact results in a primary lesion with axonal disruption and haemorrhage leading to secondary damage mechanisms including inflammation and oxidative stress. These in turn exacerbate the pathology. The development of a number of experimental models of SCI has been central to obtaining a better understanding of the cascade of cellular and molecular events that is initiated by a traumatic event, and has allowed the definition of three different time points and targets which are amenable to post-lesional intervention strategies:

1, reducing secondary tissue damage, open for neuroprotective strategies

2, promoting axonal regeneration, open for repair strategies

3, reactivating the central pattern generator in the de-afferented spinal cord, open for restorative strategies

Many highly promising experimental intervention strategies have been developed to promote neuroprotection and repair, but most still require significant development before they can enter clinical trials.

There is enormous potential for the further development of neuroprotective strategies which reduce one or more of the key mechanisms involved in secondary tissue damage, such as recruitment of inflammatory cells to the lesion site, expression of cytokines, release of prostaglandins, free radicals and other cytotoxic molecules. Central to such research will be the clear identification of the duration of the clinical window of opportunity for the range of injury types.

The versatility of stem cells and progenitors has led to substantial interest in the use of such cells for transplant-mediated replacement strategies. Although embryonic stem cells have the widest potential due to their pluripotentiality, stem cells or precursors from adult sources also require thorough investigation. The recruitment of endogeneous stem cells to promote tissue repair promises many potential therapeutic applications.

Since severed axons often have to traverse areas of scar tissue and cystic cavitation at the lesion site, a number of tissue engineering approaches have been explored to bridge the gap, and more sophisticated biomaterials are contributing to this approach.

Although there are many experimental models of SCI, the functional analyses applied to these models still rely on the relatively subjective opinion of one or more observers. The development of more objective, computer-assisted analytical methods will be of substantial importance. There is no doubt that combination of several intervention strategies will be necessary in experimental and clinical SCI to obtain clinically satisfatory functional recovery.

The current clinical approach to SCI is mainly symptomatic. The only pharmacological treatment that has been approved for use in the acute phase, high dose steroids, remains highly controversial and is often considered a treatment option rather than a standard of care. Many other drugs are being investigated for rapid clinical application, however, and some are already being tested in humans. Certain repair strategies are in phase I trials, such as implantations of autologous, incubated macrophages.

The enormous complexity of the neuroscientific problem posed by SCI demands input from a number of specialised research groups which are capable of bringing together effective combinations of treatment strategies in a coordinated manner.

Growth factors

Rearrangement of neuronal networks is required during recovery from a large number of brain diseases, from stroke to traumatic brain injury. On the other hand, aberrant connectivity is believed to underlie other brain diseases, including epilepsy, chronic pain and addiction. Glial cells actively inhibit neuronal regrowth, which seriously limits neuronal recovery after spinal cord injury and stroke. Growth factors support neuronal survival and control neuronal connectivity during development and after trauma. The expression of these growth factors is increased by exercise and enriched environment, which can also lead to enhanced recovery following brain injury. Therefore growth factors and their signalling mechanisms, viral vector delivery of neurotrophic genes or proteins and stem cell approaches are candidate treatments for a wide variety of brain diseases. Systemic delivery of small molecules that stimulate neurogenesis or trophic factors is an attractive therapeutic approach for the pharmaceutical industry.

Stem cells research

Stem cell transplantation is a promising area of research for the repair of brains damaged by neurodegenerative, affective or cerebrovascular diseases. One strategy being explored is that of cultivating the required cell type from stem cells in vitro, then grafting the differentiated cells into the damaged brain. But the transplantation technique needs to be refined. The anatomical and functional integration of grafts into pre-existing circuits is not yet good enough, and better molecular imaging methods are needed to monitor how the raft functions in vivo.

An important focus in basic research is to explore possibilities for repair by promoting regeneration and exploiting brain plasticity. Europe currently has a distinct advantage over the USA in stem cells research, and clear opportunities exist to increase European dominance in this field. Stem cells therapy has already proved beneficial in various neurological diseases, but research into its potential use in traumatic CNS injury is still in its infancy.

ii. Organisation's role or significance in the overall research effort within the field of the Concept on both the national and international scales

The Institute of Neurobiology has been studying the pathomechanisms of CNS injury due to circulatory, traumatic and metabolic disturbances from the very beginning of its existence for more than 30 years. Institute has got a solid background that grants for its development in the future. The Institute is located in a modern building, has got a good infrastructure and systematically built laboratories.
There is a relatively small, but very experienced group of scientists with well-defined areas of interest at the Institute. The Institute has a good position in both national and international community of experimental biomedicine. There are 3 researchers with the highest degree D.Sc. at the Institute, and others are preparing their docorate thesis.
Experimental research of the brain is extremely demanding from methodical point of view. During the existence of the Institute, we have preferred multidisciplinary approach. Understanding the processes in the central nervous system under both physiological and pathological conditions can be made only by contributions from all disciplines such as anatomy, physiology, and biochemistry.
The Institute, as a regionally renowned research institution, closely collaborates with Universities and clinical researchers at national level. Similarly, we sytematically collaborate on international level with the brain research-oriented Institutions from the countries of V4. Based on the both collaborations, Institute prepares mutual projects, organizes conferences, and provides research tutors and scientists for doctoral students.
Our focusing and methodologies are absolutely in agreement with the recommendations for european brain research, as defined by recent Consensus document on European brain research published by European Brain Council.
Recently, we participated on 2 project applications submitted for 6FP .

iii. Objectives of the Concept

Central to our effort is building an academic institution devoted to experimental brain research, in line with the recommendations of European Brain Council. We will continue working on basic and preclinical research focused on understanding the mechanisms of circulatory, traumatic and metabolic disorders of the central nervous system, aimed at designing and testing the promising neuroprotective strategies.

Objectives for the next 4 years

1. In vitro experiments

Many answers to important questions in neurobiology can be obtained "from the Petri dish", rather than from the whole animal experiment. It is both ethically and economically desirable to make experiments in vitro. On the other side, there is a general consensus in neurobiology, that "in vivo veritas". Our strategy will be to continue the experimental work with sophisticated in vivo models but also to utilize isolated cells and tissues.

2. Molecular approach
It is obvious that any progress in understanding the pathomechanisms of brain diseases have to be made on molecular level. We have to extend our possiblities to apply modern molecular methods for studying genomics and proteomics of neural cells in pathologic conditions. That is why it is of primary importance to involve genetically modified animals into portfolio of our research techniques.

3. Get involved into regeneration medicine
It is expected that an enormous potential of cell therapy will be evaluated in the future. It is our mission to promote application of regeneration medicine for the treatment of brain diseases. Transplatation and tissue replacement therapies must be based on understanding molecular mechanisms of ontogenesis of the nervous system.

4. Integration of neuroscience research in Slovakia
Experimental neuroscience in Slovakia has devoleped as isolated laboratories based on enthusiastic individuals. At this moment it consists of relatively small groups at various academic and clinical institutions. Each of them has its own strengths, but no one can afford complex, multidisciplinary approach for complex study of its subject of interest. We believe that integration of neuroscientists can bring a strong synergic effect for all participants.

iv. Proposed strategies and methods to be applied, and time schedule

1, Stimulation of individuals to prepare their new projects in line with the proposed objectives

2, Obtaining funds from different sources
In addition to the "traditional" research projects, we will aplly for:
a, 7th Framework Programme EU 2007-2013. 7th FP is the first programme that recognized importance of brain research in EU, and will specifically support programmes oriented on brain research. Therefore, there is a good chance to succeed with our 2 projects that are in preparation
b, Structural Funds of EU 2007-2013 are planned for building infrastructure – we have prepared 5 projects that will be submitted.
c, Launch of new State programs 2008-2015. We have submitted a project proposal entitled Regeneration medicine for the treatment of CNS diseases.

