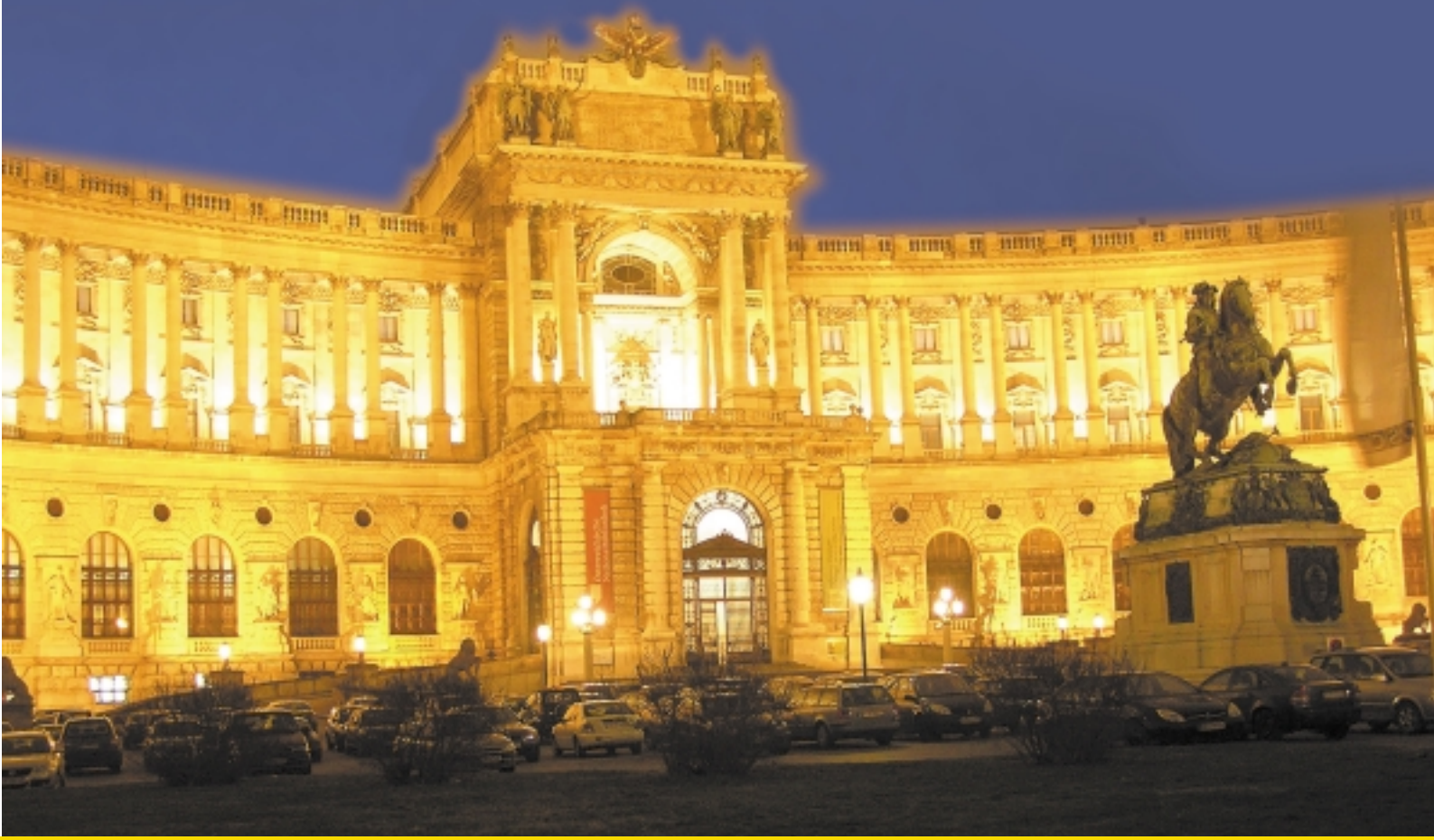
VIENNA 1 - 3 MARCH 2009

Hilton Hotel, Vienna, Austria

Second Joint Congress of GCNN and SSNN

6th Congress of the Global College of Neuroprotection & Neuroregeneration

5th Congress of the Society for the Study of Neuroprotection and Neuroplasticity



Final Program and Abstract Book

Global College of Neuroprotection and Neuroregeneration

THE SOCIETY FOR THE STUDY OF NEUROPROTECTION AND NEUROPLASTICITY

www.ssnn.ro

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Director Institute of Clinical Neurobiology
Senior Editor Acta Neuropathologica
Vienna, Austria

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Scientific Director, The Miami Project to Cure Paralysis,
University of Miami, USA

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/ in alphabetical order

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William A. Banks / USA
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Hans Christian Bauer / Austria
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Natan Bornstein / Israel
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/ in alphabetical order

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THE SOCIETY FOR THE STUDY OF
NEUROPROTECTION AND
NEUROPLASTICITY

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ORGANIZERS

THE SOCIETY FOR THE STUDY OF NEUROPROTECTION AND NEUROPLASTICITY

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CONGRESS VENUE

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CONGRESS REGISTRATION DESK

All congress materials and documentation will be available at the congress registration desk located at SSNN booth, on the congress area, Hilton Hotel, Vienna.
The congress staff will be pleased to help you with all enquiries regarding registration, congress materials and program.
Please do not hesitate to contact the staff members if there is anything they can do to make your stay more enjoyable.

OPENING HOURS

Saturday – 28th of February 2009 16:00 – 19:30
Sunday – 1st of March 2009 8:30 – 19:30
Monday – 2nd of March 2009 8:30 – 19:30
Tuesday – 3rd of March 2009 8:30 – 15:00

REGISTRATION FEES

20 Sep 08 - 15 Jan 09	15 Jan 09 - 28 Feb 09 On site registration
EUR **400**	EUR **500**

PARTICIPANTS REGISTRATION FEE INCLUDES:

Admission to all scientific sessions during the congress

Admission to Poster Exhibition

Conference materials (delegate bag, final program and abstract book etc.)

Admission to Lunches and Coffee Breaks

Admission to Welcome Dinner, 28th of February 2009

ON-SITE REGISTRATION

On-site registration will be processed on a first-come, first-served basis. Priority will be given to pre-registered delegates. Depending on the number of on-site registered delegates, availability of congress bags may be limited.

NAME BADGES

Participants are kindly requested to wear their name badge at all times during the congress. The badge constiutes admission to the scientific sessions, coffee breaks and lunches.

CONGRESS LANGUAGE

The congress language is English. Simultaneous translation will not be provided.

CHANGES IN PROGRAM

The organizers cannot assume liability for any changes in the congress program due to external or unforeseen circumstances.

CONTACT

If you need further information regarding technical details, please contact:
Ovidiu Selejan/e-mail/ovidius@ssnn.ro
For updates and details please visit our website/www.ssnn.ro

POSTER EXHIBITION

Posters will be displayed from Sunday, 1st of March until Tuesday, 3rd of March 2009 in Werfel Hall.
The poster exhibition is open to all conference delegates on:
Sunday – 1st of March 2009 8:30 h – 19:00 h
Monday – 2nd of March 2009 8:30 h – 19:10 h
Tuesday – 3rd of March 2009 8:30 h – 15:00 h

POSTER DIMENSIONS

All posters must fit into a 90 X 120 cm area.
Boards will be provided for displaying posters.
Tape and tacks will be provided.

POSTER SET UP AND REMOVAL

Set up on Sunday, 1st of March between 9:00 and 11:00
Removal on Wednesday, 4th of March from 15:00

POSTER AWARDS

All posters will be evaluated on site and the best posters will be awarded with a poster prize.

SPEAKERS CENTER

Speakers are asked to hand in their CD-ROM or USB stick containing the PowerPoint presentation (IBM format or compatible) preferably one day before their session but at the latest 90 minutes prior to the presentation.
The presention will be transfered to the central congress server. Due to time and technical reasons we kindly the speaker not to use their own notebook.
PC working stations are provided in the speakers center where speakers can also work on their PC charts in a quiet area. Tehnical staff will be glad to assist.

OPENING HOURS

Sunday – 1st of March 2009 8:30 – 19:30
Monday – 2nd of March 2009 8:30 – 19:30
Tuesday – 3rd of March 2009 8:30 – 15:00

FINAL PROGRAM AND ABSTRACT BOOK

The participants' documents include the abstract book which will be handed out together with the congress bag at the registration counter.

OFFICIAL ORGAN OF THE SOCIETY

International Journal of Neuroprotection and Neuroregeneration, IJNN
http://www.ijnn.org

Covered by Scopus/PubMed

PUBLICATION

Speakers are invited to bring a manuscript of their talk for publication in IJNN (6 000 to 15 000 Words of text excluding references, tables and illustrations).
All papers will be peer reviewed for publication according to the policy of the IJNN.

ACQUISITION EDITOR:

Manuscripts may also be submitted on-line or by e-mail to Aruna Sharma, Uppsala, Sweden
E-mail: aruna.sharma@surgsci.uu.se

MOBILE PHONES

Participants are kindly requested to keep their mobile phones turned off while attending the scientific sessions in the meeting rooms.

CURRENCY

The official Austrian currency is EURO.

ELECRICITY

Electrical current is 220 volts, 50 Hz.
Two-prong plugs are standard.

TIME

The time in Vienna is
Central European Time (GMT+1).

COFFEE BREAKS, LUNCHES, DINNERS

February 28, 2009

20:30 - 23:30 Welcome Dinner
Location: Park Congress 2&3
Note: *Free of charge to all registrated delegates.*

March 1, 2009

07:00 - 08:30 Breakfast
Location: Straus/Brahms/Mahler/Bruckner
Note: *Free of charge to all registrated delegates.*

13:00 - 14:00 Lunch
Location: Park Congress 2 and Prefunction Area
Note: *Free of charge to all registrated delegates.*

20:30 - 23:30 Gala Dinner
Location: Klimt Ballroom 1&2&3
Note: *Access permitted to delegates holding valid Invitations. Invitations can be purchased at the registration desk for 75€*

March 2, 2009

07:00 - 08:30 Breakfast
Location: Klimt Ballroom 1&2&3
Note: *Free of charge to all registrated delegates.*

13:50 - 14:35 Lunch
Location: Klimt Ballroom 1&2&3
Note: *Free of charge to all registrated delegates.*

March 3, 2009

07:00 - 08:30 Breakfast
Location: Klimt Ballroom 1&2&3
Note: *Free of charge to all registrated delegates.*

14:25 - 15:30 Lunch
Location: Klimt Ballroom 1&2&3
Note: *Free of charge to all registrated delegates.*

20:30 - 23:30 Farewell Party
Location: Klimt Ballroom 1&2&3
Note: *Access permitted to delegates holding valid Invitations. Invitations can be purchased at the registration desk for 75€*

SCIENTIFIC PROGRAM

scientific program *1st of March*

PARK CONGRESS 1

PRESIDENTIAL SESSION
Chairpersons: Franz Gerstenbrand, Laurențiu M. Popescu

8:30-8:35
Welcome Address

8:35-9:05
Kurt Jellinger / Austria
Advances in our understanding of neurodegeneration

9:05-9:35
Dafin Mureşanu / Romania
Quantum reality and neurosciences

9:35-10:05
Hari Shanker Sharma / Sweden
Blood-central nervous system barriers: the gateway to neurodegeneration, neuroprotection and neuroregeneration

10:05-10:35
Dalton Dietrich / USA
New advances in the pathophysiology and treatment of spinal cord injury

PARK CONGRESS 3

10:35 – 10:50 / COFFEE BREAK

STROKE and NEURORECOVERY
Chairpersons: Anna Czlonkowska, Michael Brainin

10:50-11:05
Anna Czlonkowska / Poland
Can we enhance post stroke rehabilitation by pharmacotherapy?

BLOOD-BRAIN BARRIER AND BRAIN EDEMA / Session 1
Chairpersons: Hans Christian Bauer, Conrad Johanson

11:55-12:15
Hans Christian Bauer / Austria
New aspects of the molecular constitutents of the Blood-Brain Barrier

scientific program *1st of March*

PARK CONGRESS 1

11:05-11:20
Diez-Tejedor Exuperio / Spain
Cerebral protection, plasticity and repair therapies in ischemic stroke

11:20-11:35
Vida Demarin / Croatia
Stroke, music and neuroplasticity

Discussions 10 min

NEUROREHABILITATION
Chairpersons: Cristian Dinu Popescu, Heinrich Binder

11:45-12:00
Cristian Dinu Popescu / Romania
Effect of active, passive and functional electrical stimulation on reorganization of hand motor area in patients with stroke and healthy volunteers: a transcranial magnetic stimulation study

12:00-12:15
Aurel Popa Wagner / Germany
Neurobiology of post-ischemic recuperation in the aged mammalian brain

12:15-12:35
Heinrich Binder / Austria
Early neurorehabilitation at the blurred margin between curative treatment and rehabilitation

12:35-12:50
Valentin Bohotin / Romania
10 Hz rTMS has opposite effects depending of the underlying cortex excitability.

Discussions 10 min

PARK CONGRESS 3

12:15-12:30
Georghe Benga / Romania
Water channel proteins (aquaporins and relatives): from their discovery in 1985 in Cluj-Napoca, Romania to their implications in the physiology and pathology of the nervous system

12:30-12:50
Conrad Johanson / USA
Aging rat dentate gyrus: amyloid retention, inflammatory reaction and gliosis in relation to reduced neural stem cell activity and poorer water maze performance.

Discussions 10 min

13:00 – 14:00 / LUNCH / RESTAURANT

scientific program *1st of March*

PARK CONGRESS 1

PARK CONGRESS 3

14:00 – 15:30
NEUROTROPHIC FACTORS – FACTS BEYOND THE DEBATE OR HOW INTELLIGENT MOLECULES CAN RECREATE THE BRAIN

Park Congress 1

14:00-14:15 Christian Stadler / Austria
Neurotrophic treatment option supports stroke recovery

14:15-14:30 Dafin Mureşanu / Romania
Neuroprotection and neuroplasticity in acute stroke. Clinical utility of neurotrophic factors therapy - data from a double blind placebo controlled clinical trial

14:30-14:45 Natan Bornstein / Israel
Neuroprotection – new hope on the horizon

14:45-15:00 Anton Alvarez / Spain
Efficacy of neurotrophic factors in moderate to moderately severe Alzheimer's disease

15:00-15:15 Alexandru V. Ciurea / Romania
Important therapeutic option to improve global outcome in Severe Brain Injury (SBI)

15:15-15:30 Hari Shanker Sharma / Sweden
Neuroprotective effects of neurotrophic factors in animal models of CNS injuries

DEMENTIA / Session 1
Chairpersons: Amos Korczyn, Leontino Battistin

15:30-15:50
Amos Korczyn / Israel
Depression and dementia

NEUROANAESTHESIA
Chairpersons: William Slikker, Lars Wiklund

15:30-15:50
William Slikker / USA
Anesthetic-induced brain injury during development: Non-invasive assessments and strategies for prevention

scientific program *1st of March*

PARK CONGRESS 1

15:50-16:10
Dafin Mureşanu / Romania
Neurotrophic factors – from bed to bench in dementia treatment; a short overview of some original data

16:10-16:25
Leontino Battistin / Italy
Alzheimer's disease: the therapeutic scenario between present and future

16:25-16:40
Bogdan O. Popescu / Romania
Presenilin-mediated signal transduction – relevance to Alzheimer's disease pathogenesis

16:40-16:55
Emil Toescu / UK
Cognitive dysfunction of normal ageing seen from a neuronal perspective

Discussions 10 min

PARK CONGRESS 3

15:50-16:10
Lars Wiklund / Sweden
Mechanisms of neuroprotection as revealed from experimental studies of long cardiac arrests and cardiopulmonary resuscitation (CPR) in young pigs

16:10-16:25
Wilhelm Behringer / Austria
Hypothermia during and after cardiac arrest

Discussions 10 min

17:05 - 17:20 COFFEE BREAK

ACUTE STROKE

Chairpersons: Natan Bornstein, Wolf Dieter Heiss

17:20-17:40
Natan Bornstein / Israel
Time is Brain-Stroke/TIA is an emergency condition

17:40-18:00
Wolf Dieter Heiss / Germany
Imaging the penumbra: the pathophysiologic basis for therapy of ischemic stroke

BLOOD-BRAIN BARRIER AND BRAIN EDEMA / Session 2

Chairpersons: Ole Petter Ottersen, William A. Banks

17:20-17:40
Ole Petter Ottersen / Norway
Unravelling the molecular and cellular routes of water entry in brain during brain edema formation

scientific program *1st of March*

PARK CONGRESS 1

18:00-18:15
Michael Brainin / Austria
Acute stroke units enhance chances for recovery

18:15-18:30
Ovidiu Băjenaru / Romania
Thrombin in the pathophysiology of hemorrhagic stroke

18:30-18:45
Ronen Leker / Israel
Stem cells and stroke

Discussions 10 min

PARK CONGRESS 3

17:40-18:00
Eugene Kiyatkin / USA
Permeability of the Blood-Brain Barrier depends on brain temperature: implications for normal brain functions, neuropathology, and drug-induced neurotoxicity.

18:00-18:30
William A. Banks / USA
Transport of Lysosomal enzymes across the Blood-Brain Barrier: induction of Mannose-6-Phosphate Receptor in adult mice

Discussions 10 min

19:00 – 19:40
Park Congress 1

19:00-19:20 Ovidiu Băjenaru /Romania
Its mode of action and possible neuroprotective properties

19:20-19:40 Dafin Mureşanu /Romania
Correlating mechanisms of action with safety and tolerability profile

20:30 GALA DINNER
KLIMT BALLROOM

PARK CONGRESS 1

VASCULAR DEMETIA
Chairpersons: Vladimir Hachinski, Christopher Chen

8:30-8:50
Vladimir Hachinski / Canada
ReWARD™: a registry based clinical trial method

8:50-9:05
Christopher Chen / Singapore
A traditional chinese medicine, in post-stroke recovery and vascular cognitive impairment

9:05-9:20
Kurt Jellinger / Austria
The enigma of vascular dementia: A neuropathologist's view

9:20-9:35
Alla Guekht / Russia
In vascular dementia – results of the randomized, double-blind, placebo-controlled multicentric clinical trial

Discussions 10 min

MULTIPLE SCLEROSIS
Chairpersons: Ovidiu Băjenaru, Klaus Toyka

9:45-10:00
Bianca Weinstock-Guttman / USA
Brain derived neurotrophic factor and anterior optic pathway in multiple sclerosis

10:00-10:20
Klaus Toyka / Germany
The multiple sclerosis treatment consensus group - immunomodulatory treatments in MS

PARK CONGRESS 3

PARKINSON
Chairpersons: Barry Hoffer, Harry Steinbusch

8:30-8:50
Barry Hoffer / USA
Aging, mitochondrial function, and Parkinson's disease

8:50-9:05
Peter Riederer / Germany
The history of MAO and MAO-I's

9:05-9:25
Harry Steinbusch / The Netherlands
Stimulation of the subthalamic nucleus in a rat model of Parkinson's disease motor and non-motor effects

9:25-9:40
Yu Luo / USA
Delayed treatment with a p53 inhibitor enhances recovery in stroke brain

Discussions 10 min

DEGENERATIVE DISORDERS
Chairpersons: Rudy Castellani, David Lovejoy

9:50-10:10
Rudy Castellani / USA
Neuropathology is neuroprotection in degenerative diseases

10:10-10:25
Mihai Moldovan / Denmark
Abnormal motor axon function in nerves deficient of the myelin protein P0 as a possible target for neuroprotective strategies

scientific program *2nd of March*

PARK CONGRESS 1

10:20-10:35
Ivan Milanov / Bulgaria
Validation of quality of life questionnaires for multiple sclerosis and cognitive impairment questionnaire – msqol-54, msis-29 and msnsq in the Bulgarian patients with multiple sclerosis.

Discussions 10 min

PARK CONGRESS 3

10:25-10:40
David Lovejoy / Canada
Hippocampus, stress and neurodegeneration: delineating a novel peptide system that affects hippocampal morphology

Discussions 10 min

10:45– 11:00 COFFEE BREAK

11:00 – 12:00
CONTINUOUS DOPAMINERGIC THERAPY - EFFICIENT CONTROL OF SYMPTOMS
Park Congress 1

11:00-11:20 Amos Korczyn / Israel
Continuous dopaminergic stimulation in the management of PD

11:20-11:40 Dafin Mureşanu / Romania
The need for continuous dopaminergic therapy

11:40-12:00 Ovidiu Băjenaru / Romania
Clinical data on continuous dopaminergic therapy

FUTURE RESEARCH PERSPECTIVES IN NEUROREGENERATION /
Session 1
Chairpersons: David Mulholland, Gioacchino Tedeschi

12:00-12:15
David Mulholland / USA
What internet search engines results teach self-determining patients about neuroprotection and neuroplasticity

FUTURE RESEARCH PERSPECTIVES IN NEUROREGENERATION
Chairpersons: Michael Thompson, Fred Nyberg

12:00-12:20
Fred Nyberg / Sweden
The role of the somatotrophic axis in neuroprotection and neuroregeneration of the addictive brain

scientific program *2nd of March*

PARK CONGRESS 1

12:15:12:30
Gioacchino Tedeschi / Italy
Resting-state Functional MRI: state of the art and future perspectives

12:30-12:45
Michal Horowitz / Israel
Environmental heat, possible role in neuroplasticity, cross-tolerance and neuroprotection

Discussions 10 min

FUTURE RESEARCH PERSPECTIVES IN NEUROREGENERATION / Session 2
Chairpersons: Gregory Oxenkrug, Laszlo Vecsei

12:55-13:10
Gregory Oxenkrug / Spain
Tryptophan - Kynurenine metabolism as a target for neuroprotective intervention

13:10-13:25
Laszlo Vecsei / Hungary
Neuroprotection and the kynurenine system: 2009

13:25-13:40
Ludwig Aigner / Austria
Neurogenesis in the adult brain: watch me if you can!

Discussions 10 min

PARK CONGRESS 3

12:20-12:35
Larissa Cheran / Canada
Nanoneuromedicine: The Final Frontier

12:35-12:50
Michael Thompson / Canada
Towards the design of a hard matter system capable of neural-like cognition

12:50-13:05
José-Vicente Lafuente Sánchez / Spain
Effects of VEGF delivery by encapsulated cells in striatum

13:05-13:20
Maximilian Mehdorn / Germany
Deep Brain Stimulation for various disorders

Discussions 10 min

13:50–14:35 LUNCH / KLIMT BALLROOM

scientific program *2nd of March*

PARK CONGRESS 1

WFNR SESSION
Chairpersons: Klaus von Wild, Volker Hömberg

14:35-14:50
Jean-Luc Truelle / France
What Quality of Life after Traumatic Brain Injury? QOLIBRI, a disease-specific quality of life tool.

14:50-15:10
Klaus von Wild / Germany
Quality of life following severest damage of the Central Nervous System (CNS)

15:10-15:25
Volker Hömberg / Germany
From motor learning to motor therapy: Translational research in rehabilitation

15:25-15:40
Zhang Tong / China
Effects of three-phrase rehabilitation treatment on acute cerebrovascular diseases: a prospective, randomized, controlled, multicenter study

Discussions 10 min

TRAUMATIC BRAIN and SPINAL CORD INJURY / Session 1
Chairpersons: A. V. Ciurea, Pieter Vos

15:50-16:10
A. V. Ciurea / Romania
How to improve the global outcome in Severe Brain Injury (SBI) early neuroprotection, neuroplasticity, neuroregeneration, neurorehabilitation and psychological support

PARK CONGRESS 3

NANOSESSION, NANOMEDICINE / Session 1
Chairpersons: Hari Shanker Sharma, Morag Robertson

14:35-14:45
Morag Robertson

14:45-15:00
Jany Raty / Finland
Seeing gene therapy to emerge from trials to products

15:00-15:15
Giovanni Tosi / Italy
Engineered polylactide-co-glycolide(PLGA) Np as drug delivery systems for the Central Nervous System

15:15-15:30
Hari Shanker Sharma / Sweden
Engineered nanoparticles from metals exacerbate Blood-Spinal Cord Barrier disturbances, edema formation and cord pathology. An experimental study in the rat

Discussions 10 min

NANOSESSION, NANOMEDICINE / Session 2
Chairpersons: Russell Andrews, Morag Robertson

15:40-16:00
Russell Andrews / USA
See no electricity, hear no electricity – but the brain speaks with electricity: sensory neuroprostheses and the neural-electrical interface

scientific program *2nd of March*

PARK CONGRESS 1

16:10-16:30
Helen M. Bramlett / USA
Progressive injury following traumatic brain injury: therapeutic implications

16:30-16:45
Pieter Vos / The Netherlands
Mild Traumatic Brain Injury, cognitive functioning and post traumatic complaints: a MRI study.

16:45-17:00
Lars Hillered / Sweden
Oxidative stress and inflammation as targets for neuroprotection in traumatic brain injury

Discussion 10 min

17:10–17:50
COFFEE BREAK

DEMENTIA / Session 2
Chairpersons: Stavros J.Baloyannis, Anton Alvarez

17:50-18:10
Stavros J.Baloyannis / Greece
Loss of cholinergic neurons of septum pellucidum in Alzheimer´s disease: a Golgi and electron microscope study

18:10-18:25
Andreas Winkler / Austria
Pain assessment in residents of neurogeriatric long-term care facilities with severe dementia

PARK CONGRESS 3

16:00-16:20
Gabriel A. Silva / USA
Imaging neural cells with functionalized quantum dots: from structure to function

16:20-16:35
Arezoo Campbell / USA
Inhalation of particulate matter and neuroinflammation

Discussions 10 min

NANOSESSION, NANOMEDICINE / Session 3
Chairpersons: Morag Robertson, Vadim Fraifeld

16:45-16:05
Vladimir Parpura / USA
Carbon nanotubes as modulators of neuronal growth

17:05-17:25
Joerg Kreuter / Germany
Nanoparticles as carriers for drug transport across the Blood-Brain Barrier

Discussions 10 min

17:35–17:50
COFFEE BREAK

MOLECULAR MARKERS AND NEUROPROTECTION
Chairpersons: Thomas Herdegen, Lars Hillered

17:50-18:10
Thomas Herdegen / Germany
Functional specificity of MAPK isoforms: don't touch the group but hit the isoform

PARK CONGRESS 1

18:25-18:40
Anton Alvarez / Spain
Double-blind clinical trial with and a combination therapy in mild to moderate Alzheimer's disease

18:40-18:55
Eckhart Ruether / Germany
Is there any realistic treatment in dementia?

Discussions 10 min

PARK CONGRESS 3

18:10-18:25
Vadim Fraifeld / Israel
At the crossroad of aging, longevity and age-related neurodegeneration: a network-based perspective

18:25-18:45
Mark Smith / USA
The causes and consequences of oxidative stress in alzheimer disease: therapeutic implications
Discussions 10 min

scientific program *3rd of March*

PARK CONGRESS 1

DEGENERATIVE DISORDERS /
Sessions 1
Chairpersons: Johannes Thome, Peter König

8:30-8:45
Johannes Thome / UK
Neural plasticity and neurodegeneration in depression and dementia

8:45-9:00
De-Maw Chuang / USA
Therapeutic potential of mood stabilizing drugs for neurodegenerative diseases

9:00-9:15
Peter König / Switzerland
Neurotrophic-like acting peptides as treatment-option in depression?

9:15-9:30
Michael Ritsner / Israel
Neuroprotection in Schizophrenia: challenges and opportunities

Discussions 10 min

DEGENERATIVE DISORDERS/
Sessions 2
Chairpersons: Christian Krarup, Antonio Federico

9:40-10:00
Christian Krarup / Denmark
Axonal degeneration and prerequisites for recovery

10:00-10:20
Antonio Federico / Italy
Mitochondrial functions and dysfunctions in some inherited neurological diseases as a model of neurodegeneration and neuroprotection

PARK CONGRESS 3

NANOSESSION, NANOMEDICINE /
Session 4
Chairpersons: Karen Martinez, Kewal Jain

9:40-9:55
Svetlana Gelperina / Russia
Nanoparticles for brain delivery: toxicological aspects

9:55-10:15
Karen Martinez / Denmark
Interfacing mammalian cells with vertical arrays of inorganic nanowires for biosensing

10:15-10:30
Kewal Jain / Switzerland
An integrated approach to neuroprotection in traumatic brain injury

Discussions 10 min

scientific program *3rd of March*

PARK CONGRESS 1

10:20-10:35
Le Weidong / USA
Autophagy is a novel therapeutic target for neurodegenerative diseases

Discussions 10 min

PARK CONGRESS 3

10:45-11:00 COFFEE BREAK

11:00-11:40
WHAT IS NEW IN PARKINSON'S DISEASE TREATMENT?
Park Congress 1

11:00-11:20 Ovidiu Băjenaru / Romania
Monotherapy with rasagiline in Parkinson's disease

11:20-11:40 Cristina Panea / Romania
Adjunctive therapy with rasagiline in Parkinson's disease

TRAUMATIC BRAIN and SPINAL CORD INJURY / Session 2
Chairpersons: Byron Kakulas, Zhang Tong

11:40-11:55
Florina Antochi / Romania
Preliminary results of a clinical study on nucleoplasty

11:55-12:15
Dalton Dietrich / USA
Therapeutic Hypothermia and CNS Injury

12:15-12:35
Byron Kakulas / Australia
Neuropathology: the basis for new treatments of human spinal cord injury

Discussions 10 min

scientific program *3rd of March*

PARK CONGRESS 1

EPILEPSY
Chairpersons: Ivan Milanov, Alla Guekht

12:45-13:00
Doru Mărgineanu / Belgium
Pharmacoresistance in epilepsy: what prospect for gap junction-related pharmacotherapy?

13:00-13:15
Onno van Nieuwenhuizen / The Netherlands
Timing of epilepsy surgery

Discussions 10 min

FUTURE PERSPECTIVES
Chairpersons: Dafin Mureşanu, Hari Shanker Sharma

13:25-13:45
Anna Lindström / Sweden
Uppsala: a science city & fervent destination for research & development

PARK CONGRESS 3

13:45 - 14:25
CAROTID ATHEROSCLEROSIS AND ARTERIAL STIFFNESS
Park Congress 1

13:45-14:05 Miklos Illyes / Hungary
Cerebrovascular deceases and arterial stiffness

14:05-14:25 Dafin Mureşanu / Romania
TensioMed™ Artheriograph - A new era in measuring arterial stiffness

14:25 – 15:30 LUNCH / KLIMT BALLROOM

20:30 FAREWELL PARTY / KLIMT BALLROOM

ABSTRACTS

abstracts

NEUROGENESIS IN THE ADULT BRAIN: WATCH ME IF YOU CAN!

Ludwig Aigner, Institute of Molecular Regenerative Medicine, Paracelsus Medical University Salzburg, Austria

Interest in adult neurogenesis has tremendously increased after its detection in the adult human brain. Thus, the continuous generation of new neurons, which is confined to regions of adult neurogenesis, may play an important role in cognitive and emotional processes under physiological and pathological condition. Moreover, it could provide the basis for functional and cellular brain repair. To date, however, a simple tool for *in vivo* visualization and quantification of neurogenesis such as optical / bioluminescent imaging, magnetic resonance imaging (mri) or positron emission tomography is lacking for rodents and humans. Currently, the vast majority of studies addressing the extent and the kinetics of neurogenesis are still based on mitotic markers, such as bromodeoxyuridine (brdu). We previously demonstrated that doublecortin (dcx) was specifically and transiently expressed in the population of neuronal precursors and young neurons and thus constituted a good marker of neurogenesis. Here, we describe a new transgenic tool designated dcx-promo-luciferase that enables *in vivo* optical imaging of developmental or adult endogenous neurogenesis and to follow the fate of transplanted neural progenitor cells. Moreover, we investigate on the possibility of using mr spectroscopy for imaging of neurogenesis. Also, the presentation will demonstrate some examples of molecular regulation of adult neurogenesis with a potential therapeutic application.

abstracts

SEE NO ELECTRICITY, HEAR NO ELECTRICITY – BUT THE BRAIN SPEAKS WITH ELECTRICITY: SENSORY NEUROPROSTHESES AND THE NEURAL - ELECTRICAL INTERFACE

Russell J. Andrews, Ames Associate, Smart Systems & Nanotechnology, NASA Ames Research Center, Moffett Field, CA USA

Sensory neuroprostheses - cochlear implants - have been augmenting hearing for decades. However, in visual neuroprostheses the neural-electrical interface more closely resembles the potential interface in other parts of the nervous system. This review of sensory neuroprostheses research focuses on (1) optimizing the neural-electrical interface, and (2) strategies for enhancing neuromodulation/neuroregeneration.