3, Collaboration at national level
Based on initiatives from Slovak Society for Neuroscience, we are planning to prepare a project for National Center of Excellence in Neurosciences under the Operation priorities of Structural Funds of EU 2007-2013. Preparation of this project will be based on experience from existing Centers of Excellence.

4, Systematically building infrastructure

Laboratories of :
Advanced confocal microscopy
Gene expresion analyses
Proteomic studies
Membrane physiology
Preparation of cell cultures

5, Repatriation grants of EU
There are many scientists from our Institute working in the USA and Canada. There is a good chance to stimulate their return to Košice with aid of new programmes for building infrastructure and Eropean repatriation grants.

III. Partial indicators of the main activities:

1. Research output

i. **List of the selected publications documenting the most important results of basic research. Total number of publications in the whole assessed period should not exceed the average number of the research employees**

1. GOTTLIEB, M.- WANG, Y.- TEICHBERG. V.I. Blood-mediated scavenging of cerebrospinal fluid glutamate. In *Journal of Neurochemistry.* Vol 87, 2003, 119–126. IF=4,604
2. LUKACOVA, .- CIZKOVA, D.- KRIZANOVA, O.- PAVEL, J.- MARSALA, M,.- MARSALA J. Peripheral axotomy affects nicotinamide adenine dinucleotide phosphate diaphorase and nitric oxide synthases in the spinal cord of the rabbit. In *Journal of Neuroscience Research.* Vol. 71(2), 2003, 300-313. IF=3,239
3. BURDA, J.- HREHOROVSKA, M.- GARCIA BONILLA, L.- DANIELISOVA, V.- CIZKOVA, D.- BURDA, R.- NEMETHOVA, M.- FANDO, L.J.- SALINAS, M. Role of protein synthesis in the ischemic tolerance acquisition induced by transient forebrain ischemia in the rat. In *Neurochemical Research.* Vol. 28, 2003, 1213-1219.IF=2,187
4. ČÍŽKOVÁ D,- CARMEL JB, -YAMAMOTO K,- KAKINOHANA O,- SUN D, -HART RP,- MARŠALA M. Characterization of spinal HSP72 induction and development of ischemic tolerance after spinal ischemia in rats. In *Experimental Neurology* Vol.185, no.1 (2004), p. 97-108 IF= 3,767
5. GARCIA, L.- BURDA, J.- HREHOROVSKÁ, M.- BURDA, R.- MARTIN, ME.- SALINAS, M. Ischaemic peconditioning in the rat brain: effect on the activity of several initiation factors, Akt and extracellular signal-regulated protein kinase phosphorylation, and GRP78 and GADD34 expression. In *Journal of Neurochemistry* Vol. 88, no.1 (2004), p.136-47. IF= 4,604
6. MARŠALA J,- LUKÁČOVÁ N,- ČÍŽKOVÁ D,- LUKÁČ I- KUCHÁROVÁ K,- MARŠALA M. Premotor nitric oxide synthase immunoreactive pathway connecting lumbar segments with the ventral motor nucleus of the cervical enlargement in the dog. In *Journal of Chemical Neuroanatomy.* Vol. 27, no.1 (2004), p. 43-54. IF= 2,453
7. ONDREJČÁK T,- VANICKÝ I,- GÁLIK J. Ischemic preconditioning does not improve neurological recovery after spinal cord compression injury in the rat. In *Brain Research*. Vol. 995, no.2 (2004), p. 267-73. IF= 2,296

8. MARŠALA M,- KAKINOHANA O,- YAKSH TL,- TOMORI Z,- MARŠALA S,- ČÍŽKOVÁ D. Spinal implantation of hNT neurons and neuronal precursors: graft survival and functional effects in rats with ischemic spastic paraplegia. In *European Journal of Neuroscience*. Vol. 20, no.9(2004), p. 2401-14. IF= 3,949
9. SASARA T,- ČÍŽKOVÁ D, -MESTRIL R, -GÁLIK J,- SUGAHARA K,- MARŠALA M. Spinal heat shock protein (70) expression: effect of spinal ischemia, hyperthermia (42 degrees C)/hypothermia (27 degrees C), NMDA receptor activation and potassium evoked depolarization on the induction. In *Neurochemistry International* Vol.44, no.1 (2004), p. 53-64 . IF=2,994
10. CHALIMONIUK M,- LANGFORT J,- LUKÁČOVÁ N,- MARŠALA J. Upregulation of guanylyl cyclase expression and activity in striatum of MPTP-induced parkinsonism in mice. In B*iochemical and Biophysical Research Communications* Vol. 324, no.1, (2004), p. 118-26. IF= 3,000
11. MARŠALA, J.- LUKÁČOVÁ, N.- SULLA, I.- WOHLFAHRT, P.- MARSALA, M. The evidence for nitric oxide synthase immunopositivity in the monosynaptic Ia-motoneuron pathway of the dog. In: *Experimental Neurology* 195 (1): 161-178 SEP 2005. (3,767 – IF2005)
12. JERGOVÁ, S.- ČÍŽKOVÁ D. Long-term changes of c-Fos expression in the rat spinal cord following chronic constriction injury. In: *European Journal of Pain* 9 (3): 345-354 JUN 2005. (2,460 – IF2005)
13. BURDA, J.- MATIAŠOVÁ, M.- GOTTLIEB, M.- DANIELISOVÁ, V.- NÉMETHOVÁ M.- GARCIA, L.- SALINAS, M.- BURDA, R. Evidence for a role of second pathophysiological stress in prevention of delayed neuronal death in the hippocampal CA1 region. In: *Neurochemical Research* 30 (11):1397-1405 NOV 2005 (2,187 – IF2005)
14. DANIELISOVÁ, V.- NÉMETHOVÁ, M.- GOTTLIEB, M.- BURDA J. Changes of endogenous antioxidant enzymes during ischemic tolerance acquisition .In: *Neurochemical Research* 30 (4): 559-565 APR 2005. (2,218 – IF2005)
15. MARSALA, M.- HEFFERAN, MP.- KAKINOHANA, O.- NAKAMURA, S.- MARSALA, J.- TOMORI, Z. Measurement of peripheral muscle resistance in rats with chronic ischemia-induced paraplegia or morphine-induced rigidity using a semi-automated computer-controlled muscle resistance meter. In: *Journal of Neurotrauma* 22(11):1348-61 NOV 2005. (2,574 – IF2005)
16. GOTTLIEB, M.- LEAL-CAMPANARIO, R.- CAMPOS-ESPARZA, MR.- SANCHEZ-GOMEZ, MV.- ALBERTI, E.- ARRANZ, A.- DELGADO-GARCIA, JM.- GRUART, A.- MATUTE, C. Neuroprotection by two polyphenols following excitotoxicity and experimental ischemia. In: *Neurobiology of Disease*. Vol. 23, No. 2 (2006) p.374-86. (4,048 – IF2005)
17. KAKINOHANA, O.- HEFFERAN, MP.- NAKAMURA, S.- KAKINOHANA, M.- GÁLIK, J.- TOMORI, Z.- MARŠALA, J.- YAKSH, TL.- MARSALA, M. Development of GABA-sensitive spasticity and rigidity in rats after transient spinal cord ischemia: a qualitative and quantitative electrophysiological and histopathological study. In: *Neuroscience*. Vol. 141, No. 3 (2006), p. 1569-83. (3,410 – IF2005)
18. CHALIMONIUK, M.- LUKÁČOVÁ, N.- MARŠALA, J.- LANGFORT, J.Alterations of the expression and activity of midbrain nitric oxide synthase and soluble guanylyl cyclase in 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine-induced Parkinsonism in mice. In: *Neuroscience*. Vol. 141, No. 2 (2006), p.1033-46. (3,410 – IF2005)