Critical for neuromodulation in general and neuroprostheses in particular is safe charge transfer from electrode to tissue. Retinal prosthesis research has addressed tissue injury from undue charge transfer, the issues including: electrode size (smaller electrodes require smaller charge transfer), electrode composition (both material and coatings, which can affect impedance and capacitance), electrode to tissue distance, and characteristics of the stimulating current (waveform, pulsewidth, frequency, etc). Research in both neuroprostheses and neuromodulation suggest that the use of penetrating arrays (for 3-D contact), polymer coatings, and carbon nanotube arrays (or carbon nanotube electrode coatings) can greatly enhance safe charge transfer.

Anatomical and/or surgical issues may influence neuroprosthesis development, e.g. in visual neuroprostheses electrode array placement may be epiretinal, subretinal, or suprachoroidal. Anatomical location of the array may be dictated by the hardware employed: multiphotodiode arrays are placed in the subretinal space, whereas microelectrode arrays (utilizing a digital camera and signal processing to transmit a signal pattern to the array) can be implanted in various locations (epiretinal or suprachoroidal – arguably simpler/safer to implant than subretinal – or even direct visual cortex stimulation). In auditory neuroprostheses for patients who are not candidates for a cochlear implant, a penetrating microelectrode array stimulating the inferior colliculus may be more effective and safer than a brainstem implant stimulating the surface of the cochlear nucleus.

A relevant strategy is the use of multiple bandwidths. For people with residual vision, a visual prosthesis consisting of a small (several mm dia) epiretinal or subretinal microelectrode array is stimulated by near-infrared 'light' (i.e. the processed data from a digital minicamera mounted on glasses). The remaining retina can then process light in the visual spectrum without 'crosstalk' between the visual light striking the retina and the near-infrared 'light' striking the implanted microarray. Another example is dual band inductive coupling to communicate between the implanted hardware (in the retina and ocular region) and the necessary external hardware (typically mounted in glasses worn by the visually-impaired person). Data transmission is at high frequency (20 MHz) while power transmission – to recharge the implanted battery – is at low frequency (1 MHz). Simultaneous data and power transmission is thus achieved.

Additional strategies include various tissue engineering and nanolevel techniques to improve neuroprostheses, e.g. stem cells, neurotrophin-eluting hydrogels, and nanoscaffolds. The possible benefit of appropriate electromagnetic fields for sensory neuroprostheses has yet to be investigated. Communcation between sensory neuroprosthesis researchers and neuromodulation/neuroregeneration researchers can result in productive cross-fertilization.

abstracts

DOUBLE-BLIND CLINICAL TRIAL WITH AND A COMBINATION THERAPY IN MILD TO MODERATE ALZHEIMER'S DISEASE

A. Alvarez[1], R. Cacabelos[1], M. Aleixandre[2], C. Linares[3], E. Granizo[3], E. Doppler[4], H. Moessler[4]
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[2]Geroclinic, Granada, Spain;
[3]Memory Clinic, Málaga, Spain;
[4]

Is a peptide mixture with neurotrophic activity being effective in Alzheimer's disease (AD) treatment. A randomized, double-blind clinical trial was conducted to evaluate the efficacy and the safety of and a combination therapy in mild to moderate AD patients.
AD patients (N=197; 45 male/152 female; age: 51-95 years) received iv infusions of Cere (10 ml) or placebo (saline) 5 days/week from weeks 1-4 and 13-16 (40 infusions) and Donepezil (5 mg for 4 weeks and 10 mg thereafter) or placebo tablets throughout the study. The effects of Cere, Donepezil and Combination on cognition, clinical global impression, activities of daily living and neuropsychiatric symptoms were evaluated with ADAS-cog, CIBIC+, ADCS-ADL and NPI. Primary efficacy parameters were CIBIC+ score and change from baseline in the ADAS-cog+at week 28.
At week 28 and in comparison with patients treated only with Donepezil: (1) Cere-treated patients showed a significant improvement in global clinical impression (CIBIC+: $p<0.05$; CIBIC+ responders rate: $p<0.01$) and no significant differences for ADAScog, ADCS-ADL and NPI scores; (2) patients receiving combination therapy showed higher scores in the CIBIC+responders rate ($p<0.01$), almost significant differences in CIBIC+ score ($p=0.068$) and ADAS-cog&CIBIC+ responders rate ($p=0,056$), and nonsignificant improvements in ADAS-cog and ADCS-ADL. Patents treated with Cere or Combination were cognitively stable and those receiving only Donepezil deteriorated after week 16.
According to the present results it is concluded that: 1) Cere is at least as efficacious as Donepezil for AD treatment; 2) The combined therapy showed a tendency for superiority with respect to Donepezil alone; 3) Cere-treated patients maintained cognitive improvement till the end of the study. Significant long-term benefits of the combination therapy are suggested.

abstracts

EFFICACY OF NEUTROPHIC FACTORS IN MODERATE TO MODERATELY SEVERE ALZHEIMER'S DISEASE

Antón Alvarez, Department of Neuropharmacology, EuroEspes Biomedical Research Centre, Santa Marta de Babío, Bergondo, 15166-A Coruña, Spain

Is a compound with neurotrophic activity shown to be effective in Alzheimer's disease (AD) in previous trials. The efficacy and safety of three different dosages were evaluated in patients
with moderate to moderately severe AD (MMSE≤ 20; n=133; ITT) enrolled in a doble-blind, placebo-controlled clinical trial.
Patients were treated with 10, 30 or 60 ml for five days per week for four consecutive weeks and thereafter two times per week for eight consecutive weeks. The patients were then without treatment for another 12 weeks until the end of the study. Primary efficacy parameters were the CIBIC+score and change from baseline in the ADAS-cog+, both measured at the study endpoint (month 6).
Patients treated with 10 ml Cere showed a mean improvement from baseline of –1.838 points in ADAS-cog+ and a significant treatment difference of –6.376 points ($p=0.046$) vs. Placebo. Responder analysis confirmed this improvement showing an odds ratio of 4.20 ($p<0.05$). Cognitive improvement did not reach statistically significance in the 30 ml (-4.531 points vs. Placebo) and 60 ml (-2.866 points vs. Placebo) groups. In the CIBIC+ , all Cere dosages significantly ($p<0.001$) improved global clinical function with a treatment difference of -1.72 (10 ml), -1.65 (30 ml), and -1.41 (60ml) points compared to Placebo. 10 and 30 ml showed also the best results in ADL functioning (DAD score); whereas the highest behavioural improvement was observed with 30-60 ml doses. Treatment with up to 60 ml per day was safe and well tolerated.
Study results demonstrate a dose-dependent treatment effect of in moderate AD patients with dosages of 10 ml and 30 ml being superior to Placebo in improving cognitive function and global clinical outcome.

abstracts

PRELIMINARY RESULTS OF A CLINICAL STUDY ON NUCLEOPLASTY

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L.Tomescu, B.Dorobat, R.Nechifor, G.Iana, Department of Interventional Radiology
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Objective: Nucleoplasty is a minimal invasive method of disc decompression which has important advantages compared to surgical methods, such as minimal tissue trauma, only local anesthesia, short duration of procedure, faster recovery time. Until now there were developed a few technical methods to perform nucleoplasty having the same target: to reduce the volume of nucleus pulpous and to decompress the nervous root. The aim of our study was to centralize the benefits and the side effects of the combination/association of two types of nucleoplasty, mechanical nucleoplasty used Dekompressor and nucleoplasty used discectomy with ozone in order to promote it from research to clinical practice.
Methods: A 36 months prospective, randomized, clinical study was start in the Neurology Department and Interventional Radiology Department of the University Hospital Bucharest with financial support of National Center of Management Program. The study included 84 patients presenting lumbar pathology. The inclusion criteria were: persistent radicular pain with or without back pain, the failure of conservative therapy, MRI showing herniation less than 6 mm and preservation of disc height (less than 50% loss). We excluded the patients with no previous conservative therapy for at least 6 weeks, significant neurological deficits, patients with disc height less than 50% of normal. The used methods were the mechanical nucleoplasty with Dekompressor and intradiscal and paravertebral ozonotherapy for first group of the patients with preservation of the anatomical integrity of the disc. Intradiscal discectomy with ozone and paravertebral ozonotherapy were used for the second group of patients with intervertebral disc extrusion.
Administration of ozone in nucleoplasty seems to prove not only decompression effect through dehidratation of nucleus pulpous but anti-inflammatory and analgesic effects and the combination of ozonotherapy to mechanical nucleplasty should improve the clinical results. Post procedural all patients received anti-inflammatory treatment for 2 weeks. The average time of hospitalization was 24 hours.
Results: Up to date there were no serious procedural related complications. After 6 months 79% of patients reported improvement of simptomatology: 89% in the group of patients with mechanical decompression associated with ozonotherapy in just one session; 75% in the second group of patients with intradiscal ozonotherapy after an average of 3 sessions**.** The preliminary results of 12 months post procedural follow-up reported 92% of patients satisfied with significant reduction of analgesic medication. A small percent - 8% of cases - was no benefit of the methods: 2% from the first group and 6% from the second group.
Conclusion: The results of the study confirm that nucleoplasty provides therapeutic benefits regard of percutaneous disc decompression techniques without severe side effects if the selection of patients was strictly done. The number of the average ozonotherapy sessions depends of the type of the nucleoplasty chosen and it is strictly related to the presence of disc extrusion.

abstracts

THROMBIN IN THE PATHOPHYSIOLOGY OF HEMORRHAGIC STROKE

Ovidiu Bajenaru, University Hospital of Emergency Bucharest, Department of Neurology, „Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania

The clinical severity and life-threatening events related to the primary cerebral hemorrhage are hematoma growth and perihematoma edema. The mechanisms of hematoma growth are complex and different according to the evolutive stage of hemorrhagic stroke. The perihematoma edema has three stages of development, related to the hydrostatic pressure and clot retraction (phase 1), the activation of coagulation cascade where the trombin production seems to be the key-event (phase 2) and the red blodd cell lysis with Hb-induced neuronal damage (phase 3). Experimental and clinical data obtained during many recent studies emphasized that trombin induces inflammation and cytotoxic effects on the blood-brain barrier, glial cells and neurons leading to the development of perihematoma edema and related pathogenic events. Very interesting data concern the relation of thrombin release and the increased expression of aquaporin-4 in the BBB, the interaction between thrombin and complement cascade, activation of matrix metalloproteinases, microglial activation; all these events seem to be integrated in a complex pathogenetic network, not yet completely understood, induced by the thrombin activation of PARs (in particular protease-activated receptor 1), of MAPK and protease nexin-1. The identification of these pathogenic mechanisms essentially differentiating hemorrhagic stroke from ischemic stroke, is probably crucial to design future neuroprotective strategies which could change significantly the prognosis of this extremely severe type of stroke.

abstracts

LOSS OF CHOLINERGIC NEURONS OF SEPTUM PELLUCIDUM IN ALZHEIMER´S DISEASE: A GOLGI AND ELECTRON MICROSCOPE STUDY

Stavros J. Baloyannis, 1st Department of Neurology, Aristotelian University, Thessaloniki, Greece

Background. Morphological and morphometric alterations have been described in the nucleus basalis in Alzheimer´s disease, resulting in progressive cholinergic deficit, which is associated with the decline of the mental faculties. In the present study we attempted to proceed in morphological and morphometric estimation of the neuronal networks of the septum pellucidum, which is also one of the main cholinergic structures of the brain.

Methods This morphological study is based on examination of fifteen brains obtained at autopsy 30 min to 2 hours after death. Samples from the septum pellucidum were excised and immediately immersed in Sotelo's fixing solution and were processed for electron microscope. The brains, which were processed for the silver impregnation techniques, were remained for two weeks in formalin. Then the septum pellucidum was excised and immersed in potassium dichromate (7g potassium dichromate in 300 ml of water) for ten days. Then the specimens were immersed in 1% silver nitrate for ten days, according to rapid Golgi method. The morphological and morphometric study was carried into effect in a Zeiss axiolab photomicroscope.The results were correlated with relevant morphological and morphometric analysis of the neuronal population of the septum pellucidum of normal brains of the same age with the patients.

Results The morphological analysis, revealed a marked change of the cytoarchitecture of the septum pellucidum of the patients suffered from Alzheimer's disease. Loss of neurons and astrocytic proliferation were also very prominent phenomena in the brains of Alzheimer´s patients. The septum pellucidum is characterized normally by the presence of numerous small round, elongated or triangular neurons arranged in round homocentric networks. In the brains of Alzheimer's patients the homocentric neuronal networks were disrupted and disarranged and large number of neurons was replaced by astrocytes. Numerous synaptic alterations concerning the dendritic spines of the small round neurons and the triangular ones were seen in electron microscope. Some of the synapses, which remained still intact, contained limited number of round synaptic vesicles and elongated, morphologically alternated, mitochondria. The morphometric analysis revealed an average loss of neurons of the septum pellucidum approaching to 70%.

Conclusions The above described morphological and morphometric observations, plead obviously in favour of substantial neuronal loss and synaptic alterations in the septum pellucidum of the brains of patients suffered from Alzheimer's disease, a fact which eventually increases the cholinergic deficit.

abstracts

TRANSPORT OF LYSOSOMAL ENZYMES ACROSS THE BLOOD-BRAIN BARRIER: INDUCTION OF MANNOSE-6-PHOSPHATE RECEPTOR IN ADULT MICE

William A. Banks,[1] William S. Sly[2], Jeffrey H. Grubb[2]
GRECC[1], Veterans Affairs Medical Center-St. Louis and Saint Louis University School of Medicine, Division of Geriatrics, Department of Internal Medicine[1], and Edward A. Doisy Department of Biochemistry and Molecular Biology[2]

Mucopolysaccharidoses (MPS) are characterized by abnormal storage of glycosaminoglycans in lysosomes of various tissues, including those of the central nervous system. These are devastating diseases that usually result in death during childhood and are caused by the lack of key enzymes. For example, MPS VII is missing beta-D-glucuronoside glucuronosohydrolase (GUS). Enzyme replacement of GUS reduces visceral lysosomal storage and will also reduce abnormal storage in brain in mice that are younger than 2 weeks of age. We have shown that phosphorylated GUS (P-GUS) is transported across the blood-brain barrier (BBB) of neonatal mice by a saturable mechanism that uses the mannose-6-phosphate receptor (M6PR). With maturation, transporter activity for P-GUS declines to undetectable levels. We hypothesized that P-GUS transport could be re-induced in adults and so allow treatment of MPS in adults. We reasoned that the transporter activity of M6PR would be vesicular dependent and that epinephrine (Epi) might stimulate such activity. We treated mice with varying doses of Epi and found that P-GUS transport, but not nonphosphorylated GUS transport, was increased. BBB disruption occurred in some mice treated with Epi, but P-GUS transport exceeded that explicable by BBB disruption and also occurred in mice that had no BBB disruption. We also showed that transport of P-GUS in Epi treated mice was mediated by reactivation of M6PR-dependent transport. We conclude that the neonatal M6PR-dependent transport of P-GUS is re-induced with Epi treatment and offers a strategy for the treatment of MPS in adults.

abstracts

ALZHEIMER'S DISEASE: THE THERAPEUTIC SCENARIO BETWEEN PRESENT AND FUTURE.

Leontino Battistin, Department of Neurology, University of Padua Medical School, Padua, Italy

Alzheimer's disease (AD), the most common form of dementia in the elderly, was first described roughly 100 years ago in Bavaria by Dr. Alois Alzheimer. AD is thought to affect 4–8% of the population over 65 years of age, with the incidence continuing to increase with increasing age. Although drugs currently available treat the symptoms with only minimal and temporary benefit, the coming years are expected to see the results of several clinical trials on novel therapeutics aimed at retarding disease progress.
In this lecture I will review the results obtained from clinical trials with symptomatic therapy and highlight the most promising new therapeutics currently under development for the treatment and prevention of AD. Given the overwhelming evidence supporting a central role for amyloid in AD pathogenesis, a great amount of research has been done on therapies targeting the cerebral accumulation of amyloid (secretase inhibitors or modulators, beta breakers, immunotherapy). In addition to senile plaques, neurofibrillary tangles are characteristic hallmarks of brain pathology in AD. Focusing on tau as a therapeutic target in AD, I will present evidence that hyperphosphorylation and aberrant aggregation of tau plays a central role in neurodegeneration and neuronal dysfunction in AD. Thus, therapies acting on this target have been proposed as an alternative therapeutic strategy for AD.
With several promising drugs now headed toward the clinic, the hope is that we will soon have novel AD therapeutics that successfully slow or reverse disease progress.

abstracts

NEW ASPECTS OF THE MOLECULAR CONSTITUTENTS OF THE BLOOD-BRAIN BARRIER

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Tissue barriers, such as the blood-brain barrier (bbb), rely on the functional interplay of transmembrane constituents linked to cytoplasmic plaque proteins. Scaffolding proteins located at the cytoplasmic surface of the junction site play a crucial role in assembling junction-related proteins at the plasma membrane and linking this so-called junctional plaque to the cytoskeleton.

Zonula occludens proteins (zops), currently comprising zo-1, zo-2 and zo-3, are scaffolding proteins which belong to the large family of maguk (membrane-associated guanylate kinase-like) proteins. These multidomain proteins are involved in the organization of epithelial and endothelial intercellular junctions. In spite of their structural similarities, zops appear to exert non redundant functions.

The nuclear targeting of zops is well documented and there is sufficient experimental evidence suggesting that zops directly interact with nuclear proteins, including various transcription factors, adaptor proteins, and even a matrix scaffolding component. However, in spite of the unequivocal demonstration of distinct nuclear activities of zops, the biological significance of their nuclear action has remained elusive.

In earlier studies we have found that zo-2 localizes to the nucleus in response to various environmental stress conditions. Here, we have focussed on the role of nuclear zo-2 in cerebral endothelial cells subjected to oxidative stress. Our results provide evidence to suggest that accumulation of nuclear zo-2 specifically downregulates the expression of matrix metalloproteinase-9 (mmp-9) and reduces apoptotis in cerebral endothelial cells following chemically induced oxidative stress. The downregulation of mmp9 was accompanied by reduction of the pore-forming claudin-2 but not of the barrier-forming claudin-1 mrna and protein. Since downregulation of mmp-9 is known to exert a protective effect on the endothelial blood-brain barrier during hypoxia/ischemia we will have to clarify whether the nuclear targeting of zo-2 may be involved in an early-response mechanism aimed at protecting the bbb during an oxidative insult.

Supported by the Austrian FWF, the Austrian National Bank and Applied Biotechnology GmbH Salzburg

abstracts

HYPOTHERMIA DURING AND AFTER CARDIAC ARREST

Wilhelm Behringer, Department of Emergency Medicine, Medical University Vienna, Vienna, Austria

Sudden cardiac arrest remains a major unresolved public health problem. In Europe and USA, approximately 425.000 people die of sudden death with very poor survival, usually less than 10%, most likely because irreversible injury to the brain and heart begins within minutes following global ischemia. Novel therapeutic concepts, different from the ones used at present, have to be found to substantially improve outcome after cardiac arrest.

Hypothermia is a re-discovered promising multifaceted treatment strategy in cardiac arrest patients. *Protective* hypothermia, induced before cardiac arrest, has to be differentiated from *preservative* hypothermia, induced during cardiac arrest, and from *resuscitative* hypothermia, induced after successful resuscitation.

Resuscitative mild hypothermia was already uded in the 1960s, but was then given up for 25 years, because experimental and clinical trials had been complicated by the injurious systemic effects of total body cooling with the means of intensive care at that time. In 2002, the results of two prospective randomised clinical trials showed that mild hypothermia initiated after successful resuscitation improved survival and neurologic outcome in cardiac arrest survivors as compared to patients treated with normothermia. In 2005, the guidelines of the European Resuscitation Council and the American Heart Association stated that unconscious patients with spontaneous circulation after cardiac arrest should be cooled to 32°C - 34°C for 12 - 24 hours. But many questions concerning resuscitative mild hypothermia are still unanswered. The optimal speed of induction, depth, and duration of resuscitative hypothermia, as well as optimal re-warming rate, are still not determined, and need further investigations.

Preservative hypothermia, i.e. induction of deep to profound hypothermia during cardiac arrest, *before* reperfusion (=Emergency Preservation and Resuscitation, EPR), might be a novel concept to further improve outcome after normovolemic cardiac arrest. In heart and brain surgery, where circulatory arrest is necessary for surgery, protective deep hypothermia is slowly induced with cardiopulmonary bypass (CPB), to protect the brain during the ischemic period. In sudden cardiac death, vital organs like the brain and heart loose their viability within minutes after the arrest. In large animals or humans, the rapid induction of deep hypothermia during cardiac arrest remains a challenge, and novel innovative techniques have to be found. In our normovolemic cardiac arrest pig model, induction of deep cerebral hypothermia was feasible within few minutes with a cold (4°C) saline flush, applied through an aortic balloon catheter, advanced into the thoracic aorta via the femoral artery. In subsequent outcome studies with 15 minutes cardiac arrest and 20 minutes resuscitation time, EPR improved 9-day neurological outcome as compared to pigs with conventional resuscitation attempts. Further experiments are necessary to optimize this novel concept of EPR, before considering clinical trials.

abstracts

WATER CHANNEL PROTEINS (AQUAPORINS AND RELATIVES): FROM THEIR DISCOVERY IN 1985 IN CLUJ-NAPOCA, ROMANIA TO THEIR IMPLICATIONS IN THE PHYSIOLOGY AND PATHOLOGY OF THE NERVOUS SYSTEM

Gheorghe Benga, Department of Cell And Molecular Biology, "Iuliu Haţieganu" University of Medicine and Pharmacy Cluj-Napoca, Cluj-Napoca, Romania

Water channels or water channel proteins (wcps) are transmembrane proteins that have a specific three-dimensional structure with a pore that can be permeated by water molecules. Wcps are a large family (over 450 members) that are present in all kingdoms of life. The first wcp, called today aquaporin 1 (aqp1), was discovered in the red blood cell (rbc) membrane by my group in 1985 in cluj-napoca, romania, reported in publications in 1986 (benga et al., biochemistry, 25, 1535-1538, 1986; benga et al., eur. J. Cell. Biol., 41, 252-262, 1986) and reviewed in subsequent years. In 1993 the name aquaporins was proposed for wcps which are specific water channels. Later, other wcps were discovered, the aquaglyceroporins, which are permeable to water and also to other small molecules (in particular glycerol). So far, thirteen wcps have been discovered in mammals. Wcps in the central nervous system (cns) appear to be of great physiological and pathological importance. Aqp1 is expressed in epithelial cells of the choroid plexus (cp) and is probably involved in the cerebrospinal fluid (csf) formation. This idea is supported by the increased csf production in cp tumours in parallel with increased expression of aqp1. As hydrocephalus is associated with csf flow abnomalities, inhibitors of aqp1 might be useful in treating this disease. Aqp1 is present in capillaries and astrocytes of astrocytomas and metastatic carcinomas. Aqp1 was also found in small-diameter sensory neurons in dorsal root, trigeminal and nodose ganglia and co-localized with markers of nociceptors, notably substance p. It was suggested that aqp1 may be involved in the pathophysiology of migraine. Aqp4 is expressed strongly throughout the brain and spinal cord, especially in astroglial cells lining ependyma and pial surfaces in contact with the csf and the blood-brain barrier, in glial cells forming the edge of the cerebral cortex and brainstem, vasopressin-secretory neurons in supraoptic and paraventricular nuclei of the hypothalamus, and purkinje cells of cerebellum. This pattern of distribution is in agrement with the major role of aqp4 to control water movements into and out of the brain. A role of aqp4 in the generation of brain edema in response to two established neurological insults (acute water intoxication and ischemic stroke) has been proposed; it was suggested that aqp4 inhibitors may reduce cytotoxic brain swelling in humans, whereas aqp4 activators or upregulators may reduce vasogenic edema and hydrocephalus. A second role of aqp4, in astrocyte migration, has been suggested. On the other hand aqp4 overexpression is a feature of astrocytomas, facilitates cancer spread and aqp inhibitors may slow tumor growth. A third role of aqp4 in brain was suggested to be the control of neuronal activity. Extracellular space (ecs) expansion has recently been proposed as an alternative mechanism to account for higher seizure threshold and prolonged seizure duration in aqp4 deficiency.

(continued next page)

abstracts

WATER CHANNEL PROTEINS (AQUAPORINS AND RELATIVES): FROM THEIR DISCOVERY IN 1985 IN CLUJ-NAPOCA, ROMANIA TO THEIR IMPLICATIONS IN THE PHYSIOLOGY AND PATHOLOGY OF THE NERVOUS SYSTEM

Gheorghe Benga, Department of Cell And Molecular Biology, "Iuliu Haţieganu" University of Medicine and Pharmacy Cluj-Napoca, Cluj-Napoca, Romania

An increased ecs volume increases the buffering capacity for k+ released into the ecs during neuronal excitation, preventing large changes in ecs [k+].
It is unclear, however, why the ecs volume is increased in aqp4-null mice. All these findings confirm our earlier conclusion of a membrane defect affecting water permeability in child epilepsy (benga, gh. And morariu, v. V. Nature 265, 636-638, 1977, clinical contribution benga ileana). The seizure phenotype data in aqp4-deficient mice raise the possibility that aqp4 modulation may also be effective in epilepsy therapy. Recently, it has been found that autoimmune reactions with autoantibodies against aqp4 appear to produce neuromyelitis optica (devic's disease) and the presence of these autoantibodies is a criterion for differential diagnosis with multiple sclerosis. Aqp9 has been observed in three cell types: endothelial cells of sub-pial vessels, glial cells (in particular tanycytes and astrocytes), and neurons. Aqp9 expression was found predominantly in one subtype of neurons, the catecholaminergic neurons, which are involved in energy balance. Consequently, a role for aqp9 in brain energy metabolism have recently been proposed. Aqp9 permeability to water, glycerol and lactate may be important in brain ischemia. In conclusion, we have world priorities in the discovery of wcps and of their role in epilepsy.

abstracts

EARLY NEUROREHABILITATION AT THE BLURRED MARGIN BETWEEN CURATIVE TREATMENT AND REHABILITATION

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Vorstand des Neurologisches Zentrums, "Rothschildstiftung Maria Theresien Schlössel"
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Early neurorehabilitation is a concept which needs somehow more precise definition. At first glance to start straight away with neurorehabilitation everybody will assent. But what does that mean: “as early as possible”. If we target normal body structures and functions we have to consider, that neurological diseases and injuries seldom are finalized incidents. Quite the contrary: One moment unnoticed but next clearly discernible beginning, the release mechanism is followed from a long lasting cascade of different pathophysiologic processes down to microbiologic domains having an effect not only on structure but also on function, activities and participation. Therefore putting aside the necessity to give precedence curative treatment though sometimes time consuming, we have to keep an eye on protection and repair of healthy or differently harmed neural tissue simultaneously. And those same are the key elements of early neurorehabilitation. But to put into practice actually is one of the most difficult problems. There is a whole string of experimental research giving hope but unfortunately little clinical trials that fulfil the hopes placed on the results of this basic research. The deciding reason is the existence of not only one but a wealth of branching pathophysiological pathways with different flow interfering with abundant possible physiologic repair mechanisms. From this the difficulty follows to do the right thing at the right time. Though we have gotten a vast overview from basic research concerning neuroprotection and repair so far early neurorehabilitation is mainly on empirical feet and furthermore on trial.

abstracts

10 Hz rTMS HAS OPPOSITE EFFECTS DEPENDING OF THE UNDERLYING CORTEX EXCITABILITY

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Background: It is well known that low frequency repetitive transcranial magnetic stimulation (rTMS) has an inhibitory effect and high frequency induce an excitatory effect. Some papers demonstrated that the effects of rTMS depend also on the excitability of the underlying cortex.
Proposal: to study the high rTMS effects when the cortical excitability is artificially increased by a previous rTMS session.
Material and method: In 7 healthy volunteers we performed two consecutive rTMS sessions on the motor area: first session to increase cortical excitability -10 Hz 18 trains of 50 pulses, interstimulus interval 15 seconds, 110 % of motor threshold (MT) - and the second session (five minutes later) with the same parameter to check the effect of high frequency rTMS on a preactivated cortex. As a measure of the cortex excitability we used the amplitude of motor evoked potential at 120 % of MT.
Results: First rTMS session induces an increase of motor evoked potentials amplitude with mean of 29 %, as compare with the baseline. The second rTMS session, administrated during the interval when the cortical excitability was increased by the first session, induces a paradoxical decrease of motor evoked potentials amplitude with a mean of 44%.
Conclusion: We demonstrate that the effects of rTMS depend not only with the frequency of stimulation but the underlying cortical excitability before stimulation has an important role for the rTMS effect.

abstracts

TIME IS BRAIN-STROKE/TIA IS AN EMERGENCY CONDITION

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Stroke is a devastating condition, the second leading cause of death and the major cause of disability in the elderly worldwide.
It was calculated that the neurocortex loses 31 million neurons/year in normal aging. Every minute in which a typical large-vessel acute stroke is untreated, the average patient loses: 1.9 million neurons,11 billion synapses and12 KM of axonal fibers. Each hour without treatment equal neuronal loss of 3.6 years of normal aging.
There are two main strategies which aim to save brain tissue in the acute phase of brain ischemia, namely REPERFUSION and NEUROPROTECTION.
Pooled analysis of all the thrombolytic (rtPA) trails have shown that the sooner the better. The likelihood(OR) to benefit from tPA within 1.5h after symptom onset is 2.8,within 3h is 1.5 and after 4.5h is only 1.4.Thus,we should treat stroke like acute trauma or MI where every minute counts.
The same concept should be applied for Transient Ischemic Attact(TIA) which should be considered as an emergency.
It was shown that after a TIA the risk of subsequent stroke is 5.3% at 48h,~10%at 7days and up to 15% at 30 days. It was also shown by two studies, EXPRESS TIA(Oxford,UK)and S.O.S -TIA(Paris, France)that the hazard of stroke after a TIA can be reduced by ~80% if treated as an emergency in acute TIA clinics.
In conclusion, acute ischemic brain event is an emergency condition and should be treated as such because TIME is BRAIN.

ACUTE STROKE UNITS ENHANCE CHANCES FOR RECOVERY

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Acute stroke units have been shown to be the most efficient structure for managing stroke care. In Austria such stroke units have been set up within the last decade following evidence-based principles. Transport times to all units are less than 45 minutes from any given region in Austria, with the exception of very few mountain regions. Stroke units have uniform standardized equipment including CT (and most also MRI), neurosonography, laboratory and monitoring of vital parameters. Also personel is standardized with a neurologist as a leader for such a unit, and therapists for rehabilitation, including physiotherapy, occupational therapy and speech therapy. An ongoing national online patient registry involves all 32 stroke units and covers more than 60% of all hospital admissions for stroke. It shows a high level of efficiency including an overall thrombolysis rate of 13%. When all patients are selected that are eligible for thrombolysis (including age under 80, etiology ischemic, NIHSS more than 5 points, arrival within 120 minutes,) the rate is more than 50%. Thus, such a system of competence can be considered ideal for managing the time constraints of acute stroke care and to give the best possible chances for recovery.

abstracts

PROGRESSIVE INJURY FOLLOWING TRAUMATIC BRAIN INJURY: THERAPEUTIC IMPLICATIONS

Helen M. Bramlett, University of Miami, USA

Recent experimental and clinical data have emphasized that following traumatic brain injury (tbi), progressive damage can occur from months to years after injury. In tbi, atrophic changes have been identified up to one year after both focal and diffuse injury. Progressive thinning of gray and white matter structures indicates complex pathomechanisms that may include both apoptotic and inflammatory cascades. This progressive damage may be significant in terms of progressive neurological symptoms as well as potential increased vulnerability to neurodegenerative diseases including alzheimer's and parkinson's disease. Recent investigations have provided evidence for prolonged apoptotic cell death involving neurons, microglia and oligodendrocytes. Neuronal degeneration at remote sites including subcortical thalamic nuclei has also been provided. In addition, evidence for prolonged inflammatory processes in the posttraumatic brain has been presented. The presence of blood borne inflammatory cells as well as microglial activation has also been shown weeks after tbi. However recently, other potential pathomechanisms have been proposed to underlie the progressive atrophy. These include chronic deficits in cerebral blood flow and metabolism along with seizure development. Therefore, therapies that target multiple pathways may prove advantageous in attenuating the progressive atrophy and chronic functional deficits seen after tbi. In this regard, modest hypothermia, combination pharmacotherapy treatments and cellular transplantation strategies may prove efficacious in improving outcome.

abstracts

INHALATION OF PARTICULATE MATTER AND NEUROINFLAMMATION

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The etiology and progression of neurodegenerative disorders depends on the interactions between a variety of factors including: aging, environmental exposures, and genetic susceptibility factors. Enhancement of proinflammatory events appears to be a common link in different neurological impairments, including Alzheimer's disease (AD), Parkinson's disease (PD), amyotrophic lateral sclerosis (ALS), and multiple sclerosis (MS). In a series of studies, we have shown a link between exposure to particulate matter (PM) and enhancement of CNS proinflammatory markers. We show that in a genetically susceptible mouse strain, exposure to ultrafine particulates is more effective in promoting inflammatory events in the CNS. In another study, using normal rats as a model, we have demonstrated that there is regional variation in response after exposure to diesel engine exhaust. Levels of the pro-inflammatory cytokines tumor necrosis factor alpha (TNF-) and interleukin-1alpha (IL-1) were greatest only in the striatum of diesel-exposed rats compared to the controls. Our results confirm that PM exposure induces inflammatory responses in the brain and now indicates that different brain regions may be more responsive to changes induced by exposure to diesel exhaust. However, more studies need to be conducted to determine the mechanism of this response and to assess if and to what extent the observed changes may impact the normal function and cellular integrity of unique brain regions.

abstracts

NEUROPATHOLOGY IS NEUROPROTECTION IN DEGENERATIVE DISEASES

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The microscopic pathology of neurodegenerative diseases focuses on proteinaceous inclusions for the simple fact that they are visible. Interestingly, the technique – sectioning, staining, and magnifying – is primitive, and detectability in and of itself is not evidence of pathogenic relevance, yet the temptation to relate inclusion to etiology has proven overwhelming. The detection and characterization of inclusion constituents has been the major driving force behind all major etiologic and pathogenic hypotheses in neurodegenerative diseases, most notably during the last twenty years since the protein components of various lesions have been identified.

In the frenzy to identify new cascades, and suggest new targets for therapy, scientists have turned a blind eye to the basic concept of significance, or the meaning of proteinaceous accumulations identified at the endpoint in the disease process, in chronic diseases that progress over decades. In Alzheimer's disease in particular, the capricious relationship between pathology and clinical disease, the focus on fundamentally different lesions comprised of different proteins depending which method is chosen, and the general inability to come up with accurate pathological criteria, suggest that the pathology and etiology are entirely unrelated. Yet the studies continue, as do the repeated modifications and repeated failures of expensive, lesion directed therapies.

In this discussion, the broad category of neurodegenerative diseases is considered, including Alzheimer's disease, Lewy body dementia, Parkinson's disease, frontotemporal dementias, other tauopathies, other synucleinopathies, and prion diseases. We hope to shed light on the time honored misconception that light microscopy is a window into pathogenesis of neurodegenerative diseases, and emphasize instead the window into cellular adaptation, cellular survival, the repertoire of host responses, and, indeed, neuroprotection.

abstracts

A TRADITIONAL CHINESE MEDICINE, IN POST-STROKE RECOVERY AND VASCULAR COGNITIVE IMPAIRMENT

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Stroke is a leading cause of death and disability worldwide. Despite improvements in acute stroke treatment, many patients only make a partial or poor recovery. Therefore, there is a need for treatments that would further improve outcome. A traditional Chinese medicine (TCM) widely used in China to improve recovery after stroke, has been compared to another TCM in two unpublished randomized clinical trials. The pooled analysis shows the good tolerability and superiority of over another TCM also approved for stroke. A large double blind randomized placebo controlled clinical trial is underway to further assess the safety and efficacy of DJ.

Studies show some benefit of DJ in restoring neurological and cellular function in animal models of stroke. A substantial proportion of patients after non-disabling stroke are cognitively impaired compared to aged and education matched community dwelling controls and have a high risk of converting to dementia. Further studies are needed to better clarify appropriate clinical criteria, rating scales and risk factors for cognitive deterioration, to identify preventive measures to interrupt cognitive or functional decline, and demonstrate effective cognition enhancing therapies.

A pilot double blind randomized placebo controlled clinical trial is being planned to assess the safety and efficacy of DJ in patients with vascular cognitive impairment after stroke.

abstracts

NANONEUROMEDICINE: THE FINAL FRONTIER

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At a time when science is looking not only for a unified theory of physics, but also for a unified theory of biology, we should finally realize that the same fabric of subatomic matter is the foundation for both the physical matter and the substance of life. Nanoneuromedicine lies at the intersection of molecular neurobiology, quantum physics and the science of consciousness. It is now the time to bring theory, experiments and philosophical perspectives together. It is said that the 20th century was the era of physics and the 21st will be the era of biology – more accurately, it may be the era that brings the sciences together in an integrated effort to understand the biological processes and the human brain in particular. Advances in micro-scale technology, the high-speed signal processing and memory capabilities of electronic devices and their perfectly matching dimensionality with the biological components of the living neuron cells allow the emergence of neurotechnologies and hybrid bioelectronic systems capable of performing fundamental studies at the molecular level, with spectacular applications in neurobiology, nanomedicine, diagnostics, drug discovery, prosthetic implants, neuron-based processors for biocomputers and even implantable information processing devices for virtual reality interfacing. The integration of neurobiology with the microtechnologies has already led to impressively successful applications: cochlear implants, neuroimplants for assisting impaired motor functions, retinal implants, electrodes for deep brain stimulation, microelectrode arrays for studying the dynamics of neural networks *in vitro* and to investigate the effect of drugs on neurons in carefully developed neuropharmacology assays.

Regenerative medicine must focus on understanding disease at molecular level, forgetting the mechanicistic and reductionistic views of the human body and concentrate on the more subtle biochemical, electrical and energetical properties of the living tissue. New exploratory methods based on vibrational electromagnetic and acoustic fields can be developed to investigate neuron regeneration and neuron plasticity, with a special focus on neurogenesis. Embryonic stem cells or stem-cells from fetal amniotic liquid source differentiated in neurons can ve used in transplants for neurotrophic factors delivery in brain regeneration. Biosensing techniques can monitor noninvasively all the stages of neural differentiation and growth until the moment of transplantation inside the damaged area of the brain. This will constitute a first step towards a personalized organ repair strategy, in which the patients' own regressed cells will be used, free of immunosupression and its cortege of related complications.

abstracts

THERAPEUTIC POTENTIAL OF MOOD STABILIZING DRUGS FOR NEURODEGENERATIVE DISEASES

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Lithium and valproate (VPA) are two major mood stabilizers used to treat bipolar mood disorder, one of the most devastating, highly heritable mental illnesses. Mechanisms underlying the therapeutic efficacy of both drugs are unclear. Our laboratory first demonstrated that lithium and VPA have robust neruoprotective effects against apoptotic insults, notably glutamate-induced, NMDA receptor-mediated excitotoxicity in cellular and animal models of neurodegenerative diseases. The neuroprotection involves multiple mechanisms including inactivation of glutamate receptors, induction of neurotrophic factors, activation of cell-survival pathways, expression of cytoprotective proteins, and suppression of insult-induced inflammatory responses. Pretreatment with lithium suppresses neurodegeneration in an excitotoxic rat model and transgenic mouse model of Huntington's disease. Post-insult treatment with lithium or VPA reduces neurological deficits and brain infarction induced by brain ischemia. Ischemia-induced cerebral inflammation is also markedly inhibited by VPA treatment through suppression of microglia activation. Research from other laboratories has substantiated the neuroprotective and neurotrophic properties of lithium and VPA in a large number of neuropathological conditions. Our very recent work showed that co-treatment with lithium and VPA causes synergistic neuroprotective effects. Additionally, lithium and VPA have been shown to induce neurogenesis and modulate neuroplasticity. Together, our results raise the possibility that mood stabilizers may have expanded use to treat excitotoxicityrelated neurodegenerative diseases. Supported by NIMH, NIH.

abstracts

HOW TO IMPROVE THE GLOBAL OUTCOME IN SEVERE BRAIN INJURY (SBI) EARLY NEUROPROTECTION, NEUROPLASTICITY, NEUROREGENERATION, NEUROREHABILITATION AND PSYCHOLOGICAL SUPPORT

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Background: Traumatic brain (TBI) and spinal cord injuries (SCI) are two of the most devastating types of injuries, especially in young people in all official data. The Centers for Disease Control and Prevention (USA) report that at least 15 million people sustain TBIs in the US annually, far more than the number of people affected by breast cancer, human immunodeficiency virus/acquired immunodeficiency syndrome, and multiple sclerosis combined. The estimated cost of TBI-related hospitalizations is $56.3 billion every year.
TBI delimitation was perfomed by Teasdale and Jennett (1974), in Glasgow Coma Scale (GCS), important standard in the assessment of these brain lesions: minor (13-15), moderate (12-9), severe (8-3). This standard ("golden") scale in TBI was established by motor (1-6p.), verbal (1-5p.), eyes (1-4p.) response at external stimuls. Severe brain injuries (GCS 3-8) represent an important cause of mortality and morbidity, especially in patients with active period of live (20-40 years old).
Material & Method: Severe brain injuries (GCS 3-8) represent an important cause of mortality and morbidity, especially in patients with active period of live (20-40 years old). Included criteria: the authors studied non selected consecutive 88 patients with SBI (between 6 – 66 years old), 53 male and 35 female in period 2003-2007 (5 years) at the Hospital "Bagdasar-Arseni", Bucharest. The distribution by age was children 30 cases (34,1%) and adults 58 cases (65,9%). The most frequent cause of SBI is represented by the **car accidents (car to pedestrian, passenger vehicle)** 58 cases (65,9%), followed by falls different higher 23 cases (26,1%) domestic accidents 4 cases (4,5%) and sport traumas 3 cases (3.4%). All intracranial haematoma was operated in the first 6 hours after admission. Excluded criteria: all patients in SBI status with multiple trauma with or without intracranial haematomas. All 88 cases were monitoring in intensive care unit (ICU). At admission GCS 3-4 was 26 cases (29,5%), GCS 5-6 was 25 cases (28,4%), GCS 7-8 was 37 cases (42%). In all cases the admission CT scan was performed in the first 6 hours; The following CT scan was performed at 24, 48, 72 hours and after 1 week to verified the brain lesion and intracranial mass lesion. In 30 cases (34,1%) intracranial mass lesions undergone to the operative procedures: extradural haematoma 14 cases (15,9%), subdural haematoma 10 cases (11,3%), intraparenchimal haematoma 6 cases (6,8%). Additional in 10 cases (11,3%) we report penetrated head injury. Also, CT scan showed hemhorragic contusion 23/88 (26,1%) SAH in 27/88 cases (30.7%), hypodense (ischemic aria lesion in 25/88 cases (28.4%), cerebral edema 40/88 cases (45.5%) and DAI 19/88 cases (21,6%); DAI was diagnosis only by MRI and the first week post-injury. In our data surgical evacuation of mass lesions was performed as needed, but only five decompression craniotomy was done.

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In our study no mortality was registered in the group of ICP < 20 mmHg, all the 28/88 cases (31.8%) which died had the ICP > 20 mmHg.
In the literature there are studies which correlate the GOS with GCS, metabolic, hematological, radiological and clinical profiles.
The predictors outcome factors in this series were: early neurotrophic drugs and active neurorehabilitation were done immediately after admission and neuroimaging diagnosis in intensive care unit. In our experience the neurorophic factors are an significant improvement in post TBI. (mixture of low molecular polypeptide, extracted from pig brain) ncrease motor function, enhance the cognitive performances, increase memory & attention, improve of brain bioelectrical activity. Also, early and active neurorehabilitation improve the brain activities and starts the redundant neural network. At admission GCS 7-8 was preponderent 37 cases (42%) which it was in concordance with the global outcome.
In our data Glasgow Outcome Scale (GOS): good recovery was in 25 cases (28,4%), moderate disability 9 cases (10,2%), severe disability 22 cases (25%), vegetative state 6 cases (6,8%), death 26 cases (29,5%). At admission GCS 7-8 was preponderent 37 cases (42%) which it was in concordance with the global outcome.
The psychological support in all SBI will be necessary to obtain social, familial and professional integration.
Conclusions: The four early important therapeutical factors may improve the outcome in SBI. Neurotrophic factors can improving the global outcome. The psychological support in all SBI will be necessary in both: patient and his/her family, for increase compliance at treatment to a very good recovery or autonomy and to obtain social, familial and professional integration and, finally, to a high QoL.
Keywords: traumatic brain injury, GCS, severe brain injury, DAI, ICP, neuroprotection, neurorehabilitation, outcome, GOS, QoL.

abstracts

IMPORTANT THERAPEUTIC OPTION TO IMPROVE GLOBAL OUTCOME IN SEVERE BRAIN INJURY (SBI)

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Traumatic brain injury (TBI) represent a very important cause of disease in all western countries. TBI delimitation was perfomed by Teasdale and Jennett (1974), in Glasgow Coma Scale (GCS), important standard in the assessment of these brain lesions: minor (13-15), moderate (12-9), severe (8-3). This standard ("golden") scale in TBI was established by motor (1-6p.), verbal (1-5p.), eyes (1-4p.) response at external stimuls. For children (0-16 years) in all hospitals was Children Coma Scale (CCS), also quantification 3-15 points.

Severe brain injuries (GCS 3-8) represent an important cause of mortality and morbidity, especially in patients with active period of live (20-40 years old). The authors studied non selected consecutive 88 patients with SBI (between 6 – 66 years old), 53 male and 35 female in period 2003-2007 (5 years) at the Hospital "Bagdasar-Arseni", Bucharest. The distribution by age was children 30 cases (34,1%) and adults 58 cases (65,9%). The most frequent cause of SBI is represented by the car accidents (car to pedestrian, passenger vehicle) 58 cases (65,9%), followed by falls different higher 23 cases (26,1%) domestic accidents 4 cases (4,5%) and sport traumas 3 cases (3.4%). All 88 cases were monitoring in intensive care unit (ICU). At admission GCS 3-4 was 26 cases (29,5%), GCS 5-6 was 25 cases (28,4%), GCS 7-8 was 37 cases (42%). In all cases the admission CT scan was performed in the first 6 hours; The following CT scan was performed at 24, 48, 72 hours and after 1 week to verified the brain lesion and intracranial mass lesion. In 30 cases (34,1%) intracranial mass lesions undergone to the operative procedures: extradural haematoma 14 cases (15,9%), subdural haematoma 10 cases (11,3%), intraparenchimal haematoma 6 cases (6,8%). All intracranial haematoma was operated in the first 6 hours after admission. Additional in 10 cases (11,3%) we report penetrated head injury.

The CT scan werw correlated with Marshall et all Scale (1991). In this study we report the preponderance of: cerebral edema 40/88 cases (45.5%), subarachnoid hemorrhage (SAH) in 27/88 cases (30.7%), hypodense (ischemic aria lesion in 25/88 cases (28.4%), showed hemhorragic contusion 23/88 (26,1%) and diffuse axonal injury (DAI) 19/88 cases (21,6%); DAI was diagnosis only by MRI and the first week post-injury. In our data surgical evacuation of mass lesions was performed as needed, but only five decompression craniotomy was done. No mortality was registered in the group of ICP < 20 mmHg, all the 28/88 cases (31.8%) which died had the ICP > 20 mmHg.

abstracts

All patients received at admission in ICU early treatment with Cerebrolysin iv, 3 vials (10 ml) per day, ten days. The neurotrophic factors are an significant improvement in post TBI. Cerebrolysin (mixture of low molecular polypeptide, extracted from pig brain) increase motor function, enhance the cognitive performances, increase memory & attention, improve of brain bioelectrical activity.
In the literature there are more than 500 substances studied for neuroprotective properties. The effect of neurotrophic factors for neuroprotection consist in activation of Calpaine system. The important additional neurotrophic factors effects are: cerebral excitability and hypoxia, improving EEG signal and motor activity after mild brain ischemia and also antioxidative properties.
The follow-up was performed by EEG, GCS score, GOS and psychological evaluation.
In our data Glasgow Outcome Scale (GOS): good recovery was in 25 cases (28,4%), moderate disability 9 cases (10,2%), severe disability 22 cases (25%), vegetative state 6 cases (6,8%), death 26 cases (29,5%). At admission GCS 7-8 was preponderent 37 cases (42%) which it was in concordance with the global outcome.

Conclusions: SBI represent an important medical and neurosurgical problem. Many therapeutical factors may improve the outcome in SBI (Early Neuroprotection, Neuroplasticity, Neuroregeneration, Neurorehabilitation and Psychological Support). Neurotrophic factors can improving the global outcome.

Keywords: traumatic brain injury (TBI), GCS, severe brain injury (SBI), DAI, ICP, neuroprotection, neurotrophic factors, global outcome, GOS.

abstracts

CAN WE ENHANCE POST STROKE REHABILITATION BY PHARMACOTHERAPY?

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The influence of pharmacological therapy on rehabilitation after cerebral injury raises increasing interest. Experimental studies have proved that a number of endogenous factors can enhance neuronal and glial activity, prolong cell life, stimulate axonal growth and creation of new neuronal junctions and cell maturation. Most of the experimental and clinical studies involve agents affecting neurotransmission. The effect depends on the time from the stress, localization and drug dose.

During treatment physical training and/or rehabilitation of cognitive functions is needed. Dextroamphetamine is one of the drugs with best evidence. It increases the amount of noradrenalin in the brain. Clinical improvement was seen in some of the trials. Enhancement of dopaminergic transmission was achieved by treatment with levodopa or bromocriptine. Improvement with these agents was observed in physical and aphasia rehabilitation. Fewer trials were performed with drugs increasing acethylocholine concentration. As depression is a common post stroke complications use of antidepressants seems a promising strategy , but there are some differences between drugs. E.g. fluoxetin improves motor function, whereas maprotilin has no effect. Growth factors like FGF (fibroblast growth factor), GDGF (glial derived growth factor) or BDNF (brain derived growth factor) are expected to have a substantial effect in rehabilitation.

It should still be remembered that a lot of drugs, e.g. antipsychotics, barbiturates, benzodiazepines, antiepileptics, clonidine and prazosin have a negative effect on rehabilitation.

abstracts

STROKE, MUSIC AND NEUROPLASTICITY

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The well known fact is that one third of stroke patients remain severely disabled. Unfortunately, acute stroke therapy is of limited value, great hope is put in rehabilitation of stroke victims. This hope for successful rehabilitation lies in novel findings of the brain plasticity, the mechanism of the human brain to adapt to environmental changes; after stroke neural pathways reorganize due to new experiences. In this process well known is the role of physical therapy. Based on historical experiences started from the ancient Greece and Rome, as well on modern studies using sophisticated technical equipment, music has significant role in human well being and healing processes. Many studies have shown number of diseases where listening or producing music had positive effect on the recovery. Stroke affects person's motor functions, speech, cognitive functions and mood. Music therapy positively influences the recovery of these functions. Listening to rhythmic melody enhances recovery of walking and normal gait. Listening to songs and singing along helps aphasic patients to learn to speak faster than by usual verbal techniques. Several studies with their results have shown that regular listening to music significantly improves cognitive function and mood in stroke patients.

Music should be introduced in every day clinical practice in early phase of stroke treatment and in rehabilitation period. During rehabilitation, patients spend in exercises only several hours a day, the rest of the time is spent in non-stimulating environment. Music therapy can be used longer during the day, offering patients valuable stimuli for brain plasticity processes.

abstracts

NEW ADVANCES IN THE PATHOPHYSIOLOGY AND TREATMENT OF SPINAL CORD INJURY

W. Dalton Dietrich, Kinetic Concepts Distinguished Chair in Neurosurgery, Professor of Neurological Surgery, Neurology and Cell Biology & Anatomy, Scientific Director, The Miami Project to Cure Paralysis, Miami, Florida, USA

Over the last 20 years, major advances have been made in understanding the pathophysiology and treatment of spinal cord injury (sci). The pathophysiology of sci is complex and recent studies have shown that therapies against excitotoxicity, apoptosis and inflammatory cascades represent important targets for therapeutic interventions. Recently, the importance of the formation of the nalp1 inflammasome after sci has provided another important molecular target for anti-inflammatory treatments. Modest hypothermia also appears to be protective in various animal models of sci and this experimental treatment is now being translated into humans. Several cell therapies are being tested to change the injured sc environment to make it more permissive for axonal regeneration. Schwann cells, olfactory ensheathing glia, genetically engineered cells as well as different types of stem cells are being used to protect and repair the injured spinal cord. Recently, the combination of schwann cell transplantation, rolipram as well as cyclic amp injections have been shown to improve walking by 70% in injured rats. These studies are currently being moved forward for an fda approved clinical trial for acute and chronic spinal cord injury. In addition, transplanted cells can be transduced with various synthetic molecules that allow the cell to synthesize and release multiple neurotrophins. These cellular therapies in combination with rehabilitation procedures are showing great potential in treating the sci patient. This talk will summarize recent advances in neuroprotection, cellular transplantation, rehabilitation and clinical trials for sci.

abstracts

THERAPEUTIC HYPOTHERMIA AND CNS INJURY

W. Dalton Dietrich[1], Coleen M. Atkins, Helen M. Bramlett[2]

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Recent experimental and clinical investigations have demonstrated the beneficial effects of mild to moderate hypothermia in conditions of cerebral ischemia and trauma. In animal models of brain and spinal cord trauma, for example, post-traumatic hypothermia has been reported to reduce contusion volume and significantly improve behavioral outcome. Data from models of cerebral ischemia and stroke have been successfully translated to the clinic where multicenter trials have shown efficacy in patients with cardiac arrest as well as neonatal hypoxia. In terms of possible mechanisms underlying hypothermia protection, studies have shown that temperature affects many of the pathophysiological events associated with secondary injury. Thus, mild cooling during or after an insult reduces free radical generation, excitotoxicity, apoptosis and various inflammatory processes. This multi-factorial nature of brain cooling may be a major reason why hypothermia has been reported to work in multiple neurological conditions. In the area of brain injury, an important consequence of stroke and traumatic brain injury is altered cognitive function. Hypothermia treatment has been shown to improve cognition in terms of water maze performance. More recently, molecular events underlying improvements in hippocampal dependent learning and memory have been described. This lecture will review some of the experimental, clinical and mechanistic questions currently being discussed in the area of therapeutic hypothermia targeting brain and spinal cord injury.

abstracts

CEREBRAL PROTECTION, PLASTICITY AND REPAIR THERAPIES IN ISCHEMIC STROKE

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Among available treatments in the acute ischemic stroke, only intravenous thrombolysis has been demonstrated to be efficacious. Although the majority of pharmacological neuroprotectants have been efficacious in experimental studies, they have failed in clinical trials. Hence, we need to consider integrated cerebral protection which includes the concept of cerebral repair by supporting cerebral plasticity. We provide our experience and a non-systematic review of the studies published on cerebral protection and repair treatments of cerebral ischemia considering the possibilities of cerebral protection, stimulating brain plasticity by trophic factors and cell therapy. The majority of the neuroprotective drugs have failed in clinical trials. Citicoline shows a benefit in meta-analysis and it is currently being explored in a new trial (ictus). Neuroprotective drugs combined with reperfusion, offer favorable results in experimental animals, but data from clinical studies are no enough. Repair therapies using cerebral plasticity stimulation (trophic factors) and cell therapy have shown certain efficacy in experimental and clinical studies and they are a developing route with clinical therapeutic perspectives.

abstracts

MITOCHONDRIAL FUNCTIONS AND DYSFUNCTIONS IN SOME INHERITED NEUROLOGICAL DISEASES AS A MODEL OF NEURODEGENERATION AND NEUROPROTECTION

Antonio Federico, Department of Neurological, Neurosurgical and Behavioural Sciences, Medical School, University of Siena, Siena, Italy

Mitochondria are well known cell organelles related to energy production , particularly important in the tissues with high energy request as nervous system and muscle. Mitochondrial dysfunctions have been recognized in a series of neurological disorders, in relationship to impairment of mitochondrial DNA and nuclear DNA and a series of syndromes called mitochondrial encephaloneuromyopathies have been described.
All are mainly clinically characterized by multisystem involvement, including brain, eye, endocrine system, muscle, hearth, nerves, etc. and some syndromes have been defined as MERRF (Mitochondrial encephalopathies with ragged red fibres), MELAS (Mitochondrial Encephalopathy Lactic acidosis and stroke-like episodes), Kearns Sayre syndrome, NARRP, etc.
Patients with disorders from mutations in the mitochondrial genome have variable phenotypes, but common to many of these disorders are underlying changes in postmitotic cells, particularly neurons and muscle fibers. The mitochondrial dysfunction caused by these mutations has been shown to be associated with signs of apoptosis and to cause cell loss.
Mutations of the mitochondrial genome have also been shown to accumulate with age and in common neurodegenerative diseases, such as Parkinson's disease.
Here, we will also discuss the potential role of mitochondrial fission and fusion in the onset and progression of neurodegenerative diseases. Specifically, an imbalance in mitochondrial fission and fusion may be the basis of familial and sporadic neurodegenerative disorders. First, hereditary mutations in the mitochondrial fusion GTPases optic atrophy-1 and mitofusin-2 cause neuropathies in humans. In addition, recent findings report increased mitochondrial fission in Parkinson's disease (PD) models and induction of mitochondrial fission by two proteins, PTEN-induced kinase 1 and parkin, which are mutant in familial forms of PD and other diseases.

We will describe
- our experience in the diagnosis of several mitochondrial disorders as a model of energy impairment neurodegeneration
- our research on oxidative stress induced apoptosis in several neurometabolic and genetic neurodegenerative diseases.
- some therapeutic approaches discussing the potential therapeutic efficacy of creatine, coenzyme Q10, idebenone, synthetic triterpenoids, and mitochondrial targeted antioxidants (MitoQ) .

This review presents recent data to show that the information gained from studying patients with mitochondrial disorders can help our understanding of the role of mitochondrial DNA mutations in brain aging and generally in neurodegeneration.

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AT THE CROSSROAD OF AGING, LONGEVITY AND AGE-RELATED NEURODEGENERATION: A NETWORK-BASED PERSPECTIVE

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Hundreds of genes have been identified as being involved in the control of lifespan in model organisms and in human age-related diseases (ARDs) including Alzheimer's disease (AD). These studies highlight that aging, longevity, and ARDs are associated with multiple factors. Yet, the trend to focus on individual genes and/or their products continues to dominate, reflecting in part a paradigm in biomedical research – searching for the specific targets that offer the potential for the development of highly specific drugs. In spite of enormous efforts and accumulated knowledge, our capabilities for tackling aging and ARDs, and ultimately to promote longevity are still very modest. What is lacking – essential knowledge of key players or efficient analytic tools, or both? Here we discuss how the existing data may be integrated and analyzed using a network-based approach, focusing particularly on the role of protein-protein interactions (PPIs) and microRNAs in linking AD with human aging, longevity, oxidative stress, and chronic inflammation. A gradual deterioration of the microRNA-regulated PPI networks is proposed to be one of the common mechanisms for both aging and AD. The analysis revealed the proteins and microRNAs that might particularly be essential for network integrity and normal functionality of the brain. Targeting these proteins and microRNAs might represent a new approach for pleiotropic neuroprotective interventions.

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NANOPARTICLES FOR BRAIN DELIVERY: TOXICOLOGICAL ASPECTS

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Among the most promising approaches to the non-invasive brain drug delivery is the binding to nanoparticles. In particular, poly(butyl cyanoacrylate) (PBCA) nanoparticles coated with polysorbate 80 (Tween® 80) delivered to the brain the antitumour antibiotic doxorubicin that cannot independently penetrate across the BBB and, therefore, is not used for the chemotherapy of brain tumours. In contrast to conventional formulations, the nanoparticle-bound doxorubicin reaches the brain in the concentrations sufficient to considerably inhibit the growth of intracranially implanted glioblastoma in rats.

The PBCA nanoparticles also have another important advantage: they are comprised of a relatively safe material. Indeed, PBCA is a biodegradable low-molecular polymer which is rapidly eliminated from the body. However, since the nanoparticles not only enable a transport across the BBB but additionally alter the overall body distribution, thorough toxicological investigations of the nanoparticle-bound doxorubicin have been performed.

It was shown that binding of doxorubicin to the nanoparticles did not enhance its acute toxicity. The intravenous injection of empty nanoparticles (up to 400 mg/kg) was not associated with adverse effects nor did it affect body weight or weight of internal organs.

The results of two other studies performed at the sublethal dose level indicated that the surfactant-coated nanoparticle formulation of doxorubicin has a favorable toxicological profile. The most important finding is the reduction of cardiotoxicity, evidenced by both, functional and histological assessment. The nanoparticles also considerably attenuated the testicular toxicity of doxorubicin. The lower toxicity of the nanoparticle formulation is most probably explained by the altered biodistribution of the drug mediated by the nanoparticles.

abstracts

NEUROTROPHIC FACTORS IN VASCULAR DEMENTIA – RESULTS OF THE RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED MULTICENTRIC CLINICAL TRIAL

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[2]

Introduction: Cerebrolysin is a peptide preparation acting like endogenous neurotrophic factors. Due to its pleiotropic effects, is regarded as potential therapeutic tool in complex diseases like stroke or dementia. The aim of this study was to compare neurotrophic factors with placebo in patients suffering from vascular dementia and to confirm and extend the findings of earlier clinical trials in a larger patient cohort.
Methods: The primary efficacy criterion was defined as the combined outcome of the two primary efficacy criteria ADAS-cog+ and CIBIC+. Primary endpoint for assessing efficacy is 168 days after the baseline assessment. Patients received a dose of 20 ml Cerebrolysin administered in two treatment-cycles as add-on therapy to basic treatment with acetylsalicylic acid.
Results: In this study 242 patients were randomized and a total of 217 (89.7 %) completed the study. The therapy with neurotrophic factors resulted in significant improvement of both primary parameters, the score change from baseline in ADAS-cog+ at week 24 and the CIBIC+ score at week 24. Cognition, as assessed by ADAS-cog+, improved by -10,628 points in the medicated group at week 24 yielding a statistically significant treatment difference compared to placebo. In the CIBIC+, there was also a statistically significant treatment difference between neurotrophic factors and placebo at week 24. The rate of ADAS-cog+ responders, defined as having an improvement of ≥ 4 points from baseline, was higher in the neurotrophic factor-treated group with 82.1 % compared to 52.2 % in the placebo group. The odds ratio for achieving a treatment response in the cognitive domain was 4.190 for Cerebrolysin versus placebo at week 24, indicating a 4.190-fold increased probability of achieving a clinically significant cognitive improvement during the study compared to placebo. In the CIBIC+, the rate of responders, defined as having a score of <4 at week 24, was also higher in the neurotrophic factor-treated group with 75.2 % compared to 37.4 % in the placebo group. The odds ratio for achieving a favourable CIBIC+ response was 5.081 for neurotrophic factors versus placebo. Responder rates of the combined response in ADAS-cog+ and CIBIC +were 67.5 % in the neurotrophic factors group compared to 27.0 % in the placebo group. The odds ratios were 5.633 for Cerebrolysin versus placebo at week 24. Also in the MMSE, measuring cognitive impairment, the neurotrophic factors were significantly superior over placebo at week 24. Same applies in the activities of daily living as measured by the ADCS-ADL and in the executive function as measured by the Trail-making test and the Clock-drawing test. Results from the subgroup analysis of patients with more advanced cognitive impairment (MMSE ≤20) have demonstrated that neurotrophic factors exerts even slightly larger treatment effects.