19. VANICKÝ. I.- ONDREJČÁK, T.- ONDREJCAKOVA, M.- SULLA, I.- GÁLIK, J. Long-Term Changes in Spinal Cord Evoked Potentials After Compression Spinal Cord Injury in the Rat. In: *Cellular and Molecular Neurobiology.* Vol.26 No.7-8 (2006) p. 1519-1537. (2,022 –IF2005)
20. ELBERS, PW.- de HAAN, P.- VANICKÝ, I.- LEGEMATE, D.- DZOLJIC, M. Effect of temporary visceral ischemia on spinal cord ischemic damage in the rabbit. In: *Annals of Thoracic Surgery*. Vol. 81, No. 3 (2006), p. 910-7. (2,229 – IF2005)

ii. **List of monographs/books published abroad -**

iii. **List of monographs/books published in Slovakia -**

iv. **List of other scientific outputs specifically important for the Organisation**

Chapters in monographs:

1. MARŠALA M., VANICKÝ I., TOKUMINE J., KAKINOHANA O, MARŠALA J. Blood brain barrier changes in global and focal cerebral ischemia. In: BLOOD-SPINAL CORD AND BRAIN BARRIERS IN HEALTH AND DISEASE, eds.Sharma, H.S.- Westman, J., Elsevier**,** 2004. ISBN 0-120639011-8, pp. 385-394
2. LUKÁČOVÁ, N.- PAVEL, J.- KUCHÁROVÁ, K.-MARŠALA, J. Plasticity of the spinal neural circuitry in nitric oxide synthase immunoreactive pathways after spinal cord hemisection. In: Trends in Neurochemistry Research,. Editor: Robert M. Coleman, Nova Science Publishers, Inc.2005, ISBN: 1-59454-418-2, p.189-222.

v. Table of research outputs

*Table **Research outputs** shows research outputs in number of specified entries; these entries are then divided by FTE employees with a university degree (from Tab. Research staff) for all Organisation at the respective year; finally these entries are divided by the total salary budget (from Tab. Salary budget).*

Research outputs	2003			2004			2005			2006			total			
	number	No. / FTE	No. / salary budget	number	No. / FTE	No. / salary budget	number	No. / FTE	No. / salary budget	number	No. / FTE	No. / salary budget	number	averaged number per year	av. No. / FTE	av. No. / salary budget
chapters in monographs, books published abroad	0	0,00	0,00	1	0,07	0,16	1	0,08	0,15	0	0,00	0,00	2	0,5	0,04	0,08
chapters in monographs, books published in Slovakia	0	0,00	0,00	0	0,00	0,00	0	0,00	0,00	0	0,00	0,00	0	0,0	0,00	0,00
CC publications	11	0,94	1,83	21	1,49	3,37	13	1,01	1,97	26	1,84	3,80	71	17,8	1,34	2,77
scientific publications indexed by other databases (specify)	0	0,00	0,00	0	0,00	0,00	0	0,00	0,00	0	0,00	0,00	0	0,0	0,00	0,00
scientific publications in other journals	21	1,79	3,50	6	0,43	0,96	18	1,40	2,73	0	0,00	0,00	45	11,3	0,85	1,75
publications in proc. of international scientific conferences	3	0,26	0,50	4	0,28	0,64	0	0,00	0,00	17	1,20	2,48	24	6,0	0,45	0,94
publications in proc. of nat. scientific conferences	0	0,00	0,00	17	1,21	2,73	7	0,54	1,06	0	0,00	0,00	24	6,0	0,45	0,94
active participations at international conferences	41	3,49	6,83	27	1,92	4,33	55	4,26	8,35	53	3,74	7,75	176	44,0	3,33	6,86
active participations at national conferences	17	1,45	2,83	1	0,07	0,16	7	0,54	1,06	0	0,00	0,00	25	6,3	0,47	0,97

vi. Renormalized publications[2]

Renormalized publications = number of CC publications in the given year times authorship's portion of the Organisation times the journal impact factor in 2005 divided by the median impact factor in the research field

[2] This information is required only from the Organisations of the Section 2 of the Slovak Academy of Sciences.

Renormalised publications	2003			2004			2005			2006		
	number	No. / FTE	No. / salary budget	number	No. / FTE	No. / salary budget	number	No. / FTE	No. / salary budget	number	No. / FTE	No. / salary budget
Renormalized publications	4,97	0,42	0,83	10,2	0,72	1,63	7,84	0,61	1,19	13,7	0,97	2,00

vii. Standard manuscript page count[3]

Standard manuscript page count	2003			2004			2005			2006		
	number	No. / FTE	No. / salary budget	number	No. / FTE	No. / salary budget	number	No. / FTE	No. / salary budget	number	No. / FTE	No. / salary budget
page count	0	0,0	0,0	0	0,0	0,0	0	0,0	0,0	0	0,0	0,0

viii. **List of patents and patent applications -**

ix. Supplementary information and/or comments on the scientific output of the Organisation

In addition to the numbers given above, scientific workers of the Institute published 49 abstracts in journals covered by the ISI database Current Contents (averaged Impact Factor 1,644) and 45 abstracts in other journals (see table below). These abstracts are regularly cited.

other research outputs	number	av. number/year	av. number/FTE	av. number/MP
CC abstracts	49	12.25	0.59	1.98
Abstracts in other journals	45	11.25	0.57	1.75

[3] This information is required only from the Organisations of the Section 3 of the Slovak Academy of Sciences.

We want to stress the productivity of the young researchers (below 35) at the Institute (averaged number 5). During the evaluated period they have published together 13 publications as first authors in peer reviewed journals covered by the ISI database Current Contents, e.g. in Brain Res., Cell. Mol. Neurobiol., Eur. J. Pain or J. Neurosci. Meth., with average Impact Factor 1.658.

Our contribution to brain-drain from Europe - during fellowships at scientific institutions abroad, researchers on long-term leaves from the Institute have published 1 chapter in monograph published abroad and 32 CC publications (averaged impact factor 3.384); these publications were not included in the list of the research outputs mentioned above.