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Discussion /Conclusion: The study demonstrated that the neurotrophic factors improve the clinical outcome of patients suffering from mild to moderately severe vascular dementia significantly by improving both the cognition and the overall clinical functioning and these benefits were shown to extend for at least 6 months. Furthermore it was safe and well tolerated by patients suffering from mild to moderately severe VD in a dose of 20 ml. This study has confirmed previous findings in clinical studies with patients suffering from vascular dementia. Together with its efficacy in the treatment of Alzheimer's disease, the neurotrophic factors are effective in the most common forms of dementia and represents a treatment approach, which might also be effective in the treatment of patients with mixed dementia, where vascular and Alzheimer's disease coexist. **Acknowledgement:** The authors are sincerely grateful to E. Bogdanov, S. Gavrilova, N. Govorin, A. Gustov, M. Ismagilov, V. Kontsevoy , G. Kozin, K. Lakunin, V. Laskov, O. Levin, N. Neznanov, L. Novikova, M. Odinak, O. Orlikova, Y. Shirshov, V. Shprakh, A. Skoromets, N. Spirin, Z. Suslina, N. Yakhno for their invaluable collaboration.

abstracts

ReWARD™: A REGISTRY BASED CLINICAL TRIAL METHOD

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The randomized clinical trial remains the standard method of evaluating treatments and interventions. However, clinical trials are becoming more complex, difficult and expensive. Moreover, they tend to be carried out by specialized investigators on selective populations. The introduction of large stroke registries allows new possibilities of evaluating treatments and procedures in real world settings.

The first prerequisite is a minimum common set of standard evaluations, record of interventions, audits, and agreed outcomes. Patients would be matched in pairs on all relevant characteristics except that one would have had the drug or intervention, and the other not. Once the sample size has accrued, a number of complementary, analytic strategies can be applied. (The ReWARD™ method)

This approach can be used for testing interventions prospectively, for example testing drugs used in some centers and not in others, and for post approval surveillance for effectiveness, safety and efficacy.

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IMAGING THE PENUMBRA: THE PATHOPHYSIOLOGIC BASIS FOR THERAPY OF ISCHEMIC STROKE

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Active treatment of acute ischemic stroke can only be successful as long as tissue in the area of ischemic compromise is still viable. Therefore, the identification of the area of irreversible damage, and its distinction from the penumbral zone, i.e., tissue with impaired function but preserved morphology, may improve the estimation of the potential efficacy of various therapeutic strategies.

Since morphological neuroimaging modalities as CT and MRI do not reliably detect irreversible damage in the first hours after stroke, functional imaging markers of penumbra and early infarction were introduced. Positron emission tomography (PET) of cerebral blood flow (CBF) and cerebral metabolic rate for oxygen (CMRO2) has been established as the gold standard. These multitracer studies have severe limitation due to complexity, invasiveness and radiation exposure, which can only partly be overcome by applying 11C flumazenil, a central benzodiazepine receptor ligand, for identification of irreversibly damaged cortical tissue. Therefore, other modalities served as surrogate markers, with perfusion / diffusion-weighted magnetic resonance imaging (PW / DWI) and perfusion computed tomography (PCT) being applied widely in clinical routine. In order to evaluate the limitations of PW / DWI a comparative study was performed in acute stroke patients in whom cerebral perfusion was assessed by PWI and H215O-PET, tissue damage was estimated by DWI and 11C-flumazenil (FMZ) PET and PW / DWI mismatch was related to the tissue with increased oxygen extraction fraction (PEF) as an indicator of penumbra. The lesions in DWI and in FMZ-PET were reliable predictors of final infarct on late MRI, but DWI showed a high false positive rate. PWI was limited in estimating flow and yielded values comparable to H215O-PET only in the range between 20 and 30 ml/100g/min. The PW / DWI mismatch overestimated the penumbra as determined by increased OEF. These limitations of PW / DWI have to be considered if used for selection of patients for treatment and might have an impact on the outcome of clinical trials based on this surrogate marker.

In several studies it was demonstrated that a large portion of the final infarct is irreversibly affected in the first few hours in many patients. A considerable tissue volume is viable but critically hypoperfused; a smaller portion of the final infarct is sufficiently perfused and in this area secondary and delayed biochemical and molecular mechanisms contribute to the damage. Based on this concept the improvement of perfusion within the time window of opportunity must be the primary goal in treatment of ischemic stroke, and neuroprotective and other strategies can only play a supportive and additive role. That this is the case can be seen from the results of many controlled therapeutic trails, in which up to now only thrombolytic therapy with a 4.5 h time window for systemic and a 6 h time window for intraarterial application proved its efficacy, whereas all trials with neuroprotective, anti-inflammatory or anti-apoptotic strategies failed. Since the direct treatment strategies are limited the acute management of stroke victims is of utmost importance. It is still to be investigated if the combination of reperfusion and neuroprotective therapy can improve the outcome after ischemic stroke.

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FUNCTIONAL SPECIFICITY OF MAPK ISOFORMS: DON'T TOUCH THE GROUP BUT HIT THE ISOFORM

Thomas Herdegen, Institute of Pharmacology, University of Kiel, Germany

The c-Jun N-terminal kinases (JNK), similar as their ERK and p38 counterparts, are essential mediators of neuronal plasticity and neuronal degeneration. However, it remains to be eluci-dated what regulates their physiological versus pathological actions. We and others have shown, that each JNK-isoform is capable to execute both, physiological or regenerative versus pathological or apoptotic actions. It is imperative to analyse each isoform on its context – de-pendent role in neurological diseases. In this lecture, I will present recent data from our lab on the control of isoform action and put these information into the context of current knowledge of intracellular signalling with a particular focus on JNK-kinases. Of particular relevance is the intracellular or intraneuronal localisation. The very same isoform can execute at the very same moment cell proliferation and apoptosis – with the consequence that inhibition of one isoform's total cellular activation will result in rescue (block of apoptosis) and coincident stop of proliferation. This explains why rescued neurons (block of JNK mediated apoptosis) do not undergo regeneration (coincident block of axonal elongation). One therapeutic option is the definition of context-specific MAPK signalosomes which – by different molecular composi-tion – trigger opposing functions.

abstracts

OXIDATIVE STRESS AND INFLAMMATION AS TARGETS FOR NEUROPROTECTION IN TRAUMATIC BRAIN INJURY

Lars Hillered, Dept Neuroscience, Div Neurosurgery, Uppsala University Hospital, Uppsala, Sweden

Oxidative stress (overproduction of reactive oxygen species; ROS) and adverse inflammatory reactions have long been implicated in the secondary injury cascade following traumatic brain injury (TBI). We have used members of the nitrone free radical scavenger family (PBN, S-PBN and NXY-059) as tools to study the role of ROS in rodent models of TBI. Both PBN and S-PBN markedly reduced the amount of ROS production following TBI[1]. All three nitrones had robust neuroprotective properties reducing brain tissue loss and improving functional outcomes following cortical contusion and fluid percussion injury[2,3] regardless of blood brain barrier (BBB) penetrating ability, opening up for alternative mechanisms of action. We hypothesized that the non-penetrating nitrones may act at the neurovascular unit interfering with ROS mediated signalling between the injured brain and the peripheral immune system. Quantification of immune cell infiltration following cortical contusion in rats revealed that S-PBN pre-treatment reduced the amount of neurotrophil infiltration by 50% and almost abolished T-cell infiltration following injury[4]. There was also a marked reduction of adhesion molecule expression (ICAM-1 and VCAM). Based on literature data we submit that the dramatic reduction of T-cell infiltration is mediating the neuroprotective effects of S-PBN and NXY-059 following TBI. The concept of signalling between the injured brain and the immune system was supported by recent data showing a robust upregulation of many inflammatory gene transcripts including several chemokines following cortical contusion in mice[5]. In order to translate these findings into the Neuro-ICU setting, biomarkers for monitoring of oxidative stress and inflammation in human TBI are urgently needed.
Supported by the Swedish Research Council and Uppsala University Hospital.

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abstracts

FROM MOTOR LEARNING TO MOTOR THERAPY: TRANSLATION RESEARCH IN NEUROREHABILITATION.

Volker Hömberg, Meerbusch, Germany

Over the last 15 years there has been a dramatic change in paradigms of motor rehabilitation resulting in a transition from "confession" to "profession".
The approaches have changed from "treating" patients to "coaching" patients. These based on elementary knowledge about motor learning from animal experiments as well as from behavioural studies in humans.
The change in motor rehabilitation paradigms is a beautiful example of translation research from basic studies to clinical usage which has been achieved in very short time.
In the lecture some example of modern evidence based motor rehabilitation approaches derived from basic science will be discussed in detail.

AGING, MITOCHONDRIAL FUNCTION, AND PARKINSON'S DISEASE

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In the case of Parkinson's Disease, (PD), classical animal models have utilized dopaminergic neurotoxins such as 6-hydroxydopamine (6OHDA) and 1-methyl 4-phenyl 1,2,3,6-tetrahydropyridine (MPTP). More recently, human genetic studies have identified several genes in familial forms of PD. Transgenic models have been made that explore the function of PD-linked genes (e.g. -synuclein, DJ-1, LRRK2, Parkin, UCH-L1, PINK1). Recent evidence also suggests mitochondrial dysfunction may play a major role in PD. This evidence comes from both the genetic studies mentioned above, and the finding that the major risk factor for PD is aging. Moreover, studies have shown that many of the "PD genes" products are localized to the mitochondria and that there are defects in mitochondrial genes that accumulate with aging and/or PD.

Manipulation of mitochondrial respiratory genes (e.g. mitochondrial transcription factor A or TFAM) also elicits a PD phenotype in mice. Transgenic mice (MitoPark) were developed that have TFAM selectively knocked out in dopaminergic neurons. The nigral dopamine neurons of MitoPark mice show respiratory chain dysfunction, accompanied by the development of intraneuronal inclusions and eventual cell death. In early adulthood, the MitoPark mice show a slowly progressing loss of motor function that accompanies these cellular changes. The MitoPark mouse enables the further study of role of mitochondrial dysfunction in DA neurons as an important mechanism in the development of PD. Transgenic technology has allowed new insights into mechanisms of neurodegeneration for a number of neurological disorders. This paper will summarize the genetics of human PD, effects of aging on nigral neuron mitochondria, and recent studies on transgenic models of Parkinson's Disease.

abstracts

ENVIRONMENTAL HEAT, POSSIBLE ROLE IN NEUROPLASTICITY, CROSS-TOLERANCE AND NEUROPROTECTION

Michal Horowitz, Laboratory of Environmental Physiology, The Hebrew University, Jerusalem, Israel

Prolonged exposure to a hot environment induces in the body concerted adaptive responses leading to enhanced endurance in hot environments. This process, defined as acclimation (AC), is a conserved feature of "within lifetime" phenotypic adaptation. It evolves via integrated remodeling of physiological, biochemical, and molecular functions. The reprogramming of gene expression leading to coordinated adaptations in overlapping cytoprotective (HSPs, antioxidative, antiapoptotic) and metabolic (eg HIF-1□) targeted pathways) networks and post-transcriptional mechanisms, in both central and peripheral organs/tissues, are essential components in the evolution of the AC phenotype. An inseparable outcome of the acclimatory processes is that in addition to the primary acclimation (to heat) the adjustment to one environmental stressor augments the degree of coping with other novel stressors. This 'cross-tolerance' phenomenon may be a critical feature of the cellular stress response found in nature via protective preconditioning effects. Heat acclimation mediated cross tolerance, in contrast to the "classical" preconditioning", has expanded time boundaries and provides protection for approximately 2-3 weeks. The effect is also committed to memory. We now have evidence that heat acclimation induces cross-tolerance against several environmental stressors associated with altered oxygen supplementation [hypoxia, ischemia/reperfusion, hyperoxia], ionizing radiation and several other traumatic situations such as noise and traumatic brain injury. Extensive studies conducted in our laboratory led to the development of a conceptual model of AC mediated cross-tolerance. AC enhances both constitutive and acute signaling responses that are expressed as (i) greater cytoprotective protein reserves, (ii) faster acute molecular dynamic response post injury and (iii) post translational modifications. Taken together, these enhancements provide a dual protective strategy - the prompt availability of cytoprotective proteins, without the need for de novo protein synthesis, plus an "alerted signaling system" that responds more rapidly to insult.

abstracts

AN INTEGRATED APPROACH TO NEUROPROTECTION IN TRAUMATIC BRAIN INJURY

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The important of neuroprotection in traumatic brain injury (TBI) is well recognized. There is no single method for providing adequate neuroprotection. Complexity of pathomechanisms of TBI requires an integrated approach to target various pathways for interrupting the chain of events that aggravate the initial impact of injury. Blast injuries due to roadside bombs are created a new pattern of TBI in Iraq and Afghanistan, not seen in previous wars. Neuroregeneration for lost brain tissue is needed and should be integrated with neuroprotection. In addition to evaluation of drugs for neuroprotective effect in TBI, hyperbaric oxygen, molecular therapies, biomarkers and nanobiotechnology are being investigated for the management of TBI. This presentation will describe some of the integrated approaches under investigation for TBI and the potential for translation into clinical application. For example nanoparticles can be used for delivery of neuroprotective agents and nanofibers can be used in conjunction with stem cells for repair of damaged brain. Neural stem cells have been retrovirally transduced to produce nerve growth factor and transplanted into the injured brain with marked improvement of cognitive and neuromotor function and rescue of neurons during the acute posttraumatic period. Active or passive immunization (vaccination) with CNS-associated self antigens has been shown to promote recovery from TBI. In spite of difficulties in translating these techniques into effective therapy in humans, they provide promising strategies for neuroprotection in TBI.

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THE ENIGMA OF VASCULAR DEMENTIA: A NEUROPATHOLOGIST'S VIEW

Kurt A. Jellinger, Professor of Neurology and Neuropathology at
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Vascular dementia/vascular cognitive impairment (VaD/VCI) is not a single entity, but a large group of conditions characterized by various clinical and morphological findings and variable pathophysiology. Clinical diagnostic criteria show moderate sensitivity (50-70%) and variable specificity (64-98%). Epidemiological studies are hampered by the lack of clear diagnostic criteria, the complexity of brain pathologies, ethnic and geographic variations. In Western clinic-based series VaD/VCI is suggested in 8-15% of cognitively impaired aged subjects, with age-standardized incidence ratios 0.42-2.6 and clinical prevalence at age 70+ of 6-15/1000 person/year. Prevalence in autopsy series ranges from 0.03 to 58% (real mean 8-15% in Western series, 22-35% in Japan). Both prevalence and incidence increase with age. Neuropathology shows multifocal and/or diffuse lesions: lacunes and microinfarcts, white matter lesions, hippocampal sclerosis or multi-infarct encephalopathy, mixed cortico-subcortical and diffuse post-ischemic lesions. They result from systemic, cardiac, local large and small vessel disease. Pathogenesis is multifactorial and cognitive decline is commonly associated with small ischemic/vascular lesions, often involving subcortical and strategically important brain areas (thalamus, frontobasal, limbic system). Pathophysiology affects neuronal networks involved in cognition, behavior, execution and memory. Vascular lesions often coexist with Alzheimer disease (AD) and other lesions, multiple pathologies greatly increasing the odds of dementia; 25-80% of demented subjects show both AD and cerebrovascular lesions. While both factors by synergistic interaction contribute significantly to the risk of dementia, AD pathology is often less severe in the presence of vascular lesions. Due to the heterogeneity of cerebrovascular pathology and its causative factors, no validated neuropathologic criteria for VaD are currently available, and a large variability across laboratories still exists in morphologic examination procedures and techniques. Harmonization of neuropathologic procedures and evaluation criteria in future prospective clinico-pathologic studies are needed to validate diagnostic criteria for VaD and to clarify the impact of vascular lesions on cognition.

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ADVANCES IN OUR UNDERSTANDING OF NEURODEGENERATION

Kurt A. Jellinger, Professor of Neurology and Neuropathology at
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Neurodegenerative diseases are characterized by progressive dysfunction and death of cells that frequently affect specific neural systems, implying some form of selective vulnerability. Morphologically, neuronal loss is associated with misfolding and aggregation of proteins leading to the relentless accumulation of abnormal extracellular and intracellular filamentous deposits in specific cell types (neurons and glial cells), representing the hallmarks of many neurodegenerative disorders, summarized as proteinopathies. A common feature of these conditions is a long run until sufficient protein accumulates, followed by a cascade of symptoms over many years with increasing disability leading to death. This provides a wide therapeutic window, especially in groups at risk identified early, and preclinical diagnosis becomes feasible. Neurodegenerative disorders have traditionally been defined as clinico-pathological entities; now they are classified either according to known genetic mechanisms or to the major components of their filamentous protein deposits. Although this has been a productive paradigm for the development of diagnostic consensus criteria, recent molecular biologic and genetic approaches have revealed that there are both overlap and intraindividual diversities between different phenotypes, related to synergistic mechanisms between the major pathologic proteins (β-amyloid, tau, α-synuclein), suggesting close relations between these disorders. The nature, time course, and molecular causes of cell degeneration and demise, the basic processes resulting in neurodegeneration, and the role of various factors in their pathogenesis are a matter of considerable debate, but recent studies have provided insight into the basic processes common to neurodegeneration and into cell death programs and their roles in this complex group of disorders, offering new ways for prohibition and treatment strategies.

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AGING RAT DENTATE GYRUS: AMYLOID RETENTION, INFLAMMATORY REACTION AND GLIOSIS IN RELATION TO REDUCED NEURAL STEM CELL ACTIVITY AND POORER WATER MAZE PERFORMANCE.

C. Johanson, M. Miller, K. Vasudevan, A. Messier, J. Donahue, G. Silverberg and E. Stopa.
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The dentate gyrus (dg), a key neurogenic zone near the csf, is vulnerable to the effects of aging. Neural stem cells in the dg are likely damaged by retained amyloid fragments (e.g., a-beta 40 and 42) with advancing age. We used brown-norway/fischer (b-n/f) rats (3, 12, 20, 30 months) to analyze the dg, and adjacent regions, for temporal and spatial immunostaining patterns of amyloid retention (linaris antibodies), gliosis (gfap and ox6) and neural stem cell activity (brdu and nestin). At 30 mo (but not 20) there was substantial injury to the csf system: lateral ventriculomegaly, structurally damaged atrophic choroid plexus, and focal denuding of the ependymal wall. At 3, 12/20 and 30 mo, respectively, there was mild, moderate and strong amyloid staining across cortex, hippocampus and dg. A-beta 40 positivity was mainly granular neuronal and vascular whereas a-beta 42 was especially strong in older hippocampal/dg neurons but substantially less at perivascular sites. Gfap increased significantly between 12 and 20 mo, whereas microglial ox6 immunostaining was markedly enhanced later, i.e., between 20 and 30 mo. In 3-mo rats brdu staining covered the entire dg, subventricular zone, ependyma and habenula. However brdu staining declined with age (12-20 mo) and was depleted in dg by 30 mo. Nestin immunostaining was present in certain sets of cells in the hippocampus and svz, peaking at 20 mo and then decreasing by 30 mo. The rats used for ihc were analyzed earlier in the morris water maze for working spatial memory. Thus, mean latency values (seconds to swim to submersed platform) during training trials were assessed across ages. Learning (cognitive) ability decreased with age ($p < 0.05$ for 3 v. 12 mo; 12 v. 20 mo; and 20 v. 30 mo). We think that during aging there are interrelated phenomena in the cns interior: altered expression of microvascular a-beta transporters, progressive amyloid retention in the dg & hippocampus, glial proliferation, functional destabilization of the choroid plexus-csf-ependyma nexus and reduction in neural stem cell activity. We postulate that these pathophysiologic factors lead to diminished cognitive ability. Supported by nih r01 ag027910 and by the richter and saunders funds.

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NEUROPATHOLOGY: THE BASIS FOR NEW TREATMENTS OF HUMAN SPINAL CORD INJURY.

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The changes which take place in the human spinal cord after injury are dynamic and continuous.At first there is edema swelling and haemorrhage followed by liquefaction and necrosis .Cytokines associated with the the inflammatory reaction cause aggravation of the damage with spreading necrosis Macrophages remove debris leading in a few weeks to a glial lined cavity into which nerve root regenerations will grow after some months Wallerian degeneration with extensive loss of axons becomes visible after about a year in the descending and ascending long tracts. Treatment in the initial stages is directed to reducing edema demyelination and secondary damage by administration of methyl prednisolone , 4-amino pyridine and the neutralisation of harmful cytokines The lesion is different in every patient and there is a variable amount of white matter preservation across the level of the injury in most .This residual white matter is exploited by the restorative neurologist to optimise the outcome.Regeneration of long tracts is necessary to restore function in the established case .This depends upon axonal re-growth which may be induced by trophic factors and / or inhibition of 'No-Go' using antibodies. Regenerated long axons need to reach their correct destination nucleus and function normally this will require re-education toward which the property of CNS plasticity may be utilised to restore normal physiology. This is a mammoth undertaking and currently beyond reasonable expectations as shown by recent reports of stem cell therapy.

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PERMEABILITY OF THE BLOOD-BRAIN BARRIER DEPENDS ON BRAIN TEMPERATURE: IMPLICATIONS FOR NORMAL BRAIN FUNCTIONS, NEUROPATHOLOGY, AND DRUG-INDUCED NEUROTOXICITY.

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Although increased permeability of the blood-brain barrier (bbb) has been reported in different physiological, pharmacological and pathological conditions that are accompanied by brain hyperthermia (i.e., environmental warming, stress, methamphetamine intoxication, opiate withdrawal), the role of brain temperature in modulating brain barrier functions remains unclear. To clarify this issue, we examined albumin and glial fibrillary acidic protein (gfap) immunoreactivity, ad morphological abnormalities of brain cells together with brain water and ion (na+, k+ and cl-) content in pentobarbital-anesthetized rats, which were passively warmed to different levels of brain temperature (32-42°c). Data were obtained for the cortex, hippocampus, thalamus and hypothalamus and compared with those obtained from drug-free awake rats with normal brain temperatures (36-37°c). We found that the number of albumin- and gfap-positive cells strongly correlates with brain temperature, gradually increasing from ~38.5°c and plateauing at 41-42°c. Brains maintained at hyperthermia also showed larger content of brain water and na+, k+ and cl- as well as structural abnormalities of brain cells, all suggesting acute brain edema. The latter alterations were seen at ~39°c, gradually progressed with further temperature increase, and peaked at maximum hyperthermia. Temperature-dependent changes in albumin tightly correlated with gfap, brain water and numbers of abnormal cells, were evident in each tested area, but showed some structural specificity. Notably, a mild bbb leakage, selective glial activation and specific cellular abnormalities were also found in the hypothalamus and piriform cortex during extreme hypothermia (32-33°c); in contrast to hyperthermia these changes were associated with decreased levels of brain water, na+ and k+, suggesting acute brain dehydration. Therefore, brain temperature is an important factor in regulating bbb permeability, alterations in brain water homeostasis, and subsequent structural abnormalities of brain cells.

Key words: hyperthermia, hypothermia, brain edema, brain pathology, albumin, brain water, neuronal damage, glia, endothelial cells

abstracts

NEUROTROPHIC-LIKE ACTING PEPTIDES AS TREATMENT-OPTION IN DEPRESSION?

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Since depression is rated one of he world's foremost disorders in human suffering and as economic burden and since the effectiveness of present therapies is only average, the search for new therapeutic approaches is legitimate. The current aetiological model of depression favours the monoamine-hypothesis, as reflected in psychopharmacological treatment. As was demonstrated by various groups, depression acts like a prolonged stressor thus causing a chronic stress-response of the hpa (hypothalamic-pituitary-adrenal) –axis resulting in hypercortisolism, which in turn by excitotoxicty acts deleteriously on neurons involved in depression. This leads to disruption of neuronal networks i.e. Functional systems of the brain, comprising the subgenual prefrontal cortex (pfc), orbital, dorso-antero-lateral pfc, amygdala, basal ganglia and dorsal raphe nuclei and certain hippocampal neurons. Neurotrophic factors (nf), among them bdnf (brain derived nf) counteract some of the effects of excitotoxicty in the neurons, thus exerting neuroprotective (and neutrotrophic) influence. Although these properties are of considerable interest in various brain- disorders e.g. Trauma, dementia, stroke etc., the limiting factor for treatment with these proteins is their molecular size, preventing passage through the blood-brain barrier. Small peptide molecules can permeate this filter and demonstrated neuroprotective and neutrotrophic properties similar to nfs. Therefore, in the context of depression, treatment with peptide molecules could prove a promising approach. For humans treatment with peptides may carry the risk of allergic reaction or other intolerance phenomena, so that a compound which has been successfully applied for years for the indication of brain-disorder e.g.trauma, dementia and stroke and which in preclinical studies proved neurotrophic, neuroprotective, even neurogenetic should be preferred. Therefore a feasibility study of neurotrophic factors in treatment of depressive disorders should be considered.

abstracts

DEPRESSION AND DEMENTIA

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Depression and cognitive impairment are both common conditions in old age, and frequently occur together. However, accurate figures are not available. The inter-relationship between the two is still not well understood. Clearly depression can be a reaction to cognitive decline, and also appear as an early symptom in dementing individuals. However, recent data suggest that depression can be a risk factor for Alzheimer disease (AD).

The relationship between the two clinical entities should be seen in view of observations of white matter changes both in AD and in depression. Since these are thought to represent vascular changes, the concept of "vascular depression" has been advanced. Neurotransmitter loss may occur in both, particularly cholinergic loss which is characteristic of AD but may occur also in depression. The same is true for hippocampal atrophy, which has been described in depression.

The relationship of stress in depressed people will be discussed in relation to the development of degenerative brain changes.

The effects of antidepressants on the incidence of cognitive decline in depressed individuals are still unknown, but should be an important target for research

abstracts

AXONAL DEGENERATION AND PREREQUISITES FOR RECOVERY

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Axonal degeneration is a consequence of loss of continuity, which sets in motion a cascade of processes that lead to disintegration of the nerve fiber, so called wallerian degeneration, and causes denervation and loss of function of end-organs. The long term clinical deficits depend on the severity and extent of the lesion. Peripheral axons have the capacity to regenerate and reinnervate end-organs but the recovery of function is dependent on a number of factors that may determine the outgrowth of fibers from the proximal nerve stump, the reconnection of appropriate regions of the central nervous system and the target organ and the physiological properties of the nerve fiber during maturation. For example inappropriate reinnervation of muscle fibers may lead to loss of control of movement; similarly reinnervation of sensory organs by inappropriate sensory fibers can lead to pain and loss of ability to localize the stimulus. Recovery of function in spite of such inappropriate connections may occur if plasticity of the central nervous system can compensate for aberrant reinnervation, and it is possible that such plasticity can be enhanced by proper functional training. It is likely that different factors localized to the neuronal cell body and proximal nerve stump, to the distal denervated segment of the degenerated nerve, to the denervated end-organ and to the central nervous system all are needed to attain proper reinnervation and recovery. It is the aim to discuss the different processes and structures that are involved in regeneration and how some of these questions can be addressed by electrophysiological and functional methods.

abstracts

NANOPARTICLES AS CARRIERS FOR DRUG TRANSPORT ACROSS THE BLOOD-BRAIN BARRIER

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The blood-brain barrier (bbb) represents an insurmountable obstacle for the delivery of a large number of drugs to the central nervous system (cns). One of the possibilities to overcome this barrier is drug delivery to the brain using nanoparticles. Drugs that have been transported into the brain and led to a pharmacological effect after intravenous injection using this carrier include the hexapeptide dalargin, the dipeptide kyotorphin, loperamide, tubocurarine, doxorubicin, and the nmda receptor antagonists mrz 2/576 and mrz 2/596. To achieve a significant transport across the blood-brain barrier the coating of the nanoparticles with polysorbate 80 (tween® 80) was a key factor.

Experiments with the extremely aggressive glioblastoma 101/8 transplanted intracranially showed a long term survival for 6 months of up to 40 % of the rats after intravenous injection of the polysorbate 80-coated nanoparticle preparation. The surviving animals showed a total remission by histological investigation. Untreated controls died within 10 - 20 days, the animals in the doxorubicin control and uncoated doxorubicin nanoparticle groups died between 10 – 50 days.

The mechanism of the drug transport across the blood-brain barrier with the nanoparticles appears to be endocytotic uptake by the brain capillary endothelial cells followed either by release of the drugs in these cells and diffusion into the brain or by transcytosis. After injection of the nanoparticles, apolipoproteins a-i or e adsorb on the particles surface promoting the interaction with receptors on the endothelial cells followed by endocytotis and thus would the uptake of naturally occurring lipoprotein particles. This hypothesis was supported by the achievement of a antinociceptive effect with loperamide-loaded albumin nanoparticles with covalently bound apo e and electron microscopy.

abstracts

EFFECTS OF VEGF DELIVERY BY ENCAPSULATED CELLS IN STRIATUM

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VEGF is the key angiogenic factor also playing a central role in neuroprotection, neurogenesis, neurorescue and neuroregeneration.

Many CNS diseases might benefit from its therapeutic use although the passage of the BBB possess a major problem when searching an accurate administration way. In our present work we have tested a novel method consisting on the intrastriatal implantation of VEGF-producing encapsulated cells.

We implanted alginate-poly-L-lysine-alginate microcapsules containing immobilized Fischer rat 3T3 fibroblasts transfected to produce VEGF in vitro into the striatum of rats previously lesioned with 6-hydroxydopamine (6-OHDA).

Microencapsulated VEGF secreting cells were stable for at least 3 weeks in vitro. Intrastriatal implantation of microencapsulated VEGF secreting cells into 6-OHDA lesioned rats caused a well tolerated lesion with minimal tisular reaction and mild brain edema. However no decrease was observed in apomorphine-induced rotations compared to values prior to implantation as well as to values obtained from the empty microcapsule implanted animals at each time point. In addition, no changes in the levels of tyrosine hydroxylase immunoreactivity were detected in the striatum.

One month after implantation, immunohistochemical detection of VEGF revealed strong immunoreactivity in the striatal tissue surrounding the microcapsules with parallel absence of tissue damage due to microcapsules implantation.

In summary, the implantation of microencapsulated VEGF secreting cells into the striatum induces a statiscally significant increase of microvascular density but no a substancial detectable behavioral improvement was observed, suggesting that other locations into the CNS for cell implantation should be explored.

abstracts

ENDOGENOUS NEURAL STEM CELLS AS A TREATMENT OPTION FOR STROKE

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Stem cells have long been considered in the treatment of stroke. Cell based strategies include transplantation of embryonic, neural or non-neural cells or manipulation of the endogenous pool of neural stem cells in order to improve outcome in the acute or chronic phases after stroke. This talk will focus on the recent basic and clinical developments in targeting the endogenous stem cell pools to induce angiogenesis and neurogenesis showing electrophysiological evidence for the integration of newborn cells into the existing circuitry. Combined with a careful clinical development program these novel strategies may bare fruit in the very near future and provide clinicians with novel strategies to combat stroke.

abstracts

HIPPOCAMPUS, STRESS AND NEURODEGENERATION: DELINEATING A NOVEL PEPTIDE SYSTEM THAT AFFECTS HIPPOCAMPAL MORPHOLOGY

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Dysfunction of the hippocampus has been linked to a number of mood and neuro-degenerative disorders. However, it is unclear what the mechanisms are that induce these effects, and may involve a number of effectors depending upon the nature of the stressor. Among these effectors, hormones of the hypothalamic-pituitary adrenal axis such as the glucocorticoids and corticotropin-releasing factor (CRF), have received considerable attention. Recently, a new peptide family, the teneurin C-terminal associated peptides (TCAP), was identified on the basis of its structural similarity to the CRF family of peptides. There are four TCAP peptides, each associated with one of the four teneurin genes. Despite TCAP's sequence similarity to CRF family members, these peptides do not activate or interfere with the normal binding of CRF family members to the CRF-R_1 and CRF-R_2 receptors. Two of the TCAP peptides, TCAP-1 and TCAP-3 are independently transcribed, but do not appear to possess a recognizable signal peptide. Thus, like other neurotrophic peptides such as ciliary neurotrophic factor (CNTF), they may be released from the cell during necrotic or apoptotic death, thereby providing both a warning and neuroprotective signal for the surrounding cells. The gene for TCAP-1 is particularly highly expressed in all major cell groups of the hippocampus as well as closely associated brain nuclei such as the amygdala, piriform cortex and bed nucleus of the stria terminalis. *In vitro*, synthetic TCAP-1 modulates neurite outgrowth and induces axon fasciculation of primary cultures of embryonic rat hippocampal cells. In *in vivo* studies, synthetic TCAP-1 dramatically reduces the CRF-induced *c-fos* expression in all major cell groups of the hippocampus. Moreover, intracerebroventricular administration of TCAP-1 modifies dendritic outgrowth of CA3 neurons, and ablates the dendritic effects of restraint stress in these neurons. These studies indicate that the TCAP family of peptides may act in part to regulate the normal morphology of the hippocampus during periods of stress.

abstracts

DELAYED TREATMENT WITH A P53 INHIBITOR ENHANCES RECOVERY IN STROKE BRAIN

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Objective: Cerebral ischemia can activate endogenous reparative processes, such as proliferation of endogenous neural progenitor cells (NPCs) in the subventricular zone (SVZ). Most of these new cells die shortly after injury. The purpose of this study was to examine a novel strategy for treatment of stroke at one week after injury by enhancing the survival of ischemia-induced endogenous NPCs in SVZ.

Methods: Adult rats were subjected to a 90-min middle cerebral artery occlusion (MCAo). A p53 inhibitor pifithrin-α (PFT-α) was administrated to stroke rats from days 6 to 9 after MCAo. Locomotor behavior was measured using an infra-red activity chamber. Proliferation, survival, migration, and differentiation of endogenous NPCs were examined using RTPCR, TUNEL, and immunohistochemistry.

Results: PFT-α enhanced the functional recovery as assessed by a significant increase in multiple behavioral measurements. Delayed PFT-α treatment had no effect on the cell death process in the lesioned cortical region. However, it enhanced the survival of SVZ progenitor cells and promoted their proliferation and migration. PFT-α inhibited the expression of a p53-dependent pro-apoptotic gene, termed PUMA (p53-upregulated modulator of apoptosis), within the SVZ of stroke animals. The enhancement of survival/proliferation of NPCs was further found in SVZ neurospheres in tissue culture. PFT-α dose-dependently increased the number and size of new neurosphere formation.

Interpretation: Delayed treatment with a p53 inhibitor PFT-α is able to modify stroke-induced endogenous neurogenesis and improve the functional recovery in stroke animals.

abstracts

PHARMACORESISTANCE IN EPILEPSY: WHAT PROSPECT FOR GAP JUNCTION-RELATED PHARMACOTHERAPY?

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About one third of epileptic patients have seizures not satisfactorily controlled with the existing antiepileptic drugs (aeds), in spite of the introduction in the last fifteen years of eleven new-generation aeds. Two popular hypotheses on the mechanisms of drug resistance in epilepsy respectively highlight the increased activity of blood-brain barrier multidrug transporter proteins and the alterations in aeds targets rendering them drug-insensitive. Both mechanisms are relevant, but insufficient to account for the complexity of brain changes involved in drug-resistant epilepsy. Recent studies on brain tissue from drug resistant epileptic patients and animal models revealed the involvement of several types of neuroplasticity phenomena, including inflammation processes, functional glial changes and altered gap junction (gj) intercellular communication. These provide additional, albeit not exhaustive examples of targets to consider for future aeds that might overcome drug resistance.

The gjs provide promising antiepileptic targets since i) the structure of their molecular components (essentially the connexins), their distribution in the brain and their supramolecular organisation are largely described, and ii) multiple pathways to pharmacologically modulate intercellular gj communication are identified, acting upon either connexin turnover or the conductance of gj channels. The in principle "drugability" of this putative novel type of antiepileptic target is supported by the fact that some endogenous mediators and several clinically used drugs actually modulate gj communication. A major current hindrance relates, however, to the presence and roles outside the brain of the same connexins that appear as candidate antiepileptic targets.

abstracts

INTERFACING MAMMALIAN CELLS WITH VERTICAL ARRAYS OF INORGANIC NANOWIRES FOR BIOSENSING

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It is of great interest for fundamental cell biology and for the development of improved cell-based drug screening assays, to gain spatial and temporal information on intracellular processes of single cells. To achieve this it is required to place a probe directly in the interior of living cells, which presents several challenges due to their micron size and complexity of the cytoplasm and the cell membrane.

Nanotechnology offers the possibility of fabricating one-dimensional nanostructures of various materials, which have recently been shown to be able to penetrate the cell membrane without causing significant damage [1]. The small diameter of the nanowires allows them to cross the lipid bilayer of the cell membrane without causing significant damage, which makes them attractive as a tool for gaining access to the intracellular environment. Moreover, the number of nanowires per cell can be controlled and they can be brought to penetrate cells simply by depositing a cell suspension on top of the array.
The interface of living HEK 293 mammalian cells with vertically aligned nanowires will be presented. The results include cross-section images of living cells with embedded NWs and scanning electron micrographs providing information on the interaction between NWs and cells.

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abstracts

DEEP BRAIN STIMULATION FOR VARIOUS DISORDERS

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On the basis of our clinical experience with Deep Brain Stimulation for a variety of disorders which we have gained since 1999 in nearly 500 patients, indications, contraindications and results will be elucidated as well as further directions of DBS research will be highlighted.

VALIDATION OF QUALITY OF LIFE QUESTIONNAIRES FOR MULTIPLE SCLEROSIS AND COGNITIVE IMPAIRMENT QUESTIONNAIRE – MSQOL-54, MSIS-29 AND MSNSQ IN THE BULGARIAN PATIENTS WITH MULTIPLE SCLEROSIS.

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Recent studies in the field of quality of life give better knowledge for the health status and care-giving in patients with multiple sclerosis (ms). On the basis of the most common used questionnaire for social functioning (sf-36) were created and adapted specific instruments to assess quality of life in patients with multiple sclerosis – msqol-54 and msis-29. In ms patients the estimation of cognitive function became of great importance as well in the last few years. The investigation of the cognitive abilities and their affection take enormous place as a part of the well-being of the patient. This method seems to be more sensitive than the functional imaging. The questionnaire with high sensitivity for detection of such impairments is the neuropsychological test in ms patients.

The main aim of this research is to research the opportunity to use these three methods for most truthful information about the health status and well-being of the patients. For the first time questionnaires for quality of life and test for cognitive dysfunction were used with bulgarian ms patients. Relations among the results from the tests were investigated too. Thirty-six ms patients with relapsing-remitting ms were interviewed two times for a month.

All included patients fulfilled the questionnaires in one and the same conditions and were asked to do this again after one month for msqol-54, and after two weeks for the other two questionnaires. The internal consistency, reliability and psychometric coefficients of the questionnaires were explored.

The results showed very high reliability and that was applicable for the bulgarian population for all the instruments: msqol-54, msis-29 and for the neuropsychological test. These three methods can be used in the everyday practice, as well as in clinical trials for additional information for the well-being and quality of life of the patients. The long-term effect of the treatment can be evaluated as well.

Key word: quality of life, multiple sclerosis, health status, neuropsychological questionnaire, effectiveness, msis-29, msqol-54, msnsq, reliability, psychometric coefficients.

abstracts

ABNORMAL MOTOR AXON FUNCTION IN NERVES DEFICIENT OF THE MYELIN PROTEIN P0 AS A POSSIBLE TARGET FOR NEUROPROTECTIVE STRATEGIES

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Mice expressing half of the normal dose of protein zero (P0+/- mice) have almost normal myelin during the first months of life and later develop a slowly progressing demyelinating neuropathy resembling human Charcot-Marie-Tooth type 1B neuropathy. In contrast, mice completely deficient of P0 (P0-/- mice) display a compromised myelin compaction and axonal loss from birth. The mechanism of axonal loss in P0 mutant mice is poorly understood.

Recent immunohistochemical studies suggested that myelin dysfunction in P0 mutant mice is associated with abnormal function and disposition of ion channels at the nodes of Ranvier. The aim of this study was to investigate the peripheral nerve excitability of P0-deficient mice by "threshold-tracking", which is an electrophysiological method that can offer clues about the nodal and internodal membrane function of peripheral nerves in vivo.

Excitability and conduction studies were carried out under anesthesia in 2-10 months P0-deficient mutant mice. Tibial nerves were stimulated at the ankle and the evoked motor responses were recorded from the plantar muscles using subcutaneous needle electrodes.

P0-/- mice revealed marked abnormalities in both conduction and excitability studies. Motor responses were at least 200% delayed and had amplitudes below 10%. Accommodation appeared remarkably increased during depolarizing threshold electrotonus. Accommodation during hyperpolarizing threshold electrotonus was decreased. The recovery cycle appeared shifted upwards with increased refractoriness at the expense of the superexcitable period that normally follows a single impulse.

During the investigated time-frame, conduction studies in P0+/- mice remained undistinguishable from controls. Nevertheless, both the nodal (refractoriness) and internodal (accommodation) excitability measures were abnormal. Deviations were largely similar to those observed in P0-/-, albeit of a lower magnitude. The only notable exception was the accommodation to depolarization that appeared unaffected, in contrast with the findings in P0-/- mice.

Our data suggest that in a mouse model of a demyelinating polyneuropathy, both the nodal and internodal membrane function of peripheral axons is abnormal, depending on the P0 expression levels. In P0 -/- mice, the paradoxical threshold increase during depolarization and the shifted recovery cycle were aggravated by cooling, consistent with the effect of ectopic nodal expression of Nav1.8 on motor axons. It is possible that Na+ overload occurring during electrical activity could precipitate axonal degeneration in P0 mutants.

abstracts

WHAT INTERNET SEARCH ENGINES RESULTS TEACH SELF-DETERMINING PATIENTS ABOUT NEUROPROTECTION AND NEUROPLASTICITY

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Overview: Studies indicate that Internet search engines (ISEs) are most often used to find information about medical diagnoses, treatment, and providers. This exploratory research addresses Internet information about neuroplasticity and neuroprotection that patients can freely access before, between, or after clinical visits. Other studies suggest that what they find in cyberspace influences demand for prescribed products and services as well as the provider-patient relationship. Consumers primarily ask physicians to consider switching to another approved medication or treatment and may not be adding new information for consideration.

Problem Statement: The dynamic Internet is largely unregulated and ISEs accept no responsibility for content quality. In fact, their underlying algorithms skew results towards ones positioned by popularity, direct advertising, and search engine optimization schemes. Hence, from search terms chosen, patients can locate misleading information, claims without clinical context, or unsuitable products and treatments. What information confronts self-directed neurological patients looking for answers about neuroplasticity and neuroprotection, possibly a new concept for them? Is it found amidst potentially influential contextual advertisements? Are treatments located by ISEs really new, and, if so, can new information benefit current treatment?

Methods: Patient Internet search behavior was simulated by entering "neuroprotection" and "neuroplasticity" into the Google search engine, the world's most popular engine. Terms were then modified to measure variation from single term results. Thirty search engine results from 18 queries were analyzed categorically to assess the range and frequencies of information providers, communication focus, and website idiosyncrasies. In addition, search result contexts were analyzed according to the placement of peripheral advertisements triggered by search terms used. Logistic regression and univariate methods were used.

Results: Patients seeking information regarding neuroplasticity and neuroprotection find information from a variety of sources intended for medical, general, student, or patient-advocate audiences. Media content analysis of 540 websites indicated significant differences between result profiles for search terms "neuroplasticity" (T1) and "neuroprotection" (T2) in the intended audience, the media form and content, and the presence of peripheral advertisements ($p<.05$). T1 results included 4 medically-related websites (13.3%) and T2 had 18 (60%). T1 yielded 4.5 solicitations for each medically-related website result and T2, 1 advertisement per 9 similar results. Adding the search term "treatment" eliminated peripheral advertisements in all cases, while including symptom or diagnostic terms resulted in websites ranging from 57-70% advertisements for products and services. Wikipedia was the top search engine result source in 8 of 18 searches (44.4%).

(continued next page)

abstracts

WHAT INTERNET SEARCH ENGINES RESULTS TEACH SELF-DETERMINING PATIENTS ABOUT NEUROPROTECTION AND NEUROPLASTICITY

David W. Mulholland, Faculty, University of British Columbia, Vancouver, Canada,
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When "Cerebrolysin" was added to English keyword searches for "neuroplasticity drugs" and "neuroprotective drugs" using Google, there were no overlaps among the first 20 ISE results. Although the keyword alone yields a higher percentage of medical research and provider information than top AD drugs, consumers are more likely to find dubious information from Wikipedia or advertisements than scientifically solid information about treatment options and little to no information about emerging treatments from within or outside the United States.

Implications: Medical providers, organizations, or advocates may help consumers by directing them towards specific websites with leading information about neuroplasticity and neuroprotection. ISE results alone provide little information to consumers for discerning appropriate or robust information among websites among which they will venture. Since consumers often search for alternate and untried treatments, patients are not likely to find desired information. More research is needed to determine the impact of provider website attitudes, utilization, and guidance on provider-patient relationships, compliance, and self-determination. Additional research is needed to understand safe, effective, and reliable methods for health care professionals, allied service providers, and drug and equipment manufacturers to inform consumers of treatment options. Finally, health-related keyword research is needed to understand how healthcare professionals can increase potentially helpful information results and reduce extraneous, potentially harmful, or illegal websites from dominating consumer queries in Cyberspace.

abstracts

QUANTUM REALITY AND NEUROSCIENCES

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Physics and neurosciences had somehow a common destiny but neurosciences were always running behind. Classic physics held that physical world is constituted of infinitesimal particles in a sea of space.

Einstein, building on the ideas of Maxwell, made classic physics into what is called a **local theory**: there is not action at a distance, all influences are transmitted by contact interaction between tiny neighbouring mathematically described "entities" and no influence propagates faster than the speed of light.

This mechanistic view – stimulus in, behavior out – evolved into contemporary neurobiological models of how the brain works: neurotransmitters in, behavior, thoughts or emotions out.

These models are useful to a certain point. This presentation aims to highlight the limitations of classic models of neurobiological action and to draw attention that new principles of quantum physics contradict the older ideas that local mechanical processes alone can account for the complex categories as: feeling, knowing, effort, moral judgment.

This new paradigm is able to cover the core phenomena of self-directed neuroplasticity.

abstracts

NEUROTROPHIC FACTORS – FROM BED TO BENCH IN DEMENTIA TREATMENT; A SHORT OVERVIEW OF SOME ORIGINAL DATA

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Every lesion in the nervous system triggers after a certain latency period an endogenous neuroprotective reaction. An endogenous repair process, known as neuroplasticity follows this as a second answer. These two processes are initiated and regulated by neurotrophic factors.

Neuroprotection and neuroplasticity, processes that are apparently independent, with different control, represent in fact two sequences of the same process.

The therapeutical efficacy of trophic factors in AD clinical trials was well demonstrated.
This presentation will highlight the results of a long cycle of experimental studies proving the therapeutical mechanisms of trophic factors in AD.

In this respect beside antiexcitotoxic, antioxidant, a direct strong antiamyloid effect was demonstrated.

A constant imbalance of neurogenesis in animal models of Alzheimer's disease was also described.

Our results strongly suggested that this feature is determined by neurotrophic factors disregulation.

Therefore, today, we are able to have a complete picture on trophic factors therapeutical mechanisms in AD.

abstracts

TIMING OF EPILEPSY SURGERY

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The majority of epilepsy patients respond well to antiepileptic drug therapy (1). About 10% remains drug resistant. Langfitt and wiebe (2) give a interesting overview of the risks of persistent seizures , such as:

1. Mortality. Higher mortality rates are observed among more severely affected populations (2). Standardized mortality ratios range from 1.6 to 3.2
2. Cognitive decline. Patients suffering from temporal lobe epilepsy have verbal memory decline in 29%.
3. Morbidity. Persistent seizures may cause considerable morbidity due to falls, burns etc. Antiepileptic drugs may have severe side effects as dizziness, nausea, increased or decreased appetite, hormonal dysfunction etc.
4. Quality of life. Quality of life may be decreased due to dependence on parents, friends etc.

Refractoriness may occur when two first line antiepileptic drug trials have failed (3). Besides ketogenic diet and vagal nerve stimulation, epilepsy surgery is an important option. Efficacy is impressive: in a randomized controlled trial (4) 68% of operated patients were seizure free after one year compared to 8% of medically treated patients.

Adequate timing of surgery is complicated. In pediatric patients, ongoing epilepsy may deteriorate in encephalopathic epilepsy, blocking development. Early operations may enhance plasticity. In early hemispherectomies (below the age of 4 years), post operative hemiparesis decreases in one year to pre-operative functioning (5). However, the emergence of the “new antiepileptic drugs” (lamotrigine, topiramate, levetiracetam, zonisamide) may offer new opportunities to become seizure free (6). This is an important issue as epilepsy surgery may cause postoperative deficits like dysphasia, visual field defects and memory decline (7).

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abstracts

THE ROLE OF THE SOMATOTROPHIC AXIS IN NEUROPROTECTION AND NEUROREGENERATION OF THE ADDICTIVE BRAIN

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During the past decades an increasing number of studies has shown (1,2) that growth hormone (gh) and its mediator insulin-like growth factor-i (igf-1) may exert profound effects on the central nervous system (cns). Gh replacement therapy has been shown to improve psychological capabilities and thereby increase life quality in patients deficient in this hormone. Beneficial effects of gh on certain functions, including memory, mental alertness, and working capacity, have been reported. In children with gh deficiency (ghd) significant improvements have been observed in many behavioral disabilities connected with their disorder. In experimental animals both gh and igf-1 were seen to produce enhancement regarding their memory and cognitive function (1,2). The mechanism underlying these effects seemed to involve glutamate transmission through the nmda receptor complex (3,4). Earlier studies have shown that chronic opiates and even alcoholism may inhibit cell growth and trigger apoptosis, which leads to impaired cognitive capabilities in both humans and other mammals. In recent work we have demonstrated that gh may reverse opiate-induced apoptosis in cells derived from prenatal mouse hippocampus. Primary hippocampal cell cultures derived from fetal mouse neurons were treated with morphine during growth in the absence or presence of recombinant human gh. We found that morphine decreased the cell content in a concentration-dependent manner and increased markers of apoptosis such as lactate dehydrogenase and caspase-3 activity, whereas gh counteracted these effects (5). Also, memory deficiency induced in rats by alcohol infusion was reversible by gh. These findings suggest that the hormone is capable of preventing or even repairing drug-induced damage to hippocampal cells and thereby restore cognition and memory function.

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abstracts

UNRAVELLING THE MOLECULAR AND CELLULAR ROUTES OF WATER ENTRY IN BRAIN DURING BRAIN EDEMA FORMATION

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While the process of brain edema formation has been studied extensively at the macroscopic level, little is known about water fluxes and volume changes at the cellular level in the initial phase of brain edema. This void of knowledge has hampered the development of efficient therapy for this condition. We employed optical imaging in living mice to record volume changes in individual gfp-labelled neocortical cells following induction of hypo-osmotic stress. Individual astrocytes were found to undergo a position-dependent increase in cell volume by a factor of two or more during edema formation. Neuronal compartments largely retained their original volume. Our data are the first to show that volume changes can be monitored at the cellular level in vivo and demonstrate that astrocytes are sites of water entry in the initial phase of brain edema formation. The uptake of water in astrocytes is likely to reflect the strong expression of aquaporin-4 in the perivascular endfeet of these cells. Thus, previous studies have shown that edema formation is blunted by selective deletion of the perivascular pool of aqp4. Insight in the cellular and molecular processes underlying water accumulation in brain could pave the way for more efficient prevention and therapy.

abstracts

TRYPTOPHAN - KYNURENINE METABOLISM AS A TARGET FOR NEUROPROTECTIVE INTERVENTION

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Tryptophan (try), the rarest of essential amino acids, is an initial substrate for non-protein metabolic pathways: try– methoxyindoles (serotonin, n-acetylserotonin and melatonin) and try–kynurenine (kyn). Kyn, in its turn, is metabolized along two competitive routes: kyn–kynurenic acid (kyna) and kyn–nicotinamide adenine dinucleotide (nad). Try is converted to nad in microglia while try metabolism in astrocytes is limited to kyn–kyna pathway and in vascular endothelium to kyn production. Prof. I.p. Lapin pioneered the studies of neuroactivity of kynurenines in 1969. Kynurenines are neurotoxic, mainly due to stimulation of n-methyl-d-aspartate (nmda) receptors; activation of inducible nitric oxide synthase and generation of free radicals. Kyna might impair cognition due to its antagonism to alpha 7-nicotinic acetylcholine receptors although it might be neuroprotective due to antagonism to nmda receptors. Upregulation of the rate-limiting enzyme of try–kyn pathway, indoleamine 2,3-dioxygenase (ido), and dysbalance between kyn–nad and kyn–kyna pathways might contribute to neuronal damage in major depressive disorder, schizophrenia, vascular and alzheimer's type dementias, huntington's disease, cerebral malaria and in psychiatric complications of interferone-alpha therapy. Ido is transcriptionally induced by proinflammatory cytokines: interferon-gamma (ifng) and tumor necrosis factor (tnf)-alpha. Ifng (+874) (t/a) and tnf-alpha (-308) (a/g) genes influencing cytokines production are polymorphic. Therefore, combination of high producer alleles (t for ifng and a for tnf-alpha) might identify individuals predisposed to superinduction of ido and, consequently, to severe neuronal damage. Ido and key enzymes of post-kyn metabolism might be the new targets for neuroprotective intervention.

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CARBON NANOTUBES AS MODULATORS OF NEURONAL GROWTH

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Neurons communicate with each other by forming synapses. The extension of a growth cone of immature neurons controls the pattern of synapse formation. Additionally, in a mature neuron, following the injury, growth cone plays a role in neurite regeneration. We are attempting to define whether carbon nanotubes (CNTs) could be used as prosthetics devices in the process of neuronal regeneration after injury. Towards that end we are investigating neuronal growth on multi-walled nanotubes (MWNTs). Neuronal growth was systematically controlled by modified MWNTs, prepared by covalently conjugating CNTs with functionalities designed to carry negative, neutral or positive charges at physiological extracellular pH. By using these CNTs as the scaffold for neuronal growth, it was found that the neurons grown on positively charged MWNTs showed more numerous growth cones, longer neurite outgrowth and more successful neurite branching than the neurons grown on negatively charged CNTs.

Similarly, we prepared chemically-functionalized water soluble single-walled carbon nanotube (SWNT) graft copolymers for modulation of outgrowth of neuronal processes. The graft copolymers were prepared by the functionalization of SWNTs with poly-*m*-aminobenzene sulphonic acid and poly-ethylene glycol (SWNT-PEG). When added to the culturing medium, these functionalized water soluble SWNTs were able to increase the length of various neuronal processes. Since SWNT-PEG were able to block stimulated membrane endocytosis as well as influx of Ca^{2+} in neurons, such actions could then explain the extended neurite length.

By spraying a film of SWNT-PEG onto hot glass coverslips we created retainable conductive substrates with which we could culture neurons. We could specifically control the conductivity of the substrate by varying the thickness of the nanotube film. This allowed us to determine how the growth of neurons is affected at different levels of conductivity. We show that conductive nanotubes are biocompatible as substrates for neuronal growth and that the specific level of conductivity is important as it affects neuronal growth and neurite outgrowth. Further studies with conductive substrates should pay attention to the resistance of the substrate and in applications where changes in neuronal growth are unwanted high conductivity should be sought in materials.

Taken together these studies demonstrate that CNTs can be used as a scaffold/ substrate for neuronal growth and that modifications of the CNTs can be employed to modulate the arborization of neuronal processes and their outgrowth. This suggests that in the future, it may be possible to employ suitably functionalized CNTs as neural prostheses in neurite regeneration.

abstracts

PRESENILIN-MEDIATED SIGNAL TRANSDUCTION – RELEVANCE TO ALZHEIMER'S DISEASE PATHOGENESIS

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Both cell death and loss of synapses account for the clinical manifestations of Alzheimer's disease (AD). Based on genetic and epidemiological data, AD is classified as either sporadic or familial. Mutated presenilins may cause familial AD by altering neuronal signal transduction pathways, by increasing beta-amyloid production and by triggering a number of pro-apoptotic mechanisms. Presenilin is part of the gamma-secretase complex, which executes the final proteolytical cut of amyloid precursor protein to yield beta-amyloid, and the activity of gamma-secretase is maintened during apoptosis. Presenilin proteins are capable of modulating various cell signal transduction pathways, the most extensively studied of which has been intracellular calcium signalling. AD-linked mutated presenilins can potentiate inositol(1,4,5)trisphosphate (InsP3) mediated endoplasmic reticulum release of calcium from this organelle. A recently described function of presenilins involves regulation of acetylcholine muscarinic receptor-stimulated phospholipase C upstream of InsP3 regulated calcium release. Moreover, presenilins regulate extracellular regulated kinase (Erk) activity by a protein kinase C alpha dependent mechanism. In conclusion, presenilins regulates both cholinergic signal transduction pathways and apoptotic cell death and presenilin mutations are responsible for both sensitizing neurons to death and altering neuronal signal transduction.

abstracts

EFFECT OF ACTIVE, PASSIVE AND FUNCTIONAL ELECTRICAL STIMULATION ON REORGANIZATION OF HAND MOTOR AREA IN PATIENTS WITH STROKE AND HEALTHY VOLUNTEERS: A TRANSCRANIAL MAGNETIC STIMULATION STUDY

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Background: Recovery of motor function after stroke represents a complex process with many mechanisms still obscure that depends on the integrity of cortical projection, on the amount of the normal surrounding cortical areas and the efficiency of the contra-lateral connections with motor system.
Aim Of The Study: to study the effect of the active and passive movements on the motor area, using transcranian magnetic stimulation (TMS).
Matherial & Methods: The study has been done in patients with unilateral recent stroke (first three months), and healthy volunteers. Using the TMS, we first detect motor "hot spot" and than measured the motor threshold and mapped the motor area on the affected side before and 30 minute after an active movement task, functional electrical stimulation or passive movements. For active movements we use a force tracking system
Results: The active movement induces an increase of cortical excitability (i.e. decrease motor threshold) and an extension of motor projection area; in functional electrical stimulation group there is an improvement of motor parameters but less evident in comparison with active movement group; in passive movement group there is no significant modification on motor parameters.
Conclusion: These modifications sustain the importance of active movement in motor recovery. The functional electrical stimulation and passive movement even that did not induce significant cortical modification in patients with severe motor deficits; they have a beneficial role in maintaining the sensory stimulation of parietal cortex as a part of sensory-motor area.

abstracts

SEEING GENE THERAPY TO EMERGE FROM TRIALS TO PRODUCTS

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As gene therapy has matured from clinical trials to the first commercial products, understanding of the mechanisms of gene delivery has increased tremendously. This has also been reflected in viral vector development, creating a number of new approaches to tackle issues in transduction efficiency, biodistribution and viral safety. One of important issues has been the viral biodistribution and development of non-invasive imaging modalities such as MRI, SPECT and PET for the use of gene therapy. These clinically relevant imaging systems have been used to monitor viral transgene expression, but they can be used to monitor viral particle biodistribution, as shown here with examples by SPECT and MRI imaging, or combination of both. While there is ongoing development of gene therapy vectors for new diseases, the first phase III trials in Western world are near completion, hopefully bringing the first products to market. The gene therapy products currently available or near market approval, based on p53 expression (Gendicine™ and Advexin™), conditionally replicative adenoviruses (Oncorine™) and thymidine kinase + ganciclovir therapy (Cerepro®), are introduced with emphasis on the molecular mechanisms of action.

abstracts

THE HISTORY OF MAO AND MAO-I'S

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Already in 1877 Schmiedeberg discovered the mechanism of "oxidative desamination" but the terminus technicus of monoamine oxidase (MAO) has been introduced by Zeller only in 1938. In the 1950th the clinical importance of MAO-inhibitors became aware and in the early 1960th especially Birkmayer and Hornykiewicz tested several such compounds in Parkinson's disease (PD) in order to potentiate L-DOPA's efficacy. Due to potential side-effects of these compounds it was only 1974 when Riederer and Youdim proposed Birkmayer to treat PD patients with (-)deprenyl (selegiline), a selective MAO-B-inhibitor. Since then by using different clinical study-designs the target of demonstrating a "disease-modifying effect" has not shown clear-cut results. Only the drug rasagiline offers such possibility as demonstrated in the ADAGIO-clinical long-term trial.

By developing the mode of actions of MAO and by using the strategy of inhibiting selectively its iso-enzymes in order to reduce the production of toxic aldehydes, radicals and avoiding the reaction of H_2O_2 with iron (Fenton reaction) MAO-B-inhibitors have contributed much to the concept of neuroprotection and to understand oxidative stress mechanisms. With rasagiline showing "disease-modifying properties" MAO-B-inhibitors enter a new class of compounds which are able to reduce PD progression significantly. If so, MAO-B inhibitors are the most innovative compounds developed for the sake of PD patients.

abstracts

NEUROPROTECTION IN SCHIZOPHRENIA: CHALLENGES AND OPPORTUNITIES

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Schizophrenia is a chronic and disabling mental disorder characterized not only by positive and negative symptoms but also by a significant decline in cognition, disturbed coping abilities, a decrease of psychosocial functioning as well as quality of life. Despite the effectiveness of antipsychotic medications in the treatment of schizophrenia, about 30% of patients who receive adequate treatments have significant persisting symptoms, especially regarding the negative symptom and cognitive domains. Consequently the development of more effective treatments is an important research goal. The neurodevelopmental and neurodegenerative models of schizophrenia lead us to explore a neuroprotective approach in the treatment of schizophrenia in tandem with the rapidly evolving areas in neuroscience. A significant body of literature indicates that mechanisms implicated in the disease process include oxidative stress, mitochondrial dysfunction, excitotoxicity and apoptosis. Furthermore, preclinical and clinical data suggest that neuroprotection is the maintenance of functional integrity of the brain in response to emotional and neurobiological stress – the "stressed brain". With the exception of dementia, the use of neuroprotective agents in schizophrenia is not yet well established. One of the oldest and most successful agents used in psychiatry, lithium, can be viewed as a prototype of such a neuroprotective agent. Neuroprotective agents as add-on therapies (e.g., modafinil, erythropoietin, glycine, D-serine, memantine) are currently being evaluated in schizophrenia and related disorders. In recent years we have investigated a few possible neuroprotective agents: neurosteroids (dehydroepiandrosterone, pregnenolone), bexarotene (which belongs to the group of synthetic medicines derived from the retinoid vitamin A), and L-Theanine (or gamma-ethylamino-L-glutamic acid, which is present almost exclusively in the tea plant) for treatment of schizophrenia patients. The mechanisms underlying neuroprotective effects of these compounds are various and independent of the classically defined dopamine and serotonin receptors. However, these placebo-controlled add-on trials involve a number of important challenges. Given the multiple antipsychotic medicines, identifying subjects eligible to participate in clinical trials can be a challenge. Generally multicenter and lengthy trials are required. Neuroprotection strategy may be a useful paradigm for treatment of prodromal and first-episode schizophrenia patients that might have a significant impact on subsequent course and outcome. This talk will expand on the recent findings, and suggest future directions for this exciting area.

abstracts

IS THERE ANY REALISTIC TREATMENT IN DEMENTIA?