2. Responses to the scientific output

*Table **Citations** shows specified responses to the scientific outputs; these entries are then divided by the FTE employees with a university degree (from Tab. Research staff) for all Organisation at the respective year; finally these entries are divided by the total salary budget (from Tab. Salary budget).*

Citations	2002			2003			2004			2005			total			
	number	No. / FTE	No. / salary budget	number	No. / FTE	No. / salary budget	number	No. / FTE	No. / salary budget	number	No. / FTE	No. / salary budget	number	averaged number per year	av. No. / FTE	av. No. / salary budget
Web of Science	110	9,4	18,3	112	7,9	18,0	126	9,8	19,1	124	8,8	18,1	472	118,0	8,9	73,6
(SCOPUS)	11	0,9	1,8	17	1,2	2,7	45	3,5	6,8	35	2,5	5,1	108	27,0	2,0	16,8
(Biorad, SCIRUS)	2	0,2	0,3	1	0,1	0,2	1	0,1	0,2	1	0,1	0,1	5	1,3	0,1	0,8
in monographs, conf. proceedings and other publications abroad	0	0,0	0,0	0	0,0	0,0	5	0,4	0,8	0	0,0	0,0	5	1,3	0,1	0,8
in monographs, conf. proceedings and other publications in Slovakia	0	0,0	0,0	1	0,1	0,2	0	0,0	0,0	0	0,0	0,0	1	0,3	0,0	0,2

i. List of 10 top-cited publications and number of their citations in the assessment period

1. Title: The deaf jerker mouse has a mutation in the gene encoding the espin actin bundling proteins of hair cell stereocilia and lacks espins
Author(s): Zheng LL, Sekerkova G, Vranich K, Tilney LG, Mugnaini E, Bartles JR
Source: CELL 102 (3): 377-385 AUG 4 2000
Citations: 44

2. Title: Neuronal nitric oxide synthase mRNA upregulation in rat sensory neurons after spinal nerve ligation: Lack of a role in allodynia development
Author(s): Luo ZD, Chaplan SR, Scott BP, Cizkova D, Calcutt NA, Yaksh TL
Source: JOURNAL OF NEUROSCIENCE 19 (21): 9201-9208 NOV 1 1999
Citations: 41

3. Title: Possible mechanisms involved in the down-regulation of translation during transient global ischaemia in the rat brain
Author(s): de la Vega CM, Burda J, Nemethova M, Quevedo C, Alcazar A, Martin ME, Danielisova V, Fando JL, Salinas M
Source: BIOCHEMICAL JOURNAL 357: 819-826 Part 3, AUG 1 2001
Citations: 25

4. Title: The role of nitric oxide in nociception.
Authors: Luo Z.D., Cizkova D.
Source: Current review of pain, 4 (6), pp. 459-466. (2000)
Citations: 23

5. Title: Expression of ionotropic glutamate receptor subunits in glial cells of the hippocampal CA1 area following transient forebrain ischemia.
Author(s): Gottlieb M, Matute C
Source: JOURNAL OF CEREBRAL BLOOD FLOW AND METABOLISM 17 (3): 290-300 MAR 1997
Citations: 18

6. Title: Domain-restricted expression of two glutamic acid decarboxylase genes in midgestation mouse embryos.
Authors: Katarova Z., Sekerkova G., Prodan S., Mugnaini E., Szabo G.
Source: Journal of Comparative Neurology, 424 (4), pp. 607-627. (2000)
Citations: 17

7. Title: Silver staining of native and denatured eukaryotic DNA in agarose gels.
Authors: Gottlieb M, Chavko M
Source: ANALYTICAL BIOCHEMISTRY 165 (1): 33-37 AUG 15 1987
Citations: 16

8. Title: Phosphorylation of the alpha subunit of initiation factor 2 correlates with the inhibition of translation following transient cerebral ischaemia in the rat.
Author(s): Burda J, Martin ME, Garcia A, Alcazar A, Fando JL, Salinas M.
Source: BIOCHEMICAL JOURNAL 302: 335-338 Part 2, SEP 1 1994

Citations: 15

9. Title: Transient spinal ischemia in the rat – characterization of behavioral and histopathological consequences as afunction of the duration of aortic occlusion.
Author(s): Marsala M, Yaksh TL
Source: JOURNAL OF CEREBRAL BLOOD FLOW AND METABOLISM 14 (3): 526-535 MAY 1994
Citations: 13

10. Title: Localization of N-type Ca2+ channels in the rat spinal cord following chronic constrictive nerve injury
Authors: Cizkova D., Marsala J., Lukacova N., Marsala M., Jergova S., Orendacova J., Yaksh T.L.
Source: EXPERIMENTAL BRAIN RESEARCH, 147 (4), pp. 456-463. (2002)
Citations: 12

ii. **List of top-cited authors from the Organisation (at most 10 % of the research employees) and their number of citations in the assessment period**

1. Maršala J. 202 citations
2. Čížková D. 145 citations
3. Vanický I. 121 citations

iii. **Supplementary information and/or comments on responses to the scientific output of the Organisation**

There is a commercially available biochemical kit produced since 1993 according to the method developed at our Institute and published by our colleagues. Producer has been citing the original paper in its catalogue:
Electrophoresis stains and tracking dyes, (Silver Stain Plus Kit), 2005
BioRad Catalog – Life Science, Research products

Title: Silver staining of native and denatured eukaryotic DNA in Agarose gels
Author(s): Gottlieb, M.- Chavko, M.
Source: ANALYTICAL BIOCHEMISTRY 165(1):33-37, aug. 1987

3. Research status of the Organisation in the international and national context

- **International/European position of the Organisation**

i. **List of the most important research activities documenting international importance of the research performed by the Organisation, incl. major projects (details of projects should be supplied under Indicator 4). Collective membership in the international research organisations, in particular within the European Research Area**

List of major international projects:

Cooperation on the project of 6.FP Network of Excellence: Molecular mechanisms of neuronal degeneration (acronyme BRADAREP) headed by prof. J. Delgado (Sevilla), Spain (submitted 27/10/2003).

Neuronal plasticity and neuronal protection – research with tryptophan metabolites and conjugates. Hungary, Department of Physiology University of Szeged – Grant OTKA T046687.

Neuroprotective vs neurodegenerative role of nitric oxide in CNS under neuropathological disorder. Poland, SAS/PAV, Centre of Medical Research – project 17/24-26.

Ischemic paraplegia: modulation by stem cells implant. USA, University of California, Anesthesiology Research Department – grant NIH-NINDS 5 RO1 NS 40386.

Translational alterations during transient cerebral ischemia and ischemic preconditioning. The role of initiation factors. Spain, Department of biochemistry, Hospital Ramon y Cajal – Grant Fondo de Investigación Sanitaria, MSyC, 02/0303.

Cooperative participation with University of Veterinary Medicine in Košice – 6 RP FOOD-CT-2003-506487

Neural Regeneration and Plasticity: Participation on COST B 30 project in the range of 7. FP EU

Collective membership in the international research organisations:

ESN (European Society for Neurochemistry) –3
IBRO (International Brain Research Organization) – 8
ANG (Anatomische Gesellschaft) – 4
Czech and Slovak Neurochemical Society – 7
Slovak Society for Biochemistry and Molecular Biology – 1
ENA (European Neuroscience Association – 1
SFN (Society for Neuroscience) – 5
World Federation of Neurology Commision for Comparative Neuroanatomy – 1
American Society for Neural Transplantation and Repair – 1
ECRO – European Chemoreceptor Organization – 1
International Association for the Study of Pain – 2

ii. **List of international conferences (co-) organised by the Organisation**

5th International Symposium on Experimental and Clinical Neurobiology, 19. – 22. September 2005, Stará Lesná. (46 participants from Slovakia, 66 participants from abroad)

11th Meeting of the Czech and Slovak Neurochemical Society: Molecular basis of Neurological and Psychiatric Disorders, Martin, Slovak Republic, Sept. 6.-10., 2006

iii. **List of international journals edited/published by the Organisation**

Physiological Research, vol.52 (1), 2003 (The 4th International Symposium on Experimental and Clinical Neurobiology)

Cellular and Molecular Neurobiology, Vol. 26 No.7-8, 2006 (The 5th International Symposium on Experimental and Clinical Neurobiology)

iv. **List of edited proceedings from international scientific conferences and other proceedings**

Folia Medica Cassoviensia, 2005 (5th International Symposium on Experimental and Clinical Neurobiology, Abstracts, Sept. 2005, p. 157)

- **National position of the Organisation**

i. **List of selected most important national projects (Centres of Excellence, National Reference Laboratories, Agency for the Promotion of Research and Development (APVV/APVT), National Research Programmes, Scientific Grant Agency of the Slovak Academy of Sciences and the Ministry of Education (VEGA), and others)**

Centres of excellence:
1, Centre of excellence for Alzheimer disease and related neurodegenerative disorders (AD CENTRUM).
Basic research centre: Institute of Neuroimmunology SAS, Bratislava
Collaborative institution: Institute of Neurobiology, SAS, Košice

2, Centre of excellence for individualization of antitumoric therapy (CEX INDICATE)
Basic research centre: Institute of pharmacology, Medical faculty of UPJŠ, Košice
Collaborative institution: Institute of Neurobiology, SAS, Košice

APVT projects:
Postraumatic regenerability of short propriospinal and long premotor truncospinal conductive systems in the spinal cord. No. of project: -51-013002 Principal investigator: Maršala Jozef, prof., MUDr., DrSc.

Retrograde ischemic tolerance as a possible tool in the prevention of delayed death of neurons in selectively vulnerable brain regions. No. of project: -51-021904 Principal investigator: Burda Jozef, MVDr., CSc.

The role of nitric oxide and substance P in the mechanisms of chronic pain and their pharmacological treatment. No. of project: -51-011604 Principal investigator: Jergová Stanislava, RNDr., PhD.

APVV projects:

Experimental transplantation of bone marrow stem cells, umbilical blood cord stem cells and spinal neural precursors for treatment of spinal cord injury. No. of project: -51-002105
Principal investigator: Čížková Dáša, MVDr., CSc.

Animal model of human gliomas based on nitosourea induced malignant transformation of neural stem cells. No. of project: -20-052005
Principal Investigator: prof. MUDr. Igor Šulla, DrSc. – Medical faculty UPJŠ, Košice
Cooperating institutions: Institute of Neurobiology, Slovak Academy of Sciences Košice, University of Veterinary Medicine Košice

VEGA projects:
The mechanisms influencing spinal cord nociceptive transmission at acute/chronic pain state and possible pharmacological treatment. No. of project: 2/1064/21 Principal investigator: MVDr. Dáša Čížková,CSc.

The origin, course and termination of truncospinal premotor nitric oxide synthase immunoreactive pathways in the spinal cord. No. of project: 2/3217/23 Principal investigator: Prof. MUDr. Jozef Maršala, DrSc.

Pathophysiology of spinal cord injury - the role of nitric oxide in the process of secondary injury in the white matter. No. of project: 2/3216/23 Principal investigator: MVDr. Ivo Vanický, CSc.

Mechanisms of translational changes in the rat brain after ischemia and subsequent reperfusion. Study focused to the selectively vulnerable neurons. No. of project: 2/3219/23, Principal investigator: MVDr. Jozef Burda, CSc.

Neurogenesis in new born, adult and aging Rats: Prospects in health and Pathology. No. of project: 2/3218/23, Principal investigator: RNDr. Eniko Račeková, CSc.

Regularities of rat neuroepithelial and ependymal cells transformation in health and pathology. No. of project: 2/2082/22, Principal investigator: MUDr. Judita Orendáčová,CSc.

Ischemia-and trauma-induced damage of the white matter and neuroprotective and neurodestructive role of nitric oxide synthase and nitric oxide No. of project: 2/2079/22, Principal investigator: RNDr. Lukáčová Nadežda, CSc.

Morphological and clinical aspects of neuroprotective effect of Tanakan on some ischemically damaged regions of the CNS. No. of project: 1/8294/22, Principal investigator: doc. MUDr. Eva Mechírová, PhD., (Deputy: MVDr. J. Burda, CSc).

Medico-legal analysis of traumatic and nontraumatic lesions of the CNS and their timing with application of immunohistochemical methods. No. of project: 1/0511/03, Principal investigator: Doc.MUDr. František Longauer, CSc. (Deputy: RNDr. Enikő Račeková, PhD.).

Risk factors of neurodegeneration: Morfological and functional study of alcohol and electromagnetic radiation effects in the rat brain. No. of project: 2/5135/25, Principal investigator: MUDr. Judita Orendáčová,CSc

The participation of nitric oxide synthase on nociceptive and proprioceptive afferentation. No. of project: 2/5134/25, Principal investigator: RNDr. Lukáčová Nadežda, CSc.

Molecular changes of neurons in CNS induced by ischemia reperfusion injury and the possibilities of protection. No. of project: 1/0034/03, Principal investigator: Prof. RNDr. Lehotský Ján, CSc., (Deputy: RNDr. N. Lukáčová, CSc.).

Genome instability in the brain tissue of the offspring of male rats exposed to some environmental genoxic factors. No. of project: 1/2353/03, Principal investigator: Prof. RNDr. Mišúrová Eva, CSc., (Deputy: RNDr. Račeková Eniko, CSc.).

Transformation of neuroepithelial and ependymal cells of the spinal central canal in development and after spinal cord trauma. No. of project: 1/2356/05, Principal investigator: Doc. RNDr. Daxnerová Zuzana, CSc., (Deputy: MVDr. Vanický Ivo, CSc.).

Distribution of spinal and supraspinal neuronal pools expressing nNOS and NK-1 receptor involved in chronic pain development. No. of project: 2/5136/26, Principal investigator: MVDr. Čížková Dáša, CSc.

Accelerating brain to blood glutamate efflux by the activation of blood resident enzymes: A novel approach for the management of neurodegenerative diseases. No. of project: 2/6210/26 Principal investigator: Gottlieb Miroslav, RNDr., CSc.

Role of second pathophysiological stress in the prevention of the delayed neuronal death. No. of project: 2/6211/26, Principal investigator: Burda Jozef, MVDr., DrSc.

The role of activated microglia/macrophages in the process of secondary damage of the white matter after CNS injury. No. of project: 2/6212/26, Principal investigator: Vanický Ivo, MVDr., CSc.

Endogenous and exogenous factors that regulate neurogenesis in adult rat brain. No. of project: 2/6213/26, Principal investigator: Račeková Enikö, RNDr., CSc.

Electrophysiological characteristics of differentiating multipotent stem cells. No. of project: 2/6214/26, Principal investigator: Gálik Ján, RNDr., CSc.

Molecular analysis of ischemia – reperfusion changes in CNS and neuroprotective mechanisms. No. of project: 1/3380/26, Principal investigator: prof. RNDr. Ján Lehotský, DrSc., (Deputy: Lukáčová Nadežda, RNDr., DrSc.)

ii. List of national scientific conferences (co)-organised by the Organisation

Mechanisms of damage and regeneration possibilities in the CNS. Košice, 16. February, 2004

iii. List of national journals published by the Organisation -

iv. **List of edited proceedings of national scientific conferences/events**

Mechanisms of damage and regeneration possibilities in the CNS. Proceedings, 2005 ISBN 80-969143-2-4, 89 pages

- **International/European position of the individual researchers**

i. **List of invited/keynote presentations at international conferences, documented by an invitation letter or programme**

1, Maršala, J., Lukáčová, N., Čížková, D., Maršala, M. Immunohistochemical and histochemical characterization of neuronal nitric oxide synthase immunoreactive terminal fields in the spinal cord of the dog. Neurochemical conference „Molecular basis of neurological diseases and new therapeutic strategies“, Warsaw, November, 2003 (plenary lecture).