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The actual development of treatment of dementive patients is based on the growing understanding of the pathogenesis of dementia. A variety of approved and upcoming drugs were developed: secretase inhibitors, statines, ß sheet brakers, vaccination, nsaid, nmda antagonist, ache-inhibitors .csf aß-peptides may reflect specific impact of distinct neurodegenerative processes on aß-metabolism and represent potential diagnostic and therapeutic biomarkers for alzheimer disease (ad), frontotemporal dementia (ftd) and dementia with lewy bodies (dlb). The aim of therapy is to stop or delay the progression of the disease. Until now the therapeutic response is limited. Therefore the competence network of dementia (cnd) in germany set up in the last five years a network of 14 university memory clinics for standardized recruitment, recognition, assessment and treatment of patients with mild cognitive impairment (mci) and dementia. Large controlled trials investigated the effects of combination therapy (ache inhibitor and nmda antagonist) on mci and ad. Improvement in the combination group measured by adas-cog exceeded the effect of treatment with ache-inhibitor alone (mci group). The cognitive decline after discontinuation of ache-inhibitor was more prominent than after withdrawal of nmda-antagonist. In the group of mci the pharmacological treatment was not associated with severe adverse events. Among the stabilisation strategies at delaying disease progression, neurotrophic agents received the most attention. In several international randomized controlled trials cerebrolysin a peptide preparation which mimics the effects of neuronal growth factors revealed a significant, dose dependent benefit on cognition, clinical global impression and activity of daily living. Overall the therapeutic strategies for dementive patients in every stage must include pharmacological and non- pharmacological tools.

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BLOOD-CENTRAL NERVOUS SYSTEM BARRIERS: THE GATEWAY TO NEURODEGENRATION, NEUROPROTECTION AND NEUROREGENERATION

Hari Shanker Sharma, Laboratory of Cerebrovascular Research, Department of Surgical Sciences, Anesthesiology & Intensive Care Medicine, University Hospital, Uppsala University, Uppsala, Sweden

The microenvironment of the central nervous system (CNS) is precisely and meticulously maintained by a set of dynamic physiological barriers located within the cerebral microvessels of the brain (Blood-Brain Barrier) and the spinal cord (Blood-Spinal Cord Barrier), as well within the epithelial cells of the choroid plexus separating the blood and cerebrospinal fluid (CSF) interface (Blood-CSF-Barrier). The physicochemical properties of these cellular barriers are quite comparable to that of an extended plasma membrane. The BBB and the BSCB are quite tight to small molecules (12 Å, Lanthanum ion), whereas BCSFB is less restrictive in nature. On the other hand, the ependymal cell linings of the cerebral ventricles and spinal canal referred to as CSF-Brain Barrier do not normally restrict passage of several molecules of small sizes. However, protein transport across these blood-CNS-barriers (BCNSB) is severely restricted. Entry of proteins into the CNS microenvironment induces vasogenic edema formation that is primarily responsible for cell and tissue injury. These BCNSB are often compromised under a wide variety of psychological, traumatic, metabolic, ischemic, environmental or chemical insults leading to neuronal, glial and axonal damage. Opening of the BCSNB to various endogenous or exogenous substances and proteins alters the molecular, cellular, biochemical, immunological and metabolic environment of the CNS leading to abnormal neuronal function and/or brain pathology. Our investigation is focused on current status of the BCSNB breakdown in experimental models of emotional stress, traumatic injuries, psychostimulants as well as key environmental health hazards, i.e., nanoparticles exposure. Breakdown of the BCNSB in these conditions altered gene expression and induced brain pathology leading to neurodegeneration. Attenuation of the BCNSB disruption with drugs or antibodies affecting neurochemical metabolism and neurotrophic factors markedly reduced the development of brain pathology. Taken together, these novel observations strongly point out the role of BCNSB as a “gateway” to the neurodegeneration, neuroprotection and/or neuroregeneration in neurological diseases.

abstracts

ENGINEERED NANOPARTICLES FROM METALS EXACERBATE BLOOD-SPINAL CORD BARRIER DISTURBANCES, EDEMA FORMATION AND CORD PATHOLOGY. AN EXPERIMENTAL STUDY IN THE RAT

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Influence of nanoparticles on the pathophysiology of spinal cord injury (SCI) is not well known. Thee are reasons to believe that silicon nanoparticles or silica dusts and copper nanoparticles from gun powders could be easily be inhaled from the environment by soldiers engaged in gulf war that could influence their health and brain function. These nanoparticles can easily be transported to brain via inhalation and thus can lead to neurotoxicity. However, the details of silicon or copper nanoparticles on human health function are still unknown. Previous reports from our laboratory show that exposure of Ag, Cu or Al nanoparticles adversely affect neuronal function following heat exposure. This suggests that nanoparticles exposure may enhance brain pathology following stressful conditions. Thus, it appears that traumatic injuries to the CNS may also be influenced by exposure to nanoparticles.

In this investigation we exposed rats to copper (Cu, 50 to 60 nm) or silicon nanoparticles (SiO2, 40-50 nm) by administering them intraperitoneally for 7 days (50 mg/kg) and then subjected them to spinal cord injury (SCI). We examined blood-spinal cord barrier (BSCB) permeability, cord edema and neuronal damage along with functional outcome and compared these results with normal animals subjected to identical SCI.

Rats treated with Cu or Si nanoparticles for 7 days did not show any significant alteration in behaviour on rota rod performances or on capacity angle tests. However, subjection of these nanoparticles treated rats to SCI resulted in a profound deterioration in motor functions compared to normal rats with spinal cord trauma. Furthermore, the magnitude of blood-spinal cord barrier (BSCB) breakdown to Evans blue and radioiodine tracers following SCI was much more aggravated in these nanoparticles treated animals compared to normal rats. The edema formation and cord pathology was significantly higher in nanoparticles treated injured animals than the normal spinal cord traumatized rats. These observations suggest that exposure of nanoparticles enhances the sensitivity of spinal cord to injuries. It remains to be seen whether nanoparticles treatment may also alter the pharmacotherapeutic effects of neuroprotective agents in SCI, a feature currently being investigated in our laboratory.

abstracts

NEUROPROTECTIVE EFFECTS OF NEUROTROPHIC FACTORS IN ANIMAL MODELS OF CNS INJURIES

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Previous reports from our laboratory suggest that a suitable combination of neurotrophic factors attenuates CNS pathologies following traumatic or metabolic insults to the brain or spinal cord. Since, Cerebrolysin contains a mixture of neurotrophic peptides, we have undertaken a series of investigations to examine the neuroprotective efficacy of the drug in various animal models of CNS injuries. We developed a new model of closed head injury (CHI) in which an impact of 0.224 N was applied on the right parietal bone under anesthesia by dropping a weight of 114.6 g on the skull from a height of 20 cm through a guide tube. This concussive CHI resulted in profound edema formation and volume swelling at 5 h after the insult that was most pronounced in the contralateral cerebral hemisphere. The microvascular permeability disturbances to protein tracers were prominent in both the cerebral hemispheres and the underlying cerebral structures. Pretreatment with neurotrophic factors (10 µl, 20 µl or 40 µl/min for 10 min) infused into the left lateral cerebral ventricle either 30 min before or 30 min after CHI significantly attenuated brain edema formation, volume swelling and brain pathology. This effect was most pronounced with 20 µl and 40 µl/min infusions. On the other hand, no reduction in brain edema, BBB permeability or brain pathology was seen when it was administered 60 min post-CHI.

Using a new model of spinal cord injury (SCI) in which an incision to the right dorsal horn at the T10-11 level induces profound disruptions of the blood-spinal coed barrier (BSCB) in rats after 5 h, the effects of topical application of neurotrophic factors was evaluated. Topical application of neurotrophic factors 5 min after SCI (100, 2000 and 400 µl over 10 min) over the traumatized cord markedly attenuated spinal cord edema formation at 5 h compared to untreated control group. This effect was dose related. In these animals neurotrophic factors treatment in high doses (200 and 400 µl) significantly improved the motor functions and reduced the BSCB breakdown, edema formation and cell injury at 5h. However, these potential beneficial effects were absent when the treatment was initiated 60 min or 90 min after SCI.

To further test the neuroprotective efficacy we used a new model of hyperthermic brain injury (HBI). HBI was produced by subjection of animals to 4 h heat stress at 38° C that resulted in massive blood-brain barrier (BBB) disruption and brain edema formation. Pretreatment with neurotrophic factors (5 ml or 10 ml/kg, i.p. 30 min, before heat stress) markedly attenuated the BBB dysfunction and brain pathology. Interestingly, treatment with high dose of cerebrolysin (10 ml/kg) 30 min after heat stress was also neuroprotective. However, administration of the drug 60 or 90 min after the onset of heat stress was ineffective in reducing brain damage.

Taken together these observations suggest that an early intervention with neurotrophic factors may have added therapeutic value for the treatment of various cases of CNS injuries.

abstracts

IMAGING NEURAL CELLS WITH FUNCTIONALIZED QUANTUM DOTS: FROM STRUCTURE TO FUNCTION

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Semiconductor quantum dot nanocrystals are nanoscale sized semiconductor particles that fluoresce at specific wavelengths and can be used for biological imaging. Following appropriate chemical modifications, quantum dots can be conjugated antibodies or peptides, which in turn can used to specifically bind antibody-quantum dot complexes to targeted antigens on and within cells. The use of quantum dot cellular imaging nanotechnology has some distinct advantages that compliment traditional organic fluorophore labeling and imaging. For example, they are very photostable, resulting in minimal photobleaching, and they display very narrow emission spectra while possessing comparatively wide absorption spectra. Furthermore, color tuning of quantum dots results from small changes to the size of the semiconductor core material, negating the necessity for different unique chemistries for different colors, as is the case with organic fluorophores. Taken together, this means that quantum dot labeling is particularly suitable for multiplexing several different specific colors to differing epitopes in a single preparation. Despite these positive attributes, ensuring specific and reproducible labeling, in particular with highly specialized cells such as neurons and glia, is tricky and can result in reproducible artifact labeling if labeling protocols are not optimized for target cells of interest. But with properly optimized protocols, this technology can result in very specific high resolution imaging of cellular structures using standard optical microscopy with very low non-specific background. We will begin by introducing and discussing work we have done optimizing quantum dot imaging protocols for neural cells, both in vitro and in situ in intact neural tissues, followed by a discussion on how antibodies bind to quantum dots and work we have done to experimentally derive the number of functionally bound antibodies available for specific labeling. Finally, we will discuss on-going work that attempts to extend the quantum dot neuroscience toolbox in order to understand both cellular structure and function.

abstracts

ANESTHETIC-INDUCED BRAIN INJURY DURING DEVELOPMENT: NON-INVASIVE ASSESSMENTS AND STRATEGIES FOR PREVENTION

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The developing brain is susceptible to anesthetic-induced injury. The window of vulnerability to these neuronal effects of anesthetics is restricted to the period of rapid synaptogenesis, also known as the brain growth spurt. Similar dependencies on dose/duration of exposure and developmental stage are observed in both the non-human primate and rodent models. The duration of anesthesia needed to induce cell death as measured by minimal exposure requirements is similar (~6 hrs) for nonhuman primate and rodent brain cells in culture, and also in vivo in rodent and nonhuman primate models. The susceptible stage or period of development has not been completely described, but in the nonhuman primate it begins somewhere before the last quarter of pregnancy and continues until shortly after birth. Behavioral studies in developing primates have confirmed functional deficits following neonatal ketamine-induced anesthesia as assessed by the NCTR Operant Test Battery. In rats previously exposed to ketamine, preliminary microPET imaging data have indicated enhanced 18F Annexin-V retention, a non-invasive marker of apoptosis. It has been postulated that up-regulation of the NR1 subunit of the N-methyl-D-aspartic acid receptor (NMDAR), a calcium channel regulator, may be an important first step in the pathway to anesthetic-induced neurotoxicity. Importantly, NMDARs are vulnerable to endogenous glutamate concentrations; in turn, the excitotoxic effects of glutamate may be mediated largely by increased Ca2+ influx through activated NMDARs. Associated with this increased Ca2+ influx is an increase in the generation of reactive oxygen species (ROS) that appears to originate in mitochondria. Several recent studies using blockers of oxidative stress such as L-carnitine, melatonin, the superoxide dismutase mimetic, M40403, the NOS inhibitor, 7-nitroindazole and hypothermia have indicated that reduction of oxidative stress may protect the developing animal from anesthetic-induced brain cell death. Recent gene expression assessments in developing animals indicate that genes involved in oxidative stress pathways are altered by anesthetic treatment. Together, the application of 'omics' approaches along with non-invasive and traditional toxicological endpoints indicates that the susceptibility of the developing brain to anesthetics is strongly influenced by oxidative stress. Supported by NICHD, NTP/NIEHS and CDER and NCTR/FDA

abstracts

THE CAUSES AND CONSEQUENCES OF OXIDATIVE STRESS IN ALZHEIMER DISEASE: THERAPEUTIC IMPLICATIONS

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We have determined that oxidative damage is limited to neuronal cell bodies in Alzheimer disease (AD) and is actually reduced as the senile plaques and neurofibrillary tangles accumulate. These correlations suggest that amyloid-ß deposition and the inflammatory response are associated with activity that lowers oxidative damage and explains why preliminary amyloid-β vaccines or specific inhibitors of inflammation have not benefited patients. In fact, our most recent data shows that amyloid-β serves as an antioxidant and metal chelator. While the causes of oxidative stress are well known, abnormalities that may initiate and promote neuronal oxidative damage are less well understood. That said, we have used *in situ* hybridization, quantitative immunocytochemistry, and redox chemistry to analyze the source of reactive oxygen in AD. First, we found that mitochondrial abnormalities (normal and 5kb-deleted mtDNA) were greatly increased and restricted to damaged mitochondria in neurons susceptible to AD. Such mitochondrial abnormalities were significantly correlated with increased RNA oxidative damage ($r = 0.93$). In that same vein, microtubule numbers are drastically reduced in AD neurons. Second, we found that cytoplasmic RNA in AD, but not controls, is associated with abundant redox-active metals that catalyze nucleic acid oxidation. Finally, we found that the heavily phosphorylated proteins, tau and neurofilament heavy subunit, control adduction by the lipid peroxidation product, hydroxynonenal. Taken together, our findings suggest that oxidative imbalance in AD is met by a series of complex responses that establish a disease-related homeostatic balance. Therefore, therapeutic intervention will be most effective when directed at the etiology and not the response. In fact, intervention in the latter may prove to be extremely deleterious.

Supported by the National Institutes of Health.

abstracts

NEUROTROPHIC TREATMENT OPTION SUPPORTS STROKE RECOVERY

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In spite of the increased availability of thrombolysis and treatment in stroke units about one third of the patients suffering from ischemic stroke are more or less handicapped when assessed three months after their cerebrovascular event. For those patients there is still no convincing pharmacological approach available. As neurotrophic factors are necessary for normal neuronal function, survival, growth, sprouting, proliferation, differentiation, neurogenesis and repair they are due to these pleiotropic effects in the focus of interest of "strokologists" - despite still unconclusive evidence from trials with good qualities.

Such remedies were used successfully in trials with animal models of ischemic stroke but this promise did not translate until now into convincing clinical effects in humans presumably due to difficult pharmacokinetics of the intact factors such low blood brain barrier (BBB) permeability, limited diffusion in the penumbra or side effects. Recently animal studies focused on small molecules such as Granulocyte-macrophage colony-stimulating factor, erythropoietin, Neotrofin (a synthetic purine) , granulocyte colony-stimulating factor bone morphogenetic protein-7, glial cell line-derived neurotrophic factor or on large molecules in Trojan Horses, transfected vectors or vehicles or even used topical. Another approach is to increase action of neurotrophic factors indirectly.

A biological preparation with the pleiotropic action of nerve growth factors in cell cultures and animal models but with peptides small enough to cross the BBB is available and in clinical use worldwide. In numerous small but well designed trials in stroke patients favorable effects included faster and more pronounced motor function recovery, enhanced participation in a program of occupational rehabilitation, improved performance in the activities of daily living and improved level of consciousness and cognition were observed, some of these repeatedly. The tolerability of this preparation was very good, side effects in trials mostly unrelated, fleeting and mild. The neurotrophic treatment can be added to any other form of treatment without risk of interactions.

abstracts

STIMULATION OF THE SUBTHALAMIC NUCLEUS IN A RAT MODEL OF PARKINSON'S DISEASE
MOTOR AND NON-MOTOR EFFECTS

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The use of stimulation electrodes implanted in the brain to control severely disabling neurological and psychiatric conditions is an exciting and fast emerging area of clinical neuroscience. As an example, high frequency stimulation (HFS) of the subthalamic nucleus (STN) has become the surgical therapy of choice for advanced Parkinson's disease (PD), and to date more than 30,000 PD patients worldwide have benefited from this procedure. Despite having important beneficial motor effects, bilateral STN HFS can be associated with the occurrence of unpleasant and debilitating psychiatric effects, including cognitive alterations, low mood, aggression, and impulsive acts and thoughts which are linked to suicide. These psychiatric effects can be a major burden to patients and their families, and often mitigate the positive effects on motor symptoms. In animals, HFS and other manipulations of the STN also produces a range of non-motor behavioural changes, including increased impulsivity and altered cognitive responses that appear to correlate with the adverse effects experienced by PD patients.

The author will discuss the potential mechanisms underlying these behavioural effects with special emphasis on the 5-hydroxytryptamine (5-HT: serotonin) system. In this respect, the author and co-workers recently found that HFS of the STN inhibits midbrain 5-HT neurons to evoke depression-related behavioural changes. Stimulation of the STN consistently inhibited the firing rate of 5-HT neurons in the dorsal raphe nucleus of the rat and evoked depressive-like behaviour in a widely used experimental paradigm of depression. Overall, these recent findings link reduced 5 HT function to the psychiatric effects of HFS of the STN observed in PD patients, and provide a rational basis for their clinical management.

abstracts

RESTING-STATE FUNCTIONAL MRI: STATE OF THE ART AND FUTURE PERSPECTIVES

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Functional Magnetic Resonance Imaging (fMRI) can be performed in the absence of experimental tasks with the patient in a "resting" state (RS-fMRI). RS-fMRI allows studying the spontaneous correlations of blood-oxygen-level-dependent (BOLD) signals between remote brain regions (resting-state functional connectivity). Resting-state functional connectivity data can be obtained from just five minutes of whole-brain repeated-single-shot-echo-planar scans with repetition times of two seconds or less and the patient lying quietly in the scanner and mentally relaxing with his eyes closed. The acquired image time-series are, then, decomposed into a series of spatio-temporal patterns of brain activity using statistical processing techniques. Among these techniques, Independent Component Analysis (ICA) is nowadays considered the method of choice for analyzing RS-fMRI time-series, because a fully automatic extraction of the RS-fMRI functional connectivity patterns can be obtained without the need of pre-specifying the exact location and extension of the brain regions involved in a given network, nor the expected temporal evolution of the BOLD signals. In a series of ICA components extracted from the RS-fMRI data, up to six reproducible functional connectivity networks have been so far discovered and characterized in terms of the known functional role of the regions involved. Altogether, the relatively easy set-up of an RS-fMRI session and the unbiased data modeling provided by ICA have boosted the neuroimaging research of brain disorders towards an extensive proposal and use of this methodology in clinical trials and population studies.
Among the main RS-fMRI functional connectivity networks, one specific network referred to as "default-mode" (DM) network, has recently attracted considerable interest in the clinical neuroscience community for its possible interpretation as the "baseline" cognitive state of a subject and for its link to memory and executive function in normal and pathological conditions. The DM network involves those areas of the anterior and the posterior cingulate cortices (ACC, PCC) which are typically deactivated during many different types of cognitive tasks.
The amount of functional connectivity measurable for the DM network as well as for any other resting-state network can be related to important population factors in the study of various neurological diseases, especially in the study of cognitive decline and impairment. The main challenge of current state-of-the-art methodological and application research with RS-fMRI is the optimal estimation and full understanding of each RS-fMRI network and the development of objective individual criteria for the evaluation of RS-fMRI patterns in relation to the diagnosis and follow-up of a given pathology.

abstracts

NEURAL PLASTICITY AND NEURODEGENERATION IN DEPRESSION AND DEMENTIA

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While neurodegeneration is a well established pathophysiological concept in the pathogenesis of dementia, there is increasing evidence that degenerative processes may also play a crucial role in the pathophysiology of neuropsychiatric disorders such as depression. Interestingly, there is a considerable phenomenological overlap in the clinical presentation of both conditions: Patients suffering from depression often exhibit cognitive deficits, while patients with dementia often present with emotional disturbances.
Further research into neurodegeneration as a key phenomenon of both, dementia and depression will help to better understand the pathomechanisms underlying these disorders. A better understanding of the physiology of neuroplasticity may contribute to develop future treatment strategies.

abstracts

TOWARDS THE DESIGN OF A HARD MATTER SYSTEM CAPABLE OF NEURAL-LIKE COGNITION

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In a previous conference we posed a number of questions for the communities of neurology and neuroscience. One of these raised the issue of the possible relevance, or not, of research in basic physical science to neurology and neurological diseases in particular. Secondly, and more fundamentally, we asked whether our modern understanding of the physical sciences is an adequate basis for the explanation of brain processes. In this context, for this presentation, we will address brain function from the completely opposite perspective of an early attempt to design an electrochemical capable of cognition.

The key concept for our work is the notion that a system based on familiar hard matter can be capable of information processing through consideration of its special internal dynamics. Our research program is inspired by the massive, multivariable information processing that occurs in the brain, which is intimately connected with pattern formation and recognition.

Our study is concerned with the electro-dissolution dynamics of nickel in acid electrolyte where the anodic current responds to three dimensional changes in the electrolyte and surface conditions, giving rise to a multitude of spatio-temporal patterns. We have been able to observe changes in the evolution of dynamics, and relate these patterns as a cognitive response to input perturbations which caused them and to which the response of the system was distinct. The work also aimed at clarifying what is meant by information processing by drawing on formalization used in computer science and information theory. By exploring the emerging theoretical field of pattern formation in nonlinear dynamical systems, we have demonstrated how transient dynamics and attractors in physical systems have all the necessary components to realize the formalization of information processing.

Experimental work includes studies on identification of control parameters, characterization of subsequent temporal patterns and examination of system response to information in the form of voltage perturbations. As part of this work, we developed the electronics, data acquisition hardware as well as the software necessary to acquire, control and process the data obtained from the system. Various data processing and pattern recognition techniques were then employed to look at the data coming from the electrode arrays, in order to attach meaning to the response from input information. Such methods include a new way of processing experimental data to look for real time phase synchrony between pairs of electrodes.

abstracts

COGNITIVE DYSFUNCTION OF NORMAL AGEING SEEN FROM A NEURONAL PERSPECTIVE

Emil C. Toescu, School of Clinical and Experimental Medicine, College of Medical and Dental Sciences, University of Birmingham, Edgbaston, United Kingdom

Ageing is an inevitable part of normal biological development, and it is characterised by a relative decrease in the function and/or development of dysfunctions in a variety of organs, including the brain. Minor or mild deficits in several defined cognitive domains are well established for the aged individual, with a tremendous heterogeneity, both inter- and intra-individual, in the range of such deficits. In the same period of the lifespan, a variety of acute and chronic diseases appear, including neurodegenerative diseases, and ageing is rightly cited as the most important risk factor for such diseases. Faced with the demographic data showing a continous ageing of the population, one of the major tasks of neuroscientists is to understand the mechansisms that determine or contribute to the normal ageing process. In this talk, i will present data to support the view that neuronal ageing is characterised by a decreased homeostatic reserve, centred on altered ca^{2+} homeostasis and mitochondrial dysfunction. It is this decreased capacity of the neurones in the aged brain to overcome and restore quickly homeostasis in face of excessive metabolic loads that explains the increased vulnerability of the aged neurones and, consequently, provides a reason why ageing is such an important risk factor for a variety of neurodegenerative diseases. Such metabolic alterations could also explain some of the changes in cognitive performance, at least in animal study models.

abstracts

EFFECTS OF THREE-PHRASE REHABILITATION TREATMENT ON ACUTE CEREBROVASCULAR DISEASES: A PROSPECTIVE, RANDOMIZED, CONTROLLED, MULTICENTER STUDY

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Objective: To research the function of three-phrase rehabilitation of stroke in China, provide a standard program for most of hospitals around the country and prognosis the outcome of stroke patients.

Method: Patients with stroke from all hospitals were selected according to the same criterion and were randomly divided into rehabilitation group and control group. The rehabilitation group patients took part in both early and convalescent rehabilitation while the control group patients only take part in early rehabilitation. Evaluate patients at 1 week and 1, 2, 3, 4, 5, 6 months.

Result: 1078 stroke patients were included. 902 patients finished all the assessments. 19 patients died and 157 were lost during follow-up. In the 902 patients, 439 were in the rehabilitation group, 266 male and 173 female, the average age is 61.37±10.63, with 278 infarction and 161 hemorrhage; 463 were in the control group, 281 male and 182 female, the average age is 59.85±11.37, with 291 infarction and 172 hemorrhage. Before rehabilitation therapy and 1 month after therapy, there was no difference between the two groups. From 2to 6 months, there was significant difference between the two groups in CNS, movement function, ADL and quality of life, and the rehabilitation group get better outcome. By the end of 6 months, most of the rehabilitation group patients can be self-dependent and the average score of Barthel Index is about 85. The incidence of post stroke depression of rehabilitation group is lower than control group. Get the formula of prognosis of score of Barthel Index at the 6 month.

Conclusion: The three-phrase rehabilitation program of stroke can get better outcome in movement function, ADL and quality of life.

abstracts

ENGINEERED POLYLACTIDE-CO-GLYCOLIDE(PLGA) Np AS DRUG DELIVERY SYSTEMS FOR THE CENTRAL NERVOUS SYSTEM

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Nanoparticulate polymeric systems (nanoparticles, Np) have been widely studied for the delivery of drugs to a specific target site. Np have been recently considered for the therapy of various brain diseases. The major problem in accessing the central nervous system (CNS) is due to the presence of the Blood-Brain Barrier (BBB). Recently, it has been shown the possibility to reach the CNS district crossing the BBB using nanoparticles (Np) made of polylactide-co-glycolide (PLGA), modified with a simil-opioid sequence and different glycosidic moieties. Firstly, PLGA was modified with different glycol-heptapetides (Glucose, Lactose, Xylose, and Mannose as sugar moieties and with a single [P] or a triple sequence of heptapeptides [3P]). Then, after i.v. administration, Np, labeled with covalent linkage with a fluorescent dye, were demonstrated to be able to cross the BBB by using confocal microscopy.

A strong analgesic effects due to the encapsulated Loperamide, a P-glycoprotein (P-gp) substrate model drug, demonstrated the ability of modified PLGA Np to cross the BBB, after i.v. administration. The effect was different in the intensity and in the time period according to the different surface modification, being the Glucose preferable when compared with the other ones. When 3P-PLGA Np were used, a different profile in the pharmacological activity was assessed, i.e. a sudden maximum analgesic effect followed by a fast decrease over the time. Finally, the biodistribution of Np loaded with Rhodamine-123 (P-gp substrate) was analyzed quantifying the fluorescent intensity in the different organs including brain, in order to better understand the fate of these modified Np.

abstracts

THE MULTIPLE SCLEROSIS TREATMENT CONSENSUS GROUP - IMMUNOMODULATORY TREATMENTS IN MS

Klaus V. Toyka, FRCP for the Multiple Sclerosis Consensus Group, Europe

When the new immunomodulatory treatments were introduced into the therapy of MS it became clear that MS experts should look for consensus in managing MS patients including new and traditional modes of treatment. A first MSTKG was formed in 1998 with about 130 MS experts from Austria, Switzerland and Germany joining together to reach consensus over these issues. The first publication in German (Nervenarzt) and an English translation (Eur J Neurol) in 1999 was followed by an update in 2004 (J Neurol) after joining with 14 other European countries. Finally it was achieved to have over 20 countries involved with many experts and the MS societies joining in which resulted in an updated MSTCG report in 2008 on immunomodulatory treatments and treatment excalation (published in J Neurol).

Other MSTCG reports appeared in 2006 dealing with symptomatic treatment of MS and in 2008 on the use of MRI. Here again, a multi national European update is on the horizon.
As a consequence, the political EU representatives have now adopted the general recommendations of the latest MSTCG report through interaction with the European MS Platform and have implemented the published treatment recommendations in their health policy to improve the MS treatment situation and help the countries that are more recent members of the EU to implement the MSTCG standard. Moreover, based on the MSTCG, requests for optimal treatment by patients advocates have now much more impact in the communication with national health systems and health insurances.

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abstracts

WHAT QUALITY OF LIFE AFTER TRAUMATIC BRAIN INJURY? QOLIBRI, A DISEASE-SPECIFIC QUALITY OF LIFE TOOL.

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Objective :
There is no disease-specific Health-related Quality of Life (HRQOL) tool dedicated to assess people after Traumatic Brain Injury (TBI) yet. QOLIBRI was developed by an international research group.

Material and method :
1568 TBI patients from 10 countries and 8 languages filled-out a preliminary version of the QOLIBRI taking into account specificities, sequelae and well-being of persons after TBI. Therefore, the QOLIBRI was developed through 3 successive versions and consecutive statistical analyses in order to obtain a psychometrically valid and self-reported questionnaire.

Results :
The QOLIBRI final version, filled-out in 15 minutes, consists of two parts. The first part assesses satisfaction level with HRQOL and is composed of 6 overall items and 29 items assigned to 4 subscales: thinking, self and emotion, autonomy in daily life and social aspects. The second part is devoted to "bothered" questions and composed of 12 items in 2 subscales: negative feelings and restrictions. The 6 subscales meet standard psychometric criteria. In addition, 2 items assess more medical aspects. The questionnaire was validated in English, Finnish, French, German and Italian.

Conclusion :
TBI patients may now be assessed, beyond objective measures including handicap and recovery, with a new subjective measure assessing the TBI patient's own opinion on his/her HRQOL, applicable across different populations and cultures.
Validations in China Mainland, Hong-Kong, Taïwan, Egypt, Indonesia, Japan, Poland, Norway, Malaya, Spain, Portugal and Brazil are on the way.

abstracts

NEUROPROTECTION AND THE KYNURENINE SYSTEM: 2009

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L-kynurenine is an intermediate in the pathway of the metabolism of L-tryptophan to nicotinic acid. This compound is formed in the mammalian brain (40%) and is taken up from the periphery (60%), indicating that it can be transported across the blood brain barrier (BBB). It was discovered some 30 years ago that compounds in the kynurenine family have neuroactive properties. L-kynurenine, the central substance of this pathway, can be converted into two other important metabolites: the neuroprotective kynurenic acid and the neurotoxic quinolinic acid. Kynurenines have been shown to be involved in many diverse physiological and pathological processes. Recently in vitro electrophysiological examinations on hippocampus confirmed the well-known findings that kynurenic acid in micromolar concentrations exerts an inhibitory effect. However, in nanomolar concentrations, kynurenic acid does not give rise to inhibition, but in fact facilitates the field excitatory postsynaptic potentials. Therefore, kynurenic acid in the concentration range between a few hundred nanomolar and micromolar displays different effects. The findings strongly suggest the neuromodulatory role of kynurenic acid under both physiological and pathological circumstances. Concerning the peripheral effects of this substance, kynurenic acid antagonizes the obstruction-induced motility responses and xanthine oxidoreductase activation in the colon. Inhibition of enteric NMDA receptors may provide an option to influence intestinal hypermotility and inflammatory changes.
In the future, it would be useful to elicit the relationship between the kynurenine pathway and diseases through the application of sensitive molecular techniques in line with the development of powerful new compounds. Administrating of kynurenic acid can be appear a promising therapeutic approach, but its use is limited because of its poorly transport across the BBB. The solution may be the development of kynurenic acid analogues (e.g. SZR-72) which can pass this barrier and disenganing in the brain, than kynurenic acid can exert its neuroprotective binding at the excitatory glutamate receptors. Furthermore, it seems hopeful to use kynurenine derivatives (e.g. 4-chloro-kynurenine) or enzyme inhibitors (e.g. Ro-61-8048) to ensure an increased kynurenic acid concentration in the central nervous system. In the face of all these challenges, it is clearly necessary to develop and spread the personal therapies of the patients with utilization of the recent results.