2, Lukáčová, N., Čížková, D., Križanová, O., Pavel, J., Lukáč, I., Maršala, M., Maršala, J. Response of NOS pools in the spinal cord after peripheral axotomy. Neurochemical conference „Molecular basis of neurological diseases and new therapeutic strategies“, Warsaw, November, 2003 (invited lecture).

3, Čížková, D. Stem Cells and Spinal Progenitors for Treatment of Spinal Cord Injury. 3-rd Annual Anti Ageing Conference London 2006 (AACL) and Incorporating The International Symposium on Regenerative Medicine, The Royal Society of Medicine, London, UK, 15-16.9.2006 (invited lecture).

4, Jergová S, Čížková, D. Changes in production of C-FOS protein in spinal cord of rat after peripheral nerve injury. VII. Czech-Slovak dialogs about pain, XIII. Slovak dialogs about pain. 13-15. October, 2005, Bojnice, Slovak Republic (invited lecture).

ii. **List of employees who served as members of the organising and/or programme committees for international conferences**

3rd Congress of the Slovak Neurosurgical Society with International Participation, 2004, 14.-16. 10., Stará Lesná, J. Maršala, – member of Scientific Committee

11th Meeting of the Czech and Slovak Neurochemical Society: Molecular basis of Neurological and Psychiatric Disorders, Martin, Slovak Republic, Sept. 6.10, 2006, J. Maršala, I. Vanický – members of Programme Committee

iii. **List of employees who served as members of important international scientific bodies (e.g. boards, committees, editorial boards of scientific journals)**

Journal of Brain Research-Berlin –(Germany) Prof. J. Maršala, DrSc. – member of Editorial Board
Neurobiology- (Hungary) – RNDr. T. Žigová, CSc. - member of Editorial Board
Prague Medical Report - Prof. J. Maršala, DrSc. - member of Editorial Board

iv. **List of international scientific awards and distinctions**

Award of R. Petr, 2004, dedicated by Czech Neurosurgical Society for publication of: Šulla I., Maršala J., Radoňák J. Ischemia, reperfusion-induced paraplegia in dogs, light microscopic observation. Rozhl. Chir. 2004; 83 (2): 91-95.

- **National position of the individual researchers**

i. **List of invited/keynote presentations at national conferences documented by an invitation letter or programme**

Lukáčová, N., Kafka, J., Čížková, D., Maršala, J. The response of nitric oxide synthesizing neurons in spinal cord after cauda equina constriction. XXII. Xenobiochemic symposium, Smolenice, June, 2003 (plenary lecture)

ii. **List of employees who served as members of organising and programme committees of national conferences**

Mechanisms of damage and regenerative possibilities in the CNS. Košice, 16. February, 2004, MVDr. I. Vanický, Ph.D., MVDr. V. Danielisová, Ph.D. (members of Organizing Committee).

iii. **List of employees serving in important national scientific bodies (e.g. boards, committees, editorial boards of scientific journals)**

Membership in Medical Scientific Board of SAS
Prof. MUDr. J. Maršala, DrSc.
MVDr. Ivo Vanický, CSc.

Membership in Molecular Biology and Genetics Board of SAS
MVDr. Jozef Burda, DrSc.
Membership in Scientific Grant Agency of the Ministry of Education of SR (Medical and pharmacological science) - MUDr. Judita Orendáčová. CSc., RNDr. N. Lukáčová, DrSc.

Czech and Slovak Neurochemical Society – (scientific secretary- RNDr. N. Lukáčová, DrSc.)

Membership in boards of the Presidium of SAS
MUDr. J. Orendáčová, CSc. – Board for high-priced equipment
RNDr. J. Gálik, CSc. – Board of communication and information technology
MVDr. J. Burda, DrSc. – Ethical commission

Slovak Society for Neurosciences of SAS
Prof. MUDr. J. Maršala, DrSc. – chairman
MUDr. J. Orendáčová, CSc. – membership
RNDr. J. Gálik, CSc. – scientific secretary
RNDr. N. Lukáčová, DrSc. – member of revision commission

iv. List of national awards and distinctions

Award of the Ministry of Education of SR for the science and technique in the category: Integrated work in the science and technique: Prof. MUDr. J. Maršala, DrSc.

Award for the best poster presentation, Lojda Symposium on Progress in basic, applied and diagnostic histochemistry - MUDr. K. Kuchárová, Ph.D., Košice, June 2004

Award (II.) of the Presidium of SAS in the Competition of young scientific workers, Bratislava, June, 2006 (RNDr. S. Jergová, Ph.D.)

Awards of Slovak histochemical and cytochemical society:
Award –(III.) for the best publication (2004) MVDr. V. Danielisová, Ph.D.
Award –(I.) for the best publication (2004) MVDr. D. Čížková, Ph.D.
Award –(I.) for the best publication (2005) RNDr. S. Jergová, Ph.D.
Award –(III.) for the best publication (2005) RNDr. E. Račeková, Ph.D.

Supplementary information and/or comments documenting international and national status of the Organisation

In connection with our scientific programme listed above and comprising several scientific research projects it is necessary to comment that many highly promising experimental interventional strategies have been developed to promote neuroprotection and repair, but most still require significant development before they can enter clinical trials. Between them, there is an enormous potential for the further development of neuroprotective strategies including stem cells and progenitors which can be perspectively used for therapeutic interventions. These items form an integral part of our research programme and, some of them, are included in our present research projects which are in progress.

Based on initiative of the Institute of Neurobiology, The Slovak Society for Neurosciences was founded in 2005 and, in connection with the registration of this society, the membership of our society was confirmed in FENS and IBRO organizations.

4. Project structure, research grants and other funding resources

- **International projects and funding**

i. List of major projects within the European Research Area – 5th and 6th Framework Programme of the EU, European Science Foundation, NATO, COST, INTAS, CERN, etc. (here and in items below please specify: type of project, title, grant number, duration, funding, responsible person in the Organisation and his/her status in the project, e.g. coordinator, principal investigator, investigator)

[1] Project – Cost B 30:
Neural Regeneration and Plasticity.
Principal Investigator: Prof. José-Maria Delgado
Responsible person in the Institute: MVDr. Jozef Burda, DrSc., delegate, investigator
Duration: 05/2006 - 07/2010
Total costs of project: 63000000,- €
Slovak funding in 2006: 65000,- SKK

ii. **List of other international projects incl. funding**

[1] Bilateral Slovak-Hungarian scientific cooperation
Neuronal plasticity and neuronal protection – Research with tryptophan-metabolites, conjugates and ischemic tolerance.
Number: MVTS SK-8/2004
Principal investigator in Slovakia: MVDr. Jozef Burda, DrSc.
Principal investigator in Hungary: Prof. Jozsef Toldi, DrSc., University Szeged
Duration: 06/2005 - 12/2006
Slovak funding: 35000,-Sk / 30000,-SKK

iii. **List of other important projects and collaborations without direct funding**

[1] Title: Translational alterations during transient cerebral ischemia and ischemic preconditioning. The role of initiation factors
Number: PI02/0304
Duration: 01/2003 – 12/2005).
Funding: 99000 €
Grant agency: Ministerio de Sanidad y Consumo. Instituto de Salud Carlos III (ISCIII).
Principal Investigator: Dra. Matilde Salinas, Department Biochemistry, Hospital Ramón y Cajal, Madrid
Slovak investigator: MVDr. Jozef Burda, DrSc.

[2] Title: Mechanisms of death and neuroprotection after brain ischemia. The role of initiation factors
Number: PI05/0312
Duration: 01/2006 – 12/2008).