(continued next page)

abstracts

NEUROPROTECTION AND THE KYNURENINE SYSTEM: 2009

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abstracts

MILD TRAUMATIC BRAIN INJURY, COGNITIVE FUNCTIONING AND POST TRAUMATIC COMPLAINTS: A MRI STUDY

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Memory deficits are frequent sequelae of Mild Traumatic Brain injury (MTBI). However cognitive deficits after MTBI are poorly understood. Two core brain regions, the medial temporal lobe (MTL) and the prefrontal cortex (PFC) both contribute to memory processes but both may be affected after injury. Both increases and decreases in PFC activity have been found with functional Magnetic Resonance Imaging (fMRI). It has been hypothesized that MTBI may impact on brain tissue structure at a microscopic level. Diffusion Tensor Imaging (DTI) is a relatively new MRI modality that measures the degree of the diffusion of water molecules in the brain. In healthy white matter, this diffusion is highly anisotropic (i.e. stronger in the direction parallel to axons than perpendicular to axons) and a reduction of anisotropy is thought to be an indication for white matter pathology. Several cross sectional studies in small samples, have detected decreased anisotropy in white matter tracts after MTBI.The goal of this study is first to identify possible anatomic substrates for impairments in a memory task to distinguish between the contribution of the MTL and the PFC in the post-acute period (< 6 weeks) after MTBI. Secondly we aim to investigate the occurrence of white matter changes both early and late after MTBI and to relate findings to clinical severity measures and outcome.We probed the functionality of the MTL and PFC within six weeks after injury in 43 patients from a consecutive cohort and matched healthy controls. In addition to neuropsychological measures of declarative memory and other cognitive domains, subjects underwent fMRI probing prefrontal and medial temporal functionality using the n-back task. DTI data were analyzed using both a voxel-by-voxel based analysis, and a region of interest approach (Fasciculus Uncinatus, Corpus Callosum and Capsula Interna) to examine within-subject changes in white matter anisotropy in the MTBI patients by comparing the data from the early and late assessment. In addition, between-group analyses are performed to see whether patients differ from healthy controls at either time-point. The Results are currently being analyzed and will be presented at the congress.

abstracts

NEUROBIOLOGY OF POST-ISCHEMIC RECUPERATION IN THE AGED MAMMALIAN BRAIN

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Old age is associated with an enhanced susceptibility to stroke and poor recovery from brain injury, but the cellular processes underlying these phenomena are uncertain.
Therefore studying the basic mechanism underlying functional recovery after brain ischemia in aged subjected it is of considerable clinical interest.
Potential mechanisms include neuroinflammation, changes in brain plasticity-promoting factors, unregulated expression of neurotoxic factors, or differences in the generation of scar tissue that impedes the formation of new axons and blood vessels in the infarcted region. Available data indicate that behaviorally, aged rats were more severely impaired by ischemia than were young rats, and they also showed diminished functional recovery. Further, as compared to young rats, aged rats develop a larger infarct area, as well as a necrotic zone characterized by a higher rate of cellular degeneration, and a larger number of apoptotic cells. Both in old and young rats, the early intense proliferative activity following stroke leads to a precipitous formation of growth-inhibiting scar tissue, a phenomemon amplified by the persistent expression of neurotoxic factors. Finally, the regenerative potential of the rat brain is largely preserved up to 20 months of age but gene expression temporally displaced, has a lower amplitude, and is sometimes of relatively short duration. Most interestingly it has recently been shown that the human brain can respond to stroke with increased progenitor proliferation in aged patients opening the possibilities to utilize this intrinsic attempt for neuroregeneration of the human brain as a potential therapy for stroke.
Given the heterogeneity of stroke, a universal anti-inflammatory solution may be a distant prospect, but probably neuroprotective drug cocktails targeting inflammatory pathways in combination with thrombolysis may be a possibility for acute stroke treatment in the future.

abstracts

AUTOPHAGY IS A NOVEL THERAPEUTIC TARGET FOR NEURODEGENERATIVE DISEASES

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It is believed that protein misfolding and aggregation in the selected neurons of central nervous system play a key pathological role in the neurodegeneration associated with Alzheimer's disease, amyotrophic lateral sclerosis, Huntington disease, and Parkinson's disease. Ubiquitin-proteasome system (UPS) and autophagy-lysosomal system (ALS) are the two most important pathways to degrade misfolded and aggregated proteins. A dysfunction in either of the two systems might trigger injury or apoptosis of cells, which is an increasingly recognized default pathogenic mechanism of these neurodegenerative diseases. In the past five years **(1)** we have documented that hypoxia can significantly enhance the abnormal production of A-β and neuritic plaque formation via autophagy-mediated γ-secretase activity in APP/PS1 mutant mouse model of Alzheimer's disease; **(2)** we have documented that autophagic alteration appears in the early onset of amyotrophic disease, which is in closely correlated with the motor neuron degeneration; **(3)** we have found that in a Parkinson's disease animal model when UPS is inhibited or its function is impaired, the autophagy activity is adaptively increased, while application of autophagy inducer such as rapamycin can significantly protect dopamine neurons against oxidative stress-induced injury. Currently we are investigating the molecular pathways of autophagy alteration in these neurodegenerative diseases, and to evaluate the therapeutic potential of several drugs targeting on autophagy. It is a hope that manipulating autophagy activity and its down-stream pathways may be a promising strategy in the future for the treatment of Alzheimer's disease, amyotrophic lateral sclerosis, Huntington disease, and Parkinson's disease

abstracts

BRAIN DERIVED NEUROTROPHIC FACTOR AND ANTERIOR OPTIC PATHWAY IN MULTIPLE SCLEROSIS

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Objectives: To investigate the genotype-phenotype associations between the *brain derived neurotrophic factor (BDNF)*SNPs *rs6265* (Val66Met) and *rs2030324* and the structural and functional integrity of the visual pathway in multiple sclerosis (MS) patients as assessed by clinical (Snellen visual acuity charts and Sloan low contrast visual acuity charts) and structural (optical coherence tomography (OCT)) parameters.

Background: Our previous work that focused on the role of *BDNF* genotype (G-to-A substitution (dB SNP ID: *rs6265*) and the T-to-C substitution (dB SNP ID: *rs2030324*)) in MS patients demonstrated that these single nucleotide polymorphisms (SNP) of *BDNF* are potentially important determinants of the extent of brain pathology. In particular, we obtained results indicating associations between *BDNF* genotypes, gray matter (GM) atrophy and neuropsychological (NP) tests of visual cognitive processing. Based on these data we continued our work on the visual pathway because: i) BDNF plays a critical role in the development and function of the entire optic pathway from retina to visual cortex and, ii) our previous work has shown that specific BDNF genotypes are associated with gray matter volume and performance on NP tests requiring visual cognitive processing in MS patients, iii) Visual function, especially the optic nerve is very often affected in MS patients. The relative contribution of BDNF and pro-BDNF (known to have contradicting effects) and visual pathway integrity will be also assessed.

Methods: Three hundred MS patients will be enrolled in this study. Patients will be clinically evaluated using the Kurtzke EDSS scale and their visual acuity using the Snellen and Sloan Charts. The optic nerve integrity will be evaluated with OCT. DNA will be obtained from peripheral blood and analyzed for multiple *BDNF* genetic variations including *rs6265 and rs2030324*. The associations between the genetic variations and RNFLT will be examined in mixed-effect analyses. The BDNF and pro-BDNF levels in serum will be analyzed using ELISA and the associations between the pro-BDNF to BDNF ratio and MRI measurements will be assessed.

Results: Preliminary results obtained from first consecutive 120 MS patients showed that RNFLT in affected ON in patients caring the Val/Val genotype was less affected (mean RNFLT: 83.2 μm) vs. the Val/Met (mean RNFLT: 76.7 μm) and Met/Met (mean RNFLT: 63.82 μm) genotype respectively while the non-affected fellow eyes had a similar RNFLT (mean of 91 μm) in all three groups.

Significance: BDNF may partly explain the inter-individual differences in clinical outcomes. The ease and directness of obtaining visual pathway function measures and their correlations with the underlying neurochemical and immunological mechanisms can help in better understanding the heterogeneity of MS pathology. The work may also open avenues for new therapies directed at limiting degenerative processes and/or promoting cell growth and plasticity.

abstracts

MECHANISMS OF NEUROPROTECTION AS REVEALED FROM EXPERIMENTAL STUDIES OF LONG CARDIAC ARRESTS AND CARDIOPULMONARY RESUSCITATION (CPR) IN YOUNG PIGS

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In spite of many methological improvements in cardiopulmonary resuscitation clinical survival of patients have long been unsatisfactory. However, after 2003 when hypothermic treatment (34-32°C for 24h) was introduced survival with better neurological outcome has been achieved. Thus, survival to discharge has improved from the level of approximately 5-7% to somewhat better than 10%, sometimes even to 15%. The mechanisms behind the neuro-protective effect of hypothermia (HTH) and experimental pharmacological interventions are largely unknown. Hence, we have conducted experimental studies trying to elucidate both mechanistic similarities and differences between HTH and pharmacological intervention with the nitric oxide effect inhibitor methylene blue (MB) or the spin scavenger S-PBN.
Methods: Ten to twelve week old anaesthetized pigs of both genders have been investigated after due approval of the animal review board. After instrumentation for circulatory measurements and control measurements ventricular fibrillation was initiated by a transthoracic alternating current. The animals were then left in circulatory arrest without any treatment for 12 min. After this mechanic ventilation and thoracic compressions (100/min) by a mechanical device (Lucas®, Jolife AB, Lund, Sweden) was administered for 8 min after which attempts were made to defibrillate the pig's heart and, thus, restore spontaneous circulation. If that was successful the pig was cooled to the designated body temperature. The pigs allocated to pharmacological treatment received the pharmacological agents indicated above already after 1 min of CPR in order to protect the brain from ischaemic injury. After 3h monitoring of the circulatory parameters of the animal, it was sacrificed by an injection of potassium chloride after which the brain was removed, one hemisphere placed in formalin pending embedding, sectioning and immunostaining. The other hemisphere was put in liquid nitrogen for later whole genome activity analysis.
Results: Blood-brain barrier disruption was obvious shortly after cardiac arrest. Such disruption was less after hypothermic and MB treatments. Immunostaining of isoforms of nitric oxide synthase revealed early and sustained activity of especially nNOS that was mitigated by both MB and hypothermia. The effect of MB, however, lasted only as long as MB was administered. Whole genome analysis revealed many similarities between MB and hypothermia while effects of S-PBN largely were different.

abstracts

QUALITY OF LIFE FOLLOWING SEVEREST DAMAGE OF THE CENTRAL NERVOUS SYSTEM (CNS)

WHAT SHOULD NEUROSURGEONS TELL PATIENTS AND FAMILY MEMBERS REGARDING RESTORATION OF IMPAIRED MENTAL-COGNITIVE AND NEUROBEHAVIORAL FUNCTIONING IN RESPECT TO SOCIAL RE-ENTRY?

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The question of quality of life and social re-entry of individuals who survive severest damage to the central nervous system (CNS) is the main target in multidisciplinary neurotraumatology and restoration of impaired neural functioning, however a matter of ongoing and controversial debate in the scientific literature and in the lay press too. There are different opinions which kind of medical treatment is clearly effective to improve CNS functioning after brain damage. To how long could severest impaired patients live and for how long do they have to be treated in special rehabilitation environments before admittance to nursing homes, or going back home to stay with relatives. What shall physicians, what shall the neurosurgeon tell the next of kin regarding final outcome and social re-entry? TBI specific instruments to measure patient's quality of life are still missing.

In following the Helsinki Declaration of the World Medical Association, published in 1964, and its numerous amendments, doctors are obliged to use all available means to help their patient and to leave nothing untried. Based on a broad consensus among doctors, other medical and rehabilitation professionals, and next of kin there is main demand in the central European community that medical and rehabilitative treatment interventions and adequate activating nursing should be provided for all fully dependent individuals, who remain e.g. in an Apallic Syndrome AS/ Vegetative State (VS) full stage respectively in an early remission phase or in a long lasting looked–in syndrome. The WHO-ICF 10 does not explain the neuro-trauma related quality of life.

Personal experience in multidisciplinary neurotraumatology over 40 years have shown that up to now nobody can tell what a so called unconscious and minimally conscious patient does really feel and experience mentally. Functional imaging and neurophysiology are not able to demonstrate humanity and quality of life. This, however, means to maintain comfort, to eliminate complications, and to optimize physical and higher cortical functioning and recovery in following the Hippocratic Oath. This is despite divergent statements of national and international ethical consensus conferences and diametrically opposed national penal laws and penal decisions concerning with treatment-limiting and withdrawal of nutrition and hydration. Long term follow up in a young woman and two old male individuals will demonstrate that personal good quality of life after quite unexpected outcomes with successfully social re-entry can be possible. And the QOLIBRI , a new measurement tool, can help to define HRQoL in adults trans-culturally.

Maintenance of lifelong neurorehabilitation is essential for the individuals social wellbeing and sustainability. This will be a challenge with respect to social re-entry and QoL for the future besides all medical efforts and support. The QOLIBRI measurement offers new perspectives for the assessment TBI related QoL. Sustainability is an open field in socio-economic health care and neuroscience. Broad humanitarian, medico-ethical consensus and a new definition of health related quality of life following severest CNS damage is needed to overcome ongoing and dependent most selfish, social- economic interests as to prevent disastrous legal regulations or passing new bills.

abstracts

UPPSALA: A SCIENCE CITY & FERVENT DESTINATION FOR RESEARCH & DEVELOPMENT A GLORIOUS TRADITION AND HISTORY FROM 15TH CENTURY

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Uppsala is the fourth largest city in Sweden and a perfect destination for International Conferences and concerts. The city retains the charm of a small town while offering major urban opportunities and attractions. Uppsala plays a predominant role in the history of Sweden. Some times called cradle of the nation, the city has always been a centre for both religion, trade, science and research. Here are two universities, Uppsala University the oldest university in the Nordic countries-established in 1477 and Swedish University of Agricultural Science. Today's outstanding research and education are deeply rooted in history and amongst the inhabitants in Uppsala. The long history of Uppsala University is a natural part of academic life and everyday life in Uppsala and constitutes the foundation on which today's students and researchers are creating the universities of tomorrow. The city has a solid base of knowledge and tradition from which to progress. At the same time, the atmosphere is youthful, and more than 40,000 university students are a significant factor to this exuberance. Anywhere you look, Uppsala is teeming with liveliness.
Here is also Swedish oldest botanical gardens, the largest cathedral in Scandinavia, one of Sweden,s most famous locations of prehistoric artifacts (Old Uppsala), the unique anatomical theatre built by Olof Rudbeck the Elder, and many more marvelous sites and attractions. Well known classical figures in science such as Carl von Linné, Celsius, Scheele, Ångström and Siegbahn have been affiliated with Uppsala University. Over the years, Uppsala has been the home of many internationally renowned persons including the film director, Ingmar Bergman, and the former UN Secretary General, Dag Hammarskjöld.

posters

ACUTE OBSTRUCTIVE THREEVENTRICULAR HYDROCEPHALUS CAUSED BY HUGE CEREBELLAR INFARCTION. 2 CASES REPORT

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According to European Stroke Council surgical aspiration of the cerebellar infarction compressive on the fourth ventricle are life saving with good recovery.

CASE 1.

Male, 47 years, admitted in CHU Caen, for sudden HIC Syndrome from 7 hours. The neurologic examination: cerebellar ataxia.
CT Scann, MRI: infarction in the right cerebellum, threeventricular hydrocephalus.
Surgical treatment: aspiration of necrotic tissue, external ventricular drainage 2 days.
Postoperativelly: minimal cerebellar right deficit.
The patient received cerebrolysine 30 mg/day, 6 months.

CASE 2.

Female, 77 years, admitted in CECH, Constanta, for sudden HIC Syndrome from 24 hours. The neurological examination: left neocerebellar and arhicerebellar syndrome.
CT scan, MRI: infarction in the left cerebellar hemisphere and the vermis threeventricular hydrocephalus.
Surgical treatment: aspiration of necrotic cerebellar tissue.
Postoperativelly: minimal neocerebellar left deficit. The patient received Cerebrolysine 30 mg/day, 5 months.

Conclusion:
Agressive surgical therapy: aspiration of the infarcted cerebellar tissue +/- external ventricular drainage is lifesaving.

posters

HAS THE USE OF ANGIOTENSIN-CONVERTING ENZYME INHIBITORS A POTENTIAL BENEFITS IN STROKE?

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Introduction: angiotensin-converting enzyme inhibitors (ACEI) are under the study concerning the better outcome in stroke and some studies presume that ACEI are involved in reducing the incidence of stroke in population with high vascular risk. The aim of this paper is to study the potential effect of ACEI in primary prevention and in outcome of stroke.

Methods: we recruited 180 patients with ischemic stroke. Some of these patients (52%) were under the ACEI treatment at the moment of stroke. We assessed the effect of prestroke medication with ACEI.

Results: in the group of patients with pre-treatment with ACEI the severity of stroke were significantly low comparative with the group without this treatment (assessed with cranial MRI and clinical disability score). Also the treatment with ACEI before the stroke was associated with better outcome of stroke.

Conclusions: the treatment with ACEI is associated with a decreased the risk of severity of stroke. This effect is based on the angiotensin II blocking which leads to decrease of AT1 receptors activation, and, consequently to improved endothelial function. By endothelial function improved the neuronal protection in ischemic areas is achieved.

posters

ANKLE-FOOT ORTHOSIS IN POST STROKE GAIT REHABILITATION

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Objective: To determine the influence of ankle-foot orthosis on gait rehabilitation for hemiparetic persons with stroke

Design: Prospective, randomized, controlled study
Material and Method: We investigated patients with hemiparesis from stroke with 3 to 6 month of evolution after stroke. They were selected 40 patients that were able to walk 3 minutes with or without assistive device. Patients with associated pathology that can interfere with gait pattern were excluded from study (severe arthrosis, orthopedic pathology). Patients were divided in two groups, group A and group B. All patients were trained on treadmill, two sessions every day, for three consecutive weeks. Patients from group A had an ankle –foot orthosis during gait training and througout the daily activities and group B have no orthotic device. The gait assesment was done at the begining of the study and at the end by mesuring the step length and the walking speed.

Results: Patients from group A after three weeks of gait training showed that the use of the ankle-foot orthosis resulted in an significant increase in preferred walking speed and step length.

Conclusions: Gait performance in patients with stroke is typically characterized by decreased walking speed, decreases step length and increased energy cost. This will predispose patients to limit their activities of daily living and become deconditioned by inactivity. So, improving gait pattern is an important goal in rehabilitation. Using an ankle-foot ortothosis device improved gait pattern by increasing gait speed and step length.

posters

DECOMPRESSIVE CRANIECTOMY FOR MALIGNANT BRAIN EDEMA IN FIVE PATIENTS PRESENTING BRAIN INFARCTION DUE TO MIDDLE CEREBRAL ARTERY OCCLUSION-CLINICAL, IMAGISTIC AND INTRAOPERATIVE ASPECTS

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In patients with brain infarction due to middle cerebral artery occlusion treated only by conservative means, mortality rises up to 80% (Berrouschot et.co.,1998).
Recent European multicentric studies (Lancet, 2007) showed significant improvement of survival rate from 28 to 80% in cases treated by decompressive craniotomy.
Out of a group of 50 patients with brain infarction due to middle cerebral artery occlusion (Hancu, Davidescu et co., 2007) we present a number of five cases in which decompressive craniectomy was performed in the Department of Neurosurgery- County Emergency Clinical Hospital Constanta with the written permission from the patients families.
The criteria for the patient to undergo surgical treatment was a worsening of their clinical status combined with CT and/or MRI signs of intracranial hypertension.
In four cases, clinical and imagistic CT/MRI data are in correlation with intraoperative findings.

posters

NEUROREHABILITATION PARTICULARITIES IN VISUAL SPATIAL NEGLECT RIGHT HEMISPHERIC ISCHEMIC STROKE SUBJECTS THAT ASSOCIATE VISUAL FILED DEFICITS

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Introduction: Visuo-spatial neglect(VSN) is sometimes associated with visual filed deficits(VFD).Both are a negative predictors for neurorehabilitation.

Purpose: To determine if the association of VFDtoVSNin the right hemispheric acute ischemic stroke subjects determines a poorer neurorecovery when compared to VSNisolated.

Material and method: 48consecutive subjects were included with the following inclusion criteria:right hemispheric ischemic stroke confirmed by CT,orMRIwithin 12hours from admission,VSN,VFDor both at admission.There were two study groups:groupA–26subjects with VSNandVFD;groupB–22subjects with VSNonly.They were evaluated using the behavioral inattention test(BIT) and the NIHSScale at admission,7 and 21days.Both groups followed early rehabilitation from day one.

Results: In groupA the NIHSSmedian score at admission was 20.6points, 16.6at 7days, and 12.4at 21days.GroupB had a median NIHSSscore at admission of 19.8and 9.8at 21days.GroupA had a more severe neurological status on the NIHSS($p<0.001$,CI95%) at admission and at 7days,but statistically insignificant at 21days.However, in subgroup analysis at 21days,11patients continued to show VSNwhich was associated to an average 3points higher NIHSS score($p<0.001$;CI95%) when compared to VSNfree subjects.

Conclusions: The concomitance of VFDandVSN in right hemispheric ischemic stroke subjects is associated to a more severe neurological status during the first week of the disease onset.The persistence of VSNafter three weeks of evolution is associated to a poorer outcome on the NIHSSscale.

posters

SUCCESFUL TREATMENT WITH NEUROTROPHIC FACTORS IN BRAIN HEMATOMA

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AIM-to point that treatment in acute brain hematoma with neurotrophic factors is well received and has a high efiency.

METHOD-the study was made on 12 cases of brain hematoma,with small or medium dimensions,at pacients males and females,registred in neurological clinic .Usual, the hematomas appeared after high blood preasure crisis and the simptomatology join hemiplegia,afasia,sleep disorders,agitation,depression.

ROUTINE BLOOD TESTS-in general reveale high cholesterole,dislipidemia,some of them increased glicemia.

NEUROIMAGING of the brain reveale acute brain hematoma,small or medium
The patients were treated with 30 ml cerebrobrolysin daily.

CONCLUSION-beside treating the comorbidities and the reducing risk factors,the tretment with CRB in acute brain hematoma is quite reccomended.Clinical simtomatology was highly improved after 3-4 weeks and finaly,the patients were spectacularly recovered.
After the acute phase the patients continuated the treatment with 10ml/day,10 days/month,in the following 6 months

posters

BILATERAL FACIAL NERVE PALSY – UNUSUAL ONSET OF A T-CELL NON-HODGKIN LYMPHOMA

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Background:
Bilateral facial nerve involvement is a rare clinical sign of lymphomatous meningitis.
Leptomeningeal/CSF metastases or lymphomatous meningitis (LM) is the most common CNS complication of metastatic non-Hodgkin's lymphoma (NHL) and it is observed in 4 to 15% of all patients with systemic NHL.

Material and method:
A 49 years old male presented the onset of left peripheral facial palsy interpreted as Bell's palsy and treated with methylprednisolone. A right peripheral facial palsy occurred three weeks later. Neurological examination revealed: bilateral peripheral facial nerve palsy without ageusia and hypo/hyperacusia no other neurological signs and at general examination we observed a testicular tumor.
Cerebral MRI without gadolinium was normal, CSF examination showed 35 cells (predominantly lymphocytes). Surgical removal of the right testis was performed and hystological examination revealed malign lymphocite proliferation, diffuse, polymorphic, predominantly with large cells. Immunehistochemistry identified T cell CD3 positive.

Discusssion:
The patient was diagnosed with lymphomatous meningitis and T cell non-Hodgkin lymphoma, treated with methotrexate intrathecally, cranial radiotherapy and polichemotherapy.

Conclusion:
Lymphomatous meningitis is a rare cause of bilateral facial nerve palsy. One of the possible ethiologies of cranial nerve palsies may be non-Hodgkin lymphoma.

posters

A CASE OF PARRY-ROMBERG SYNDROME ASSOCIATED WITH CONGENITAL CARDIAC MALFORMATIONS.

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Introduction: Parry-Romberg syndrome, also known as progressive hemifacial atrophy is an uncommon disorder characterized by a slow and progressive atrophy, generally unilateral, of facial fat in the dermal and subcutaneous tissues. The muscles and bones of the face may be affected. Certain central nervous system abnormalities (headache, trigeminal neuralgia, facial palsy, seizures) referable to the ipsilateral side may be observed. The cause of this condition rests unknown. It is considered a form of lipodystrophy but the role of some neural growth factors are suggested. Trauma, viral infections, endocrine disturbances, autoimmunity and heredity are believed to be associated to the pathogenesis of this disease.

Case report: We report the case of a 31 years old woman with progressive left hemifacial atrophy. The reasons for neurological examination were frontal left headache with recent onset and asymmetry of the face. She had a history of atrial and ventricular septal defects which were surgically corrected at age of 17 years with no complications. The physical examination showed no neurological deficit but a mild facial asymmetry with discrete left deviation of lips and nose. CT scan reveals no cerebral or facial bones abnormalities (MRI not performed because of the thoracic metallic clips). The electrophysiological (electroencephalography and electromyography) investigations were negative. The fundus oculi examination was normal. The laboratory results yielded immunological abnormalities (including cerebrospinal fluid). Six months later, there was an aggravation of the clinical signs. The patient had visible left facial hemiatrophy with enophthalmy and tongue atrophy. Electromyografic examination revealed left nasalis muscle atrophy. The diagnosis of Parry-Romberg syndrome was established.

Discussion: This is a case of Parry-Romberg syndrome without major neurological complications but associated with congenital cardiac malformations, a previously not described association. Congenital cardiovascular malformations usually result from altered embryonic development of normal structures caused by genetic or environmental factors. Parry-Romberg syndrome may be also considered as a result of dysgenetic process originated during the first stages of embryogenesis. Therefore, we may speculate on the existence of a common causal factor for the two disorders, acting during fetal life.

Conclusion: The significance of this association is unclear but it doesn't seem to be fortuitous. The two conditions may share common etiopathogenic mechanisms linked to genetic or environmental causes present during embryogenesis.

posters

EFFICIENCY OF THE ADJUVANT TREATMENT WITH NEUROTROPHIC FACTORS IN THE REHABILITATION OF ISCHAEMIC STROKE PACIENTS

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Cerebrolysin is a mixture of peptides obtained by standardized biotechnological methods of enzymatic breakdown of purified porcine brain proteins. It's a neurotrophic and neuroprotective drug wich reduces excitotoxic damages, blocks overactivation of calcium-dependent proteases and scavenges free oxygen radicals in the ischaemic zone.

Aim: to study the efficiency of neurotrophic factors in pacients undergoing rehabilitation after cerebral infarction .

• Material and method: in this study were included 38 pacients, aged between 32-85 years, admitted for rehabilitation after brain ischaemic stroke, in the Department of Rehabilitation Medicine, within 3-6 weeks of onset. Patients with severe renal impairment, epilepsy or history of previous cerebral infarction were excluded.The patients were randomly divided in two groups of 19 patients each. Both groups received the specific basic medication for ischaemic stroke and a standard physical therapy.The study group received adjuvant treatment in daily dosage of 30ml IV in physiologic saline for 21 days.The patients were evaluated at the day of admission, the day of the discharge(after 21 days) and at four weeks after the discharge, by utilising clinic scales:

- Barthel Index (BI)-using Total Living Score (TLS) to quantify the assessment of the improvement in the BI
- Clinical Global Impression (CGI)
- MMSE (Mini Mental Status Examination)

Results: After three weeks of treatment, neurotrophic factors -treated patients demonstrated improvement in the BI, MMSE and CGI. There were five dropouts, only one due to adverse events(one patient reported a transient and mild in severity chill episode).

Conclusions: These results suggest that neurotrophic factors might be an useful treatment to improve the recovery of patients with ischaemic stroke and encourages the conduction of confirmatory clinical trials.

Key words: ischaemic stroke, rehabilitation.

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posters

EARLY DETECTION OF ENDOTELIAL DYSFUNCTION BY ULTRASOUND EXAMINATION OF CAROTID ARTERIES IN PATIENTS WITH LIVER CIRRHOSIS.

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Background: Atherosclerosis could be an important issue in patients with cirrhosis awaiting liver transplantation

Aim: Assessment of endothelial dysfunction syndrome by eco Doppler of carotid arteries in patients with liver cirrhosis.
Patients and methods 39 patients with liver cirrhosis with different ethiologies and Child scores, were admitted to Compartment of Gastroenterology of the City Hospital Timisoara.They undertook standard biochemical liver test, serum glucose and fat profile, titer of C reactive protein(CRP)..They also did upper digestive endoscopy, abdominal us scan.Carotidian eco Doppler images were acquired using an 8.0 MHz linear array transducer in a high-resolution ultrasound system ESAOTE MEGAS CVX/GPX.
We measured IMT(intima- media thickness) at the distal part of the commune carotid artery, Doppler parameters at the bilateral commune,internal and external carotid arteries.The plaque was defined as a focal thickening of the intima over 1,2mm with regard to the age and sex of the patients.

Results: 8 patients(20,51%), 5 men,3 women, mean age= 65,5±8,9 years
had a significant thickness of the intima.IMT over1,2 mm, specific velocity for atherosclerosis.Etiology of cirrhosis was C viral infection in 7 patients and alcoholic in 1 patient.The Child classification was:A=3 patients,B=4 patients,and C= 1.Clinical assessment revealed that 5 male patients had smoking history, 2 patients had metabolic synbrome with BMI over30 kg/m^2., diabetes mellitus 3 patients, mild hipertension 1 patient, positive CRP 5 patients. 4 patients had multiple cardio-vascular risk factors(10,25%), 3 of them with calcification at carotidian plaques. Early features of atherosclerosis were seen in12,82%(.5 patients) 4 with Child B score and 1 with Child C score. Advanced aspects of atherosclerosis with plaque calcification, significant narrowing of carotid arteries and clinical signs of ischemia were seen in 3 patients with Child A score, males, age over 62 years, smokers, diabetic and HCV infected.

Conclusions: Despite the classic view that patients with liver cirrhosis have a low cardio-vascular risk, ecoDoppler assessment of carotid arteries revealed specific features for endothelial dysfunction syndrome and atherosclerosis in 20,51%.These aspects should not be overlooked when evaluate patients awaiting for liver transplantation.

posters

ACTUAL TRENDS IN THE TREATMENT OF CEREBRAL VASOSPASM AFTER SUBARCHNOID HEMORRHAGE IN ORDER TO PREVENT SECONDARY BRAIN DAMAGE-AN OVERVIEW

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Cerebral vasospasm associated with aneurysmal subarachnoid hemorrhage (SAH) which is angiographically caracterized as the persistent luminal narrowing of the major extraparenchymal cerebral arteries, affects cerebral microcirculation and caused decreased cerebral blood flow and delayed ischemic neurological deficits. Autoregulation of the microcirculation is impaired during the vasospasm and cerebral blood flow is vulnerable to change due to the changes of arterial blood pressure.
Vasospasm is the most frequent complication of SAH that occur in 20-40% of patients with ruptured aneurysms and determine a mortality between 40-60% of cases within 30 days from the aneurysm rupture. One of the most important and critical aspects of SAH-induced vasospasm is its failure to consistently respond to treatment. Pharmacological interventions have been tried in experimental models and clinical trials with only partial success.

A large number of studies on this subject brought us new data who require the reconsideration of the actual methods of clinical therapy of the vasospasm, due to a new approach of the molecular mechanisms and microcirculation studies.
Actual methods in the treatment of the cerebral vasospasm secondary to aneurysmal rupture include the next:
-surgical evacuation of the clots, when mass effect hematomas occur
-clipping the aneurysm in the first 48 hours after the rupture with evacuation of the blood located in the basal cisterns
-calcium channel blockers administrated orally or i.v, the most used being nimodipine.
-routine "3H"therapy, including hypertension, hypervolemia and hemodilution when the biological and neurological status of the patient allows
-transluminal angioplasty in cases resistant to the medical treatment.
-pharmacological dilatation of the arteries by local or intra-arterial administration of papaverine or nimodipine.
All these methods can not treat efficiently the vasospasm, even in the situation of adequate surgical clipping, and in some of the patients, on unpredicted criteria, vasospasm evolves severely to decease. Actual treatment did not address to the vasoconstrictor elements but to the collateral circulation ("3H" therapy), or directly to the vessels (angioplasty). Molecular effects of the vasospasm associated to the subarachnoid hemorrhage are not yet precise.

(continued next page)

New therapeutic trends of this intractable effect include:

- nitrous oxide supplements directly into the arterial walls by intrathecal administration of sodium nitroprusiate or levo-arginine
- endotelin releasing factors
- blocking the inflammatory response in involved in the development of the vasospasm with lazaroids or high doses of glucocorticoids, ibuprophen or U-74006 aminosteroid.
- administration of local anesthetics or serotonine antagonists
- gene therapy for inducing the increase of specific proteins in the arterial wall-unavailable yet.
- nicardipine has been used to treat cerebral vasospasm in patients withaneurysmal subarachnoid hemorrhage. Intra-arterial infusion of high concentrationsof nicardipine decreases procedure time, but it may affect hemodynamic parameters. In addition, a quantitative measurement of improvement of vessel diameter on the angiograms has not been performed.
- the pharmacological treatment of cerebral vasospasm now includes the experimental use of controlled-release biocompatible compounds that deliver a desired drug locally into the subarachnoid space. A controlled-release system consists of an active material that is incorporated into a carrier, usually in the form of a pellet or a gel. With such systems, the desired agent is delivered slowly and continuously, for long periods of time, directly to the desired site. This technology makes it possible to achieve high local concentrations of therapeutic agents while minimizing systemic toxicity and circumventing the need to cross the blood-brain barrier. This review describes controlled-release systems developed to date for local drug delivery in the treatment of cerebral vasospasm in both animal models and humans. Recent studies agree for a new protocol in the clinical treatment of the vasospasm in the favor of normotension and normovolemia and hemodilution, who seems to be more adequate in prevention of the delayed infarction events, but clinical studies did not confirm this ipothesis.

The previous method of therapy"3H" could not to be changed after more of two decades, despite of his limitations, and probably soon, other specific techniques will improve the surviving and morbidity.

Subarachnoid hemorrhage remains a devastating manifestation of cerebrovascular disease that results in the deaths of approximately 30 to 50% of affected patients

posters

NEUROTROPHIC FACTOR FOR CHRONIC SPINAL CORD INJURY

St M Iencean, N Ianovici , AV Ciurea

We present our experience of seven patients with spinal cord injuries and the results of the microsurgical resection of the spinal scar and the implant of bone-marrow tissue in the site of the spinal cord lesion.

Methods: Seven patients with chronic thoracic spinal cord injury and paraplegia underwent a laminectomy to expose the site of the spinal cord injury and partial resection of the medular scar and implant of bone-marrow tissue with a mixture of drugs in the site of spinal cord injury .
Postoperatively all patients received the similar treatment in the neuromotor rehabilitation centre. . Four patients were treated with neurotrophic factors : three patients received 5 - 10 mL/day for three to five months and one patient have received 10 mL/day for 24 months postoperatively.

Results: Sensory improvements were noticed to all patients , but no significant motor improvements were observed twelve to eighteen months afterwards.
The patient with T10-T11 complete spinal cord injury five years earlier received neurotrophic factors two years postoperatively. The result is the complete sensory recovery , return of sensation of passive legs movements, return of bladder control and return of both patellar reflex .

Conclusions: This surgical procedure consist of microsurgical remove of the spinal cord scar and implanting of the bone-marrow tissue into the spinal cord injury site .

Only the patient who received neurotrophic factors postoperatively for two years and the neuromotor rehabilitation treatment have complete sensory recovery and return of bladder control and return of both patellar reflex. Therefore the neurotrophic factors werethe neurotrophic factors were clinically effective in the treatment for a long time of one patient with chronic spinal cord injury.
This result is promising, but much follow-up work is needed to document long-term benefits.

posters

NEUROPROTECTION BY THIOPENTAL AND BARBITURIC ACID DURING OXYGEN-GLUCOSE DEPRIVATION

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Background: Reports of barbiturate neuroprotection in cell culture models independent of neurovascular effects are variable: protective against high dose(1) but harmful with lower dose NMDA(2), no effect with anoxia(1), harmful with glucose deprivation(1), and protective with oxygen-glucose deprivation(OGD)(3). Harmful effects have been attributed to inhibition of the mitochondrial respiratory chain(2). It is possible that some protection derives from the antioxidant effects of the barbituric acid moiety, independent of its effects on neuronal metabolism. We have tested the effect of thiopental and barbituric acid during oxygen-glucose deprivation.

Methods: Organotypic hippocampal slice cultures were prepared from neonatal (8-11 days old) rats, cultured for 14 days, then exposed to OGD for 60 min in serum free medium at 37 C, under a gas phase of 95% nitrogen and 5% carbon dioxide, using methods similar to those previously described(4). Test compounds were present from 30 min prior to OGD until 24 hours after OGD. Neuronal death was assessed at 24 hr by fluorescence microscopy with propidium iodide(PI), by calculating the percentage area of the CA1 region in which PI fluorescence occurred above background. N=24 cultures for each test compound concentration, and N=48 for OGD alone.

Results: Neuronal death was 39.2±3.5% (SEM) for OGD alone, and was fully attenuated to 0.1±0.07% by the control free-radical scavenger MnTBAP 0.1 mM. Thiopental was neuroprotective at 0.05 mM (17.6±2.8% death), 0.10 mM (9.3±2.8% death), and 0.30 mM (11.4±2.7% death). Protection by 0.05 mM barbituric acid was not statistically significant (28.7±3.8% death), but was significant at 0.10 mM (18.7±3.1% death) and 0.30 mM (19.6±3.3% death).

Conclusions: The data presented confirm that thiopental at clinically used concentrations is neuroprotective against OGD in hippocampal slice cultures. Surprisingly, barbituric acid was also neuroprotective in similar concentrations. Literature review suggests that this is the first test of barbituric acid for possible neuroprotection. Barbituric acid is not an anesthetic, and does not inhibit the mitochondrial respiratory chain as do the barbiturates. Barbituric acid and the barbiturates are effective free radical scavengers, suggesting that this may be a component of barbiturate neuroprotection. Further studies will be required to confirm this hypothesis.

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posters

THE EVALUATION OF NEUROPROTECTIVE EFFECT IN ALZHEIMER'S DISEASE WITH PSYCHOTIC SYMPTOMS ON ANIMAL MODEL

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Aims/Objectives:
The Alzheimer's disease with psychotic symptoms model on animal experiment is validated through the cholinergic blockade and dopaminergic agonists (bromcriptine). The neurodegenerativ-type mechanisms is accelerated by hypoxia, vascular ischemia and D2 Receptors blockade realised by Haloperidole. The neurotrohic factors can realise neuroprotection towards hypoxia and ischemia and potentially towards D2 Receptors blockade.

Methods:
We evaluated the neuroprotective role on animal model (Winstar rat), within the cholinergic blockade with vascular component.
We studied 8 lots of 5 adults rats each, held in temperature, humidity, food and ambient stressless conditions.

N1 – cholinergic blockade;
N2 – neurotrophic factors +cholinergic blockade;
N3 – cerebral ischemia +cholinergic blockade;
N4 – cerebral ischemia +cholinergic blockade +neurotrophic factors;
N5 – haloperidole;
N6 – cholinergic blockade + haloperidole;
N7 – cholinergic blockade +haloperidole +neurotrophic factors;
N – control;

A single dose (5ml/kg/day) of neurotrophic factors was administrated 10 days before and 7 days after the cholinergic blockade, cerebral ischemia or haloperidole. The rats were sacrificed during the 18th day, 6 hours after the last administration.

Results:
The cholinergic blockade produces changes in frontal cortex and hippocamp, the ischemia and D2 Receptors blockade amplifies the lesional changes. The neurotrophic factors decreased these changes.

Conclusions:
The neurotrophic factors prove it's neuroprotective value in Alzheimer's Disease with psychotic symptoms.

posters

AXOTOMY INDUCED REGENERATIVE CHANGES IN THE SCIATIC NERVE OF CIRRHOTIC RATS

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Introduction: Liver cirrhosis is characterized by the structural alterations of the liver parenchyma due to increased production and deposition of collagens. Cirrhosis ultimately leads to hepatic encephalopathy, a condition characterised by impaired brain functions. However, studies on the effect of cirrhosis on peripheral nerve structure and axonal regeneration are lacking. Therefore, the focus of this study is to understand the structural and axotomy induced regenerative changes that occur in the sciatic nerves of cirrhotic rats.

Materials and methods: Adult male Wistar rats were used in this study. Cirrhosis was induced using a hepatotoxic drug, thioacetamide that is commonly used to induce liver cirrhosis in experimental animals. For studies on nerve regeneration, the animals were anaesthetized and the left sciatic nerves were transacted at mid-thigh level and the animals were allowed to recover. Three, five and seven days following surgery, the animals were anaesthetized and distal and proximal end of the transected sciatic nerves were removed and processed routinely for light and electron microscopic observation.

Results: Light and electron microscopic studies indicate that the nerve fibers in cirrhotic rats were of small diameter as compared to that of the control rats. Delayed axonal regeneration was noticed in the sciatic nerve of cirrhotic rats. Further studies have shown that the level of cellular antioxidant enzymes such as superoxide dismutase and glutathione peroxidase were significantly low in the serum of cirrhotic rats as compared to normal animals, suggesting that free radicals may be involved in the development of neuropathies and other hepatic disorders in cirrhotic animals.

Conclusion: In conclusion, the data presented in this study suggest that cirrhosis leads to abnormalities in the peripheral nerve structure that could lead to various neurologic symptoms including changes in reflexes and delayed axonal regeneration.

Key words: Sciatic nerve, Axonal regeneration, Free radicals, Superoxide dismutase, Glutathione peroxidase

posters

MYOCARDIAL INFARCTION – POSSIBLE NEUROPROTECTIVE MECHANISM BY REMOTE ISCHEMIC PRECONDITIONING IN CEREBRAL ISCHEMIC STROKE SUBJECTS

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Background: Cerebral stroke risk after myocardial infarction is 0.6%-2.5%, but laboratory studies show the possibility of remote organ ischemic preconditioning in case of heart and brain, offering a better tolerance to ischemia if an ischemic precedent occurs in the other organ's vascular territory, with respect to a time frame.

Purpose: To find the relationship between the severity of stroke in MI and stroke subjects when compared to singularly cerebral stroke subjects.

Material and method: There were included 97subjects, 50with MI and cerebral stroke within 2-6days from the MI, and 47subjects as age–sex–matched control group of stroke solely individuals. The inclusion criteria were:confirmed ischemic stroke by CTor MRIexam, time frame compliance(stroke occurred at day 2-6from MI), EKG or enzymes suggested/excluded MI. The subjects were assessed using the NIHSS as well as ankle–brachial index measurement, pulse pressure, TC/HDL-c ratio, and history of cardiovascular diseases monitored.

Results: Significant correlations were found among the vascular risk factors and stroke severity in both groups(ABI<0.9,CT/HDL-c>5.4,AF;p<0.001). The MI and stroke group showed a higher incidence of CVDhistory, peripheral-artery-disease or dyslipidemia. The NIHSSscores at admission, 15days, and at 30days revealed that there is a significant lower severity of stroke in MI and stroke subjects at admission (-4points on the scale,p<0.001,CI95%,-6.08--1.77) that is still statistically significant at 30days of evolution (-3points on the scale,p<0.001,CI95%,-4.25--1.24) when compared to the control group.

Conclusion:MI and stroke subjects associate more CVrisk factors, but they are likely to present milder strokes with better clinical evolution at 30days when compared to solely stroke subjects.

posters

CAROTID ATHEROMATOSIS IN OBESE PATIENTS WITHOUT NEOUROLOGICAL SIGNS OF DISEASE

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Objectives: To analyze the correlation between cerebrovascular atheromatosis and metabolic impairment (obesity and metabolic syndrome).

Methods: We studied a group of 90 obese patients (54 patients with metabolic syndrome and 36 patients without metabolic syndrome), with a normal neurological examination, aged 35 years or older, referred to Elias University Hospital of Emergency between September 2007-October 2008. We used a standard protocol of clinical and paraclinical investigations, that included determination of all components of metabolic syndrome, according to NCEP ATP III criteria, and presence of atheromatous plaques by Doppler ultrasonography method. Data obtained were analyzed using descriptive statistic methods.

Results: We found carotid atheromatosis in 20% (N=18) of the patients. In the subgroup of patients with carotid atheromathosis, mean age (48.44 years) was greater than in the subgroup of patients without carotid atheromatosis (N=72, mean age 46.02 years). Metabolic syndrome was present in 10 (55.5%) patients with carotid atheromatosis, and in 44 (61.1%) patients without carotid atheromatosis. Triglycerides mean values were greater in the subgroup of patients without carotid atheromatosis (152.5 vs. 121.7) and mean values difference between the subgroups was statistically significant (p=0, 0403), while in the same group adiponectin mean values were lower (13.78 vs. 17.16), but without statistical significance.

Conclusions:

1. Carotid atheromatosis is present in a significant proportion of obese patients without clinical manifestations.
2. Metabolic syndrome doesn't represent a risk factor for focal atheromatosis, but can be correlated with increase of intima-media thickness (a marker of extended atherosclerosis)

posters

STUDY ABOUT RELATIONSHIP OF ROPINIROLE AND COGNITIVE STATE IN PATIENTS WITH PARKINSON`S DISEASE

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Objective:
The goal was to assess the influence of ropinirole in the cognitive profile of early Parkinson`s Disease (PD) patients.

Methods:
We studied 26 patients(10 men and 16 women) admitted to Clinic of Neurology from Craiova during 6 months. They presented age between 62 and 67 years, at least 9,5 years of education, established diagnosis of PD in stage I or II on Hoehn and Yahr Scale. The patients received monotherapy with dopamine agonist (ropinirole in doses≤ 7,5 mg/day).We assessed the cognitive state using Mini Mental State Examination(MMSE) and Montreal Cognitive Assessment(MoCA) at baseline, 3 months and 6 months later.The results were analysed by Student test.

Results:
The mean values for the MMSE assessment were: at baseline 28,1;after 3 months 28,4 and 6 months later 28,6($p<0,05$).
The mean scores for MoCA test were: at baseline27,5 points;at 3 months 27,7 and at 6 months follow-up 27,9($p<0,05$).

Conclusions:
We observed that the use of ropinirole did not impaire the cognitive profile of PD patients. However, it is unclear whether ropinirole have any neuroprotective role; further studies are required to identify any neuroprotective activity of ropinirole.

posters

COGNITIVE FUNCTION AND DIABETES MELLITUS IN THE ELDERLY

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The objective of the study was to establish the influence of diabetes mellitus on cognitive function in the elderly. We investigated 187 consequently admitted elderly patients with diabetes mellitus. The age range was 65 to 85 years, mean age 75, and 73% were women and 27% men. Two age groups were considered: young-old (65-74 years) and old-old (75-85 years). Patients with a past medical history of stroke and dementia were excluded. Patients with a score of 8 or more on the Short version (15 items) Geriatric Depression Scale (Yesavage) were also excluded. Cognitive function was evaluated using MMSE, Clock-drawing Test, Five Words Test and Stroop Test (score >42 was considered normal). We used HbA1c to assess long term response of the patients to anti-diabetic treatment (>7% was considered abnormal). Irrespective of age-group, a past medical history of diabetes mellitus >10 years correlated with a higher prevalence of mild cognitive impairment (correlation coefficient r=0.88). There was a significant difference between the scores on Five Words Test and Stroop Test in patients with HbA1c >10% as compared to those with HbA1c < 7% ($p<0.001$) irrespective of age-group and gender. A poor control of diabetes mellitus could be a significant risk factor for cognitive impairment in the elderly. Moreover, diabetes mellitus itself makes these patients prone to cognitive impairment possibly due to macro- and microvascular complications of this metabolic disease. A systematic screening of cognitive function needs to be performed in elderly diabetics in order to establish an early diagnosis of mild cognitive impairment and to start an adequate and timed therapy.

posters

DUAL DIAGNOSIS OF SCHIZOPHRENIC IN – PATIENTS – AN OBSERVATIONAL STUDY

D. Prelipceanu, MD, PhD, Elena Calinescu, MD, Laura Ghebaur, MD

Schizophrenia is a disabling psychiatric disorder and patients frequently abuse other substances to compensate decreasing level of social abilities and integration.

Aims. This article reviews several aspects of dual diagnosis among people with schizophrenia, including the prevalence of this co – occurrence, biological and psychosocial factors that contribute to this relationship, the effects of DD on the course and outcome of schizophrenia considering the frequnce of relapses, the hospital re – admissions and their duration, treatment issues, and indirect public policy implications.

Methods. A retrospective analysis of 525 in – patients, 18 – 64 years old, medical records, with ICD – 10 diagnosis of schizophrenia was conducted in Clinical Psychiatric Hospital "Al.Obregia", in Bucharest.

Results. General data concerning frequency of DD were comparable with the literature data. However alcohol abuse and addiction are probably underdiagnosed, and failed to become a traitment target in a frame of rehabilitation approaches when patients are between hospital admissions, and there are not an objective of medical interventions for these patients with multiple needs in the community.

posters

PREDICTIVE FACTORS FOR COGNITIVE DETERIORATION IN ALCOHOLISM

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Background:
The dis-adaptative use of alcohol is correlated with the dopaminergic deficit by decreasing the neurotransmitter's secretion and/or D2 receptors, leading to cortical-subcortical disconectivity, with direct impact on the cognitive function.

Objectives:
Identify symptoms and their evolution induced by alcohol addiction, correlated with the cognitive deficit.

Method and Results:
In a 10 years retrospective study, on 680 patients diagnosed with addiction disorder according to DSM IV –R, 35% presented a withdrawal syndrome, with or without psychotic elements. Out of these, 10 % repeated the withdrawal, 10% presented epilepsy crisis. 13% of all patients developed psychotic disorders. The alcohol use was restarted in 91% of patients after first admission. In 30% the deterioration index was low, by alterarea thinking functions. Out of them, for 45 % computer tomography highlighted cerebral atrophy, mainly in the frontal lobe.

Conclusions:
Patients with multiple withdrawal episodes, epilepsy crisis and psychotic decompensations presented cognitive deterioration, highlighted by cerebral atrophy.
Abstinences, even with restart of alcohol use, represent protection factors for the cognitive function.
The patients whose therapeutic scheme included the neuroprotection factor presented some sort of standstill in the deterioration of the cognitive function, even if for 40% of them the alcohol use was restarted.

posters

THE QUANTIFICATION OF BRAIN INFARCT VOLUME AND WATER CONTENT AFTER TREATMENT WITH CLINICALLY USED NEUROPROTECTIVE DRUGS

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We tested the infarct volume and water depletion capacity of 5 drugs on an experimental animal model of focal cerebral ischemia.The animals were Wistar-Bratislava rats from the animal breeding facility of Cluj-Napoca University of Medicine.We used 6 groups of 30 animals each (5 controls and one witness).The drugs were administered intraperitonealy

From each group ten brains were used to quantify the cerebral edema. The rest of the brains in each group were included in paraffin and cut. The infarct volume was calculated using the thionine stained sections. All drugs showed reduction of the infarct volume compared to the controls.

We also evaluated the water content in each of the 6 groups. All drugs manage to reduce the water content , with neurotrophic factors reducing it with 12,38%, whereas the others reduced it with aprox 4,85 %.

posters

THE QUANTIFICATION OF NEURONAL APOPTOSIS AFTER TREATMENT WITH CLINICALLY USED NEUROPROTECTIVE DRUGS

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We tested the neuronal apoptosis on an experimental animal model of focal cerebral ischemia, after treatment with five clinically used drugs. The animals were Wistar-Bratislava rats from the animal breeding facility of Cluj-Napoca University of Medicine.We used 6 groups of 30 animals each (5 controls and one witness).The drugs were administered intraperitonealy.

The apoptotic cells were marked with propidium iodide, DAPI (4',6-diamidino-2-phenylindole), caspase 3, PARP. By comparing the apoptosis markers and neuronal markers, we could determine the percentage of apoptotic neurons. The comparison was made between propidium iodide and sinaptophysin and between DAPI and presenilin.

The average number of apoptotic cells droped significantly in the treated groups compared with the controle.

posters

COGNITIVE PERFORMANCES IN PATIENTS WITH LEUCOARAIOSIS TREATED WITH NEUROTROPHIC FACTORS

Diana Stanca, Cornelia Zaharia, Carmen Albu, Oana Alexandru, Valerica Tudorica, Denisa Pirscoveanu, Olivian Stovicek
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Objective: The aim of our study was to evaluate the cognitive decline in the patients with leucoaraiosis treated with neurotrophic factors.
Patients and method: A number of 27 elderly subjects (16 women and 11 men) aged between 64 and 80 years who were diagnosed with leucoaraiosis on cerebral MRI were enrolled in our study. The subjects were selected to have at least 8 years of education. The patients were divided in two groups:

- Group A composed of 15 patients (9 women and 6 men) with medium age 67,2 years who received Cerebrolysin 10 ml/day two weeks in a months for 3 months consecutively.
- Group B composed of 12 patients (7 women and 5 men) with a medium age 69,4 years who did not receive neurotrophic factors.

All the patients received proper treatment for the risk factors (arterial hypertension, diabetes mellitus, hypercholesterolemia).
We performed to each patient Mini Mental State Examination (MMSE), Trail Making Test Part B, Digit Span Test Forward and Digit Span Test Backward, and Word Fluency Test.
We evaluated the patients in the beginning of the study and then one month, three months and six months later. The results were analyzed by Student's Test.

Results: The patients in group A obtained significantly statistic improvement of the scores at the end of the study. The patients in group B obtained insignificantly statistic improvement of the scores in the end of the study.

Conclusion: The patients who received neurotrophic factors had a better evolution of cognitive performances.

posters

ANTIPHOSPHOLIPID ANTIBODIES AND COGNITIVE IMPAIRMENT IN INFLAMMATORY SYSTEMIC DISEASE PATIENTS

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The antiphospholipid syndrome (APS) is defined by the presence of antiphospholipid antibodies (aPL), associated with thrombosis or recurrent spontaneous abortions. APS can occur alone or secondary to other conditions, especially associated to inflammatory systemic autoimmune diseases. Among the neurological manifestations associated with aPL, only ischemic stroke is recognized by the actual classification criteria for APS. Dementia and cognitive impairment have been, however, reported in case studies of APS patients, and neurodegeneration related to aPL was proposed as alternative mechanism to ischemia. We studied retrospectively the association between cognitive impairment, cerebral ischemia and aPL in 428 patients with inflammatory connective tissue diseases admitted in the Neurology and Internal Medicine Departments of Colentina Hospital-Bucharest. Patients with cognitive features that could be influenced by the treatment were excluded. 82 (19,2%) patients had cognitive deficiencies (all types considered). We found no relevant association between aPL and cognitive impairment (P = 0.5; OR= 1.2, 95% CI: 0.7 - 1.9). In patients with cognitive impairment, there was a slightly significant association between aPL and cerebral ischemia (P = 0.05. OR= 2.8, 95% CI: 1.0 - 7.6). Several error factors could influence the results: lack of accurate neuropsychological examination; occurrence of several other mechanisms in the genesis of cognitive disorders. Further study is needed in patients in which ischemia is not involved in the genesis of cognitive impairment, aiming to isolate patient profiles for whom alternative neurodegenerative mechanisms can be discussed.

posters

STUDY ON COGNITIVE PERFORMANCES IN THE PATIENTS WITH VASCULAR DEMENTIA TREATED WITH NEUROTROPHIC FACTORS

Valerica Tudorică, Cornelia Zaharia, Diana Stanca, Denisa Pirscoveanu, Oana Alexandru, Carmen Albu, Olivian Stovicek
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Objective: The aim of our study was to evaluate the evolution of cognitive performances in the patients with vascular dementia treated with neurotrophic factors.

Patients and method: We studied 25 patients (11 women and 14 men) aged between 65 and 80 years who fulfilled NINDS-AIREN criteria for diagnosis of vascular dementia. We also calculated for each patient Hachinski Ischemic Score. The patients were divided in two groups:

- Group A composed of 15 patients (7 women and 8 men) with medium age 67,2 years who received Cerebrolysin 10 ml/day two weeks in a months for 3 months consecutively.
- Group B composed of 10 patients (4 women and 6 men) who did not receive neurotrophic factors.

All the patients received proper treatment for the risk factors (arterial hypertension, diabetes mellitus, and hypercholesterolemia).
We performed to each patient Mini Mental State Examination (MMSE), Hierarchic Dementia Scale (HDS), Quality of Life in Dementia (QLD) and Activities of Daily Living (ADL) Index.
We evaluated the patients in the beginning of the study and then one month and three months later.
The results were analyzed by Student's Test.

Results: The patients in group A obtained in the beginning of study 22,6 points on MMSE, 256,2 points on QLD, 165,2 points on HDS and 28,4 points on ADL-Index. These scores improved significantly statistic on QLD, ADL-Index and MMSE in the end of the study. The patients in group B obtained insignificantly statistic improvement of the scores in the end of the study.

Conclusion: The patients who received neurotrophic factors had a better evolution of cognitive performances.

posters

DEPRESSION AND DEMENTIA

Catalina Tudose, Florin Tudose

The presentation reviews the clinical and assessment particularities of Late Life Depression in the daily psychiatric assessment practice. There are mentioned the difficulties in recognition and differentiation of depression in elderly, taking into account the important somatic comorbidity as well as the multiple psychotraumatic events specific for this life stage.

Depression in late life, whether is Early Onset Depression and Late Onset Depression is often associated with cognitive impairments. Historically these cognitive deficits had been regarded as benign and reversible (referred as pseudodementia or depression with reversible dementia); now it is recognized that many such patients experience persisting cognitive impairment after amelioration of depression or are in the process of developing a diagnostically distuinguishable dementia that became unmasked by the presence of depression.

Some other depression can be etiologically linked with cerebrovascular diseases; the high risk of relapse and recurrence of major depression, specific clinical features as cognitive deficits, psychomotor retardation, reduced interest in activities, neurological syndromes, associated with executive dysfunction.

Post-Stroke Depression is another clinical condition that needs attention
Complex evaluation both clinical (performed by a multidisciplinary team) and paraclinical (neuroimaging investigations) means a modern approach of this particular pathology.

posters

THE NEUROPROTECTIVE EFFECT OF NEUROTROPHIC FACTORS IN CHARCOT-MARIE-TOOTH DISEASE

Vitalie Vacaras[1], Damian Popescu[1], Zoltan Zsigmond Major[2], Mariana Marginean[3], Radu Antonescu[4], Ioan Marginean[1]
1. University of Medicine and Pharmacy Cluj, Neurology Department
2. University of Medicine and Pharmacy Cluj, Pharmacology Department
3. University of Medicine and Pharmacy Cluj, Histology Department
4. County Emergency Hospital Cluj, Neurology Department

Purpose: Charcot-Marie-Tooth disease is a heterogeneous, inherited, neurological disorder that is characterized by loss of muscle tissue and touch sensation, predominantly in the feet and legs but also in the hands and arms in the advanced stages of disease. Our purpose was to evaluate the neuroprotective effectat a pacient with Charcot-Marie-Tooth disease type II, using clinical evaluation and electromyography.

Methods: Cerebrolysin 10ml was administered to a patient diagnosed with CMT disease type II every 3rd day for 3 months, with a 3 month pause, over a period of 2 years. Clinical evaluation and EMG were performed at the inclusion and after 2 years of drug administration.

Results: Conduction velocities on peroneal, tibial, median and ulnar nerves were not modified after 2 years of drug administration.

Conclusion: Taking into account the degrading, progressive evolution of CMT disease, use of neurotrophic factors may prove usefull in slowing down the progression of this illness. Further, ongoing research on wider number of patients is needed to confirm this.

posters

STUDY ON COGNITIVE PERFORMANCES IN THE PATIENTS WITH MULTIPLE LACUNAS TREATED WITH NEUROTROPHIC FACTORS

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Objective: The aim of our study was to evaluate the evolution of cognitive performances in the patients with multiple small ischemic infarcts treated with neurotrophic factors.

Patients and method: We studied 63 patients (33 women and 30 men) diagnosed with multiple small ischemic infarcts, aged between 65 and 75 years, at least 8 years of education and no previous psychiatric disorders. The diagnosis was sustained by CT scan exam which revealed between 3 and 10 lacunas for each patient, associated with cerebral atrophy in some patients. The patients were divided in two groups according to the treatment:

- Group A composed of 35 patients (17 women and 18 men) who received Cerebrolysin 30 ml/day for two weeks and then 10 ml/day 10 days in a month for two months consecutively;
- Group B composed of 28 patients (16 women and 12 men) who did not receive Cerebrolysin.

All the patients were properly treated for the risk factors (hypercholesterolemia, arterial hypertension, diabetes mellitus).
We assessed the cognitive performances of the patients by Mini Mental State Examination (MMSE), Activities of Daily Living (ADL)-Index and The Clock Drawing Test (CDT).
The patients were evaluated in the beginning of the study, one month and two months later. The results were analyzed by Student's Test.

Results: In the beginning of the study the patients in both groups obtained scores below those corresponding to their age and educational level on MMSE and The Clock Drawing Test. In the end of the study the patients in group A had significantly statistic better performances in comparison to group B.

Conclusion: The treatment with neurotrophic factors improved cognitive performances in patients with multiple small ischemic infarcts.

posters

ABNORMAL WAVEFORMS OF THE FLASH VEPS IN SUBJECTS WITH MS

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3- University of Medicine and Pharmacy Cluj, Histology Department

Purpose: Pattern reversal visual evoked potentials frequently present abnormal morphology, such as bifid P100, W shaped P100 or oscillatory activity in patients with diseases of the visual pathways. Our purpose was to evaluate if similar changes appear with the flash technique also.

Methods: VEPs were recorded in 36 MS patients with EDSS score lower than 3,5. Reference values were taken from the Visual evoked potential standard (2004).

Results: 72,22% of the recorded VEPs presented pathological signs. Conventional VEPs were replaced by abnormal waveforms in 44,44%, 30,56% with W shape and 13,89% oscillatory activity. 12,5% of these were monocular presences of the abnormal shape, the remaining 87,5% binocular. The frequency of the abnormal shapes was slightly, elevated in men, compared to women, significantly only for the oscillatory activity (18,18% vs 12%). Among the patients with normal waveforms, 47,37% presented prolonged P2 latency, 21,05% binocular and 26,32% monocular prolongation.

Conclusion: The presence of abnormal waveforms in such an elevated percent can be seen as an indicator of impaired visual pathway functions in low EDSS score MS patients using the flash VEPs, even if in these cases P2s are ambiguous. Further, ongoing research on wider number of patients is needed to confirm this.

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THANK YOU