Funding:177310 €
Grant agency: Ministerio de Sanidad y Consumo. Instituto de Salud Carlos III (ISCIII).
Principal Investigator: Dra. Matilde Salinas, Department Biochemistry, Hospital Ramón y Cajal, Madrid
Slovak investigator: MVDr. Jozef Burda, DrSc.

[3] Title: The molecular bases of neurodegeneration
Grant agency: Gobierno Vasco
Principal Investigator: Prof. Carlos Matute Almau, PhD, Departmet Neurobiology, University of Basque Country, Bilbao-Leioa
Duration: 2005/2007
Funding:120000 €
Slovak investigator: RNDr. Miroslav Gottlieb, PhD.

[4] Title: New therapy for prevention of oligodendroglial death and treatment of multiple sclerosis.
Grant agency: Fundación La Caixa
Principal Investigator: Prof. Carlos Matute Almau, PhD, Departmet of Neurobiology, University of Basque Country, Bilbao-Leioa
Duration: 2001/2004
Funding:100000 €
Slovak investigator: RNDr. Miroslav Gottlieb, PhD.

[5] Title: Neuroprotection by antioxidants in cellular and animal models of neurodegeneration
Grant agency: Ministerio de Salud y Consumo
Principal Investigator: Prof. Carlos Matute Almau, PhD, Departmet of Neurobiology, University of Basque Country, Bilbao-Leioa
Duration: 2005/2007
Funding:80000 €
Slovak investigator: RNDr. Miroslav Gottlieb, PhD.

[6] Bilateral Slovak-Polish scientific cooperation
Title: Neuroprotective vs neurodegenerative role of nitric oxide in CNS under neuropathological disorder.
Number: SAS/PAS 17/24-26
Principal investigator in Slovakia: RNDr. Nadežda Lukáčová, DrSc.
Principal investigator in Poland: Dr. Malgorzata Chalimoniuk, Ph.D., Medical Research Center, Polish Academy of Sciences, Warsaw, Poland
Duration: 01/2004 - 12/2006

[7] Agreement on international collaboration with Prof. J. Strosznajder, Institute of Experimental and Clinical Medicine, Polish Academy of Sciences, Warsaw, Poland
Title: Acitivity of nitric oxide synthase and cGNP in the brain on model of Parkinson disease and during ischemia and spinal cord trauma. (2001-2003)

- **National projects and funding**

i. **List of projects supported by the Agency for the Promotion of Research and Development (APVV/APVT), National Research Programmes, and their funding**

[1] Postraumatic regenerability of short propriospinal and long premotor truncospinal conductive systems in the spinal cord.
Number: APVT-51-013002
Principal Investigator: Prof. MUDr. Jozef Maršala, DrSc.
Duration: 08/2002 – 12/2005
Funding: 1200000,-SKK

[2] Retrograde ischemic tolerance as a possible tool in the prevention of delayed death of neurons in selectively vulnerable brain regions.
Principal Investigator: Burda Jozef, MVDr., PhD.
Number: APVT-51-021904
Duration: 01/2005 - 01/2007
Funding: 1200000 ,-SKK

[3] The role of nitric oxide and substance P in the mechanisms of chronic pain and their pharmacological treatment.
Number: APVT-51-011604
Principal Investigator: Jergová Stanislava, RNDr.
Duration: 01/2005 - 01/2007
Funding: 1262000,-SKK

[4] Experimental transplantation of bone marrow stem cells, umbilical blood cord stem cells and spinal neural precursors for treatment of spinal cord injury.
Number: APVV-51-002105
Principal Investigator: Čížková Dáša, MVDr., PhD.
Duration: 06/2006 - 06/2008
Cooperating institution: Tissue bank, Košice
Funding: 3145000,- SKK

[5] Animal model of human gliomas based on nitosourea induced malignant transformation of neural stem cells.
Number: APVV-20-052005
Principal Investigator: prof. MUDr. Igor Šulla, DrSc. – Medical faculty UPJŠ, Košice
Duration: 01/2006-12/2008
Cooperating institutions: Institute of Neurobiology, Slovak Academy of Sciences Košice, University of Veterinary Medicine Košice
Funding: 7.638.000 SKK

ii. Number of projects supported by the Scientific Grant Agency of the Slovak Academy of Sciences and the Ministry of Education (VEGA) for each year, and their funding

VEGA	2003	2004	2005	2006
number	7	7	10	11
funding (millions of SKK)	0,941	0,901	0,817	0,979

- **Summary of funding from external resources**

External resources	2003	2004	2005	2006	total	average
external resources (millions of SKK)	1,491	1,401	1,769	2,718	7,379	1,845
external resources transfered to coooperating research organisations (millions of SKK)	0,015	0,020	0,120	0,228	0,383	0,096
ratio between external resources and total salary budget	0,248	0,225	0,269	0,397	1,139	0,285
overall expenditures from external as well as institutional resources(millions of SKK)	12,338	13,046	14,460	14,024	53,868	13,467

Supplementary information and/or comments on research projects and funding resources

Institute of Neurobiology has participated on 2 networking centers of excellence

1, Center of excellence for Alzheimer disease (AD CENTRUM).
Principal Investigator: Prof. Michal Novák, DrSc., Institute of Neuroimmunology SAS, Bratislava
Cooperating institution: Institute of Neurobiology SAS
Duration: 05/2005 do 05/2009
Funding: 125 000,-SKK

2, Center of excellence for individualization of cancer therapy (CEX INDICATE)
Principal Investigator: Prof. Ladislav Mirossay, DrSc., Medical Faculty, University of P. J. Šafarik, Košice
Cooperating institution: Institute of Neurobiology SAS
Duration: 06/2006 do 06/2010

5. Organisation of PhD studies, other pedagogical activities

i. List of accredited programmes of doctoral studies (as stipulated in the previously effective legislation as well as in the recently amended Act on the Universities)

1) 15-01-9 General biology
2) 4.2.16. Neurosciences

ii. Summary table on doctoral studies (number of internal/external PhD students; number of students who completed their study by a successful thesis defence; number of PhD students who quitted the programme)

PhD study	31.12.2003			31.12.2004			31.12.2005			31.12.2006		
number of potential PhD supervisors	11			9			9			11		
PhD students	number	defended thesis	students quitted	number	defended thesis	students quitted	number	defended thesis	students quitted	number	defended thesis	students quitted
internal	8			5			3	3		3	3	
external	1			1						1		
supervised at external institution by the research employees of the assessed organisation												

iii. Postdoctoral positions supported by

a) external funding (specify the source) -

b) ***internal funding - the Slovak Academy of Sciences Supporting Fund of Stefan Schwarz***

1, MVDr. Miroslava Némethová, PhD.
2, RNDr. Stanislava Jergová, PhD.

iv. Summary table on pedagogical activities in undergraduate programmes for each year

Teaching	2003	2004	2005	2006
lectures (hours/year)	52	52		20
practicum courses (hours/year)	20	20	108	108
supervised diploma works (in total)	5	6	6	11
members in PhD committees (in total)	3	3	2	5
members in DrSc. committees (in total)	1	1	1	1
members in university/faculty councils (in total)	1	1	1	1
members in habilitation/inauguration committees (in total)	1	1	2	1

v. List of published university textbooks -

vi. Number of published academic course books -

vii. List of joint research laboratories/facilities with the universities

1) Histochemical and Imunohistochemical laboratory, with participation of
- Institute of Biology and Ecology, Faculty of Science UPJŠ Košice
- Institute of Anatomy, Faculty of Medicine UPJŠ Košice

2) Biochemical and Electrophysiological laboratory, with participation of
- Neurosurgical Clinic, Faculty of Medicine UPJŠ Košice
- 2nd Surgical Clinic, Faculty of Medicine UPJŠ Košice
- Institute of Pharmacology, Faculty of Medicine UPJŠ Košice
- Institute of Histology and Embryology, Faculty of Medicine UPJŠ Košice
- Institute of Medical Biochemistry, Jessenius Faculty of Medicine, UK Martin

3) Laboratory of nonionizing radiation, with participation of
- Dept. Theoretical Electrotechnics and Electrical Measurement, Faculty of Electrical Engineering and Informatics TU Košice

4) Laboratory of Tissue Cultures, with participation of
- Institute of Parazitology and Infectious Diseases, UVM Košice
- Tissue Bank, University Hospital of UPJŠ Košice

viii. Supplementary information and/or comments on doctoral studies and pedagogical activities

The Institute of Neurobiology has received accreditation in collaboration with the Medical Faculty UPJŠ Košice, for postdoctoral study in the field of Neurosience (4.2.16). The education in this field has started in November 1st, 2006 when the first internal PhD student has been accepted for 4 years' study.
In addition, three internal/external PhD students of the Medical Faculty UPJŠ Košice and Faculty of Science UK Bratislava, provide their experimental work under leadership of senior scientific workers at the Institute of Neurobiology.
The Institute has applied for accreditation in the field of Animal Physiology (4.2.10) in cooperation with the Faculty of Science UPJŠ Košice. We expected to receive accreditation in the beginning of 2007.
Two PhD students had in 2006 pedagogical activities at the Institute of Histology and Embryology, Medical Faculty UPJŠ Košice and Institute of General and Anorganic Chemistry, Faculty of Theology CU Ružomberok.
Three internal PhD students of the Institute of Neurobiology will be defending their Theses in 2007.
During the evaluated period, four PhD students from Spain, Czech Republic and Russia visited the Institute of Neurobiology to learn special methods connected with their doctoral studies field.

6. Direct output to the society (applications of results, popularisation and outreach activities)

i. List of the most important results of applied research project -

ii. List of the most important studies commissioned for the decision-making authorities, the government and NGOs, international and foreign organisations -

Prof. MUDr. Jozef Maršala, D.Sc., expert participation on preparation of legislation related to use of human cells and tissues for research. Slovak Medical University, November 2006 Bratislava

iii. List of the most important popularisation activities

Articles in press - 6
Presentations on TV shots - 6

Presentations on radio broadcasting - 11

Press conferences - 2
European week of Science - Open door at the Institute - 2

iv. List of patents issued abroad, incl. revenues -

v. List of the patents issued in Slovakia, incl. revenues -

vi. List of licences sold abroad, incl. revenues -

vii. List of licences sold in Slovakia, incl. revenues -

viii. List of contracts with industrial partners, incl. revenues –

ix. List of research projects with industrial partners, incl. revenues –

x. Summary of outreach activities

Outreach activities	2003	2004	2005	2006	total
studies for the decision sphere, government and NGOs, international and foreign organisations			1		1
articles in press media/internet popularising results of science, in particular those achieved by the Organization		2	2	2	6
appearances in telecommunication media popularising results of science, in particular those achieved by the Organization	2	5	3	7	17
public popularisation lectures			1	1	2

xi. Supplementary information and/or comments on applications and popularisation activities

In collaboration with the Slovak Society for Neurosciences, the Open door day 2006 has been organized as a two days' action. In addition to public and invited vistors from collaborating institutions, we have presented neuroscience research at the Institute to more than 300 organized visitors (students from high schools and universities).

7. Background and management. Staffing policy and implementation of findings from previous assessments

i. Summary table of personnel

Personnel	2003	2004	2005	2006
all personel	29	31	29	30
research employees from Tab. Research staff	12	14	13	15
FTE from Tab. Research staff	11,74	14,09	12,9	14,16
averaged age of research employees with university degree	48,5	46,9	48,42	47,18

ii. Professional qualification structure

Number of	2003	2004	2005	2006
DrSc.	2	1	1	3
PhD / CSc.	14	15	16	12
Prof.	1	1	1	1
Doc./Assoc. Prof.	1			

iii. Status and development of research infrastructure incl. experimental, computing and technical base (description of the present infrastructure, premises, and material and technical resources. Infrastructure, instrumentation and major technical equipment necessary for the achievement of the objectives specified in the research Concept)

Present equipment:
Vivaria for experimental animals (rats and rabbits)
Operating theatres, equipped with systems for aspetic operation technique, inhalation anesthesia, stereomicroscopes, systems for monitoring physiological functions during experiments.
Histological laboratories, equipment for routine histology: microtomes, cryostats, vibratome, embedding and staining equipment,
Fluorescent microscopy – microscope Olympus BX51 with digitalization of images

Electron microscopy, microscope Tesla 500, laboratory for sample preparation. Biochemical laboratories, labs for tissue homogenization, ultracentrifugation (Beckman L8), specrophotometric analyses. Certified laboratory for radioassays (Beckman LS 3801). Protein assays, electrophoresis and Western blotting.
Electrophysiological laboratory – EEG, evoked potentials, recording of unit activity and analysis.

Major investments needed
Vivaria for genetically modified animals, rats and mice
Advanced confocal microscopy
Laboratory for gene expresion analyses (real time PCR)
Laboratory for proteomic studies (purification, protein sequencing)
Equipment for membrane physiology recording
Cell and tissue cultivation laboratory, cell separation and storage systems

iv. Status and development of bibliographic resources, activities of the Organisation's library and/or information centre

Institute of Neurobiology runs a library with more than 2000 titles, most of them are from years before 1998. Majority of new information resources are available via Internet databases from Central Library of Slovak Academy of Sciences in Bratislava.

v. Describe how the results and suggestions of the previous assessment were taken into account

1, Too many publications from research workers on long-term scholarships abroad.
We have adopted internal regulation limiting the long-term leave from the Institute to maximum 2 years.

2, Equipment of the laboratories out of date.
Every possible effort has been made to gain sources for investments. We have succeeded in getting support for buying
i, a microplate spectrophotometer (a workhorse for the biochemical lab)
ii, CO2 incubator
iii, Laminar box (safety class I.)
iv, Two steromicroscopes with digital camera

3, Recommendation to apply for APVT/APVV projects
We have submitted 10 applications, out of them 4 were succesful.

4, Number of defended theses and doctoral dissertations too low.
Within the evaluated period, research workers at the Institute defended 6 PhDs, and 2 D.Sc.s.

5, presentations for PhD. students and seminars in english.
During the whole evaluated period, institutional seminars are every other week in english.

6. Popularisation of own results too low.

Foundation of Slovak Society for Neuroscience, organization of Opened door days, many presentations in press and broadcasting media.

vi. Supplementary information and/or comments on management, research infrastructure, and trends in personnel development

The most prominent problem is persisting brain-drain of perspective research workers. In Slovakia, there is are no funds for supporting postdoctoral positions, and for supporting repatriation of prominent researchers working abroad. This should be priority #1 for the future.

Other information relevant to the assessment

Results gained at the Institute have a direct output to clinical practice. Method of epidural cooling developed at the Institute of Neurobiology on experimental animals has been adopted as a neuroprotective measure applied during major surgery on aorta in human patients with aortic aneurysms. This method of spinal cord protection is being continually used in prominent departments of vascular surgery in the USA, and more recently, in Japan. In clinical experience reports, our original experiments have been repeatedly cited, and since 2000, this method is listed as a standard neuroprotective measure in a textbook of vascular surgery (R. Rutheford: Vascular Surgery).