SNC'13

SiNAPSA Neuroscience Conference '13

Ljubljana, Slovenia, September 27-29, 2013

CELLULAR NEUROSCIENCE

SYSTEMS NEUROSCIENCE

CLINICAL NEURO SCIENCE

COGNITIVE NEUROSCIENCE

CLINICAL NEUROSCIENCE

MOLECULAR NEUROSCIENCE

MOLECULAR NEUROSCIENCE

Sinapsa Neuroscience Conference '13
Faculty of Medicine, Ljubljana, 27–29 September 2013

Organised by
SiNAPSA, Slovenian Neuroscience Association and
Faculty of Medicine, University of Ljubljana

SNC'13 Programme Committee
Maja Bresjanac (Chair), David Neubauer, Peter Pregelj, Boris Rogelj, David B. Vodušek

SNC'13 Organising Committee
Blaž Koritnik (Chair), Jure Bon, Mateja Drolec Novak, Judita Jeran, Grega Repovš, Martina Starc

YNFL'13 Organising Committee
Nadja Jarc (Chair), Simon Brezovar, Matej Markota, Miha Pelko, Klara Tostovršnik

Conference was supported by
Lundbeck, Janssen, Genzyme, Apta Medica, Krka, Droga Kolinska, City of Ljubljana

Editors
Judita Jeran, Blaž Koritnik

Design
Katja Komljanec Koritnik, Damjan Osredkar, Grega Repovš

Publisher
SiNAPSA, Slovenian Neuroscience Association
www.sinapsa.org

CIP – Kataložni zapis o publikaciji
Narodna in univerzitetna knjižnica, Ljubljana

616.8(082)
612.8(082)

SINAPSA Neuroscience Conference (2013 ; Ljubljana)
Book of abstracts / Sinapsa Neuroscience Conference '13, Ljubljana, Slovenia, September 27-29, 2013 ; organized by Sinapsa, Slovenian Neuroscience Association and Faculty of Medicine, University of Ljubljana ; editors Judita Jeran, Blaž Koritnik. - Ljubljana : Sinapsa, Slovenian Neuroscience Association, 2013

Način dostopa (URL): http://www.sinapsa.org/SiNC13/media/files/SNC13_Book_of_Abstracts.pdf

ISBN 978-961-91704-5-8
1. Jeran, Judita, 1984- 2. Sinapsa - Slovensko društvo za nevroznanost 3. Medicinska fakulteta (Ljubljana)
268905728

SNC'13

SiNAPSA Neuroscience Conference '13

Ljubljana, Slovenia, September 27-29, 2013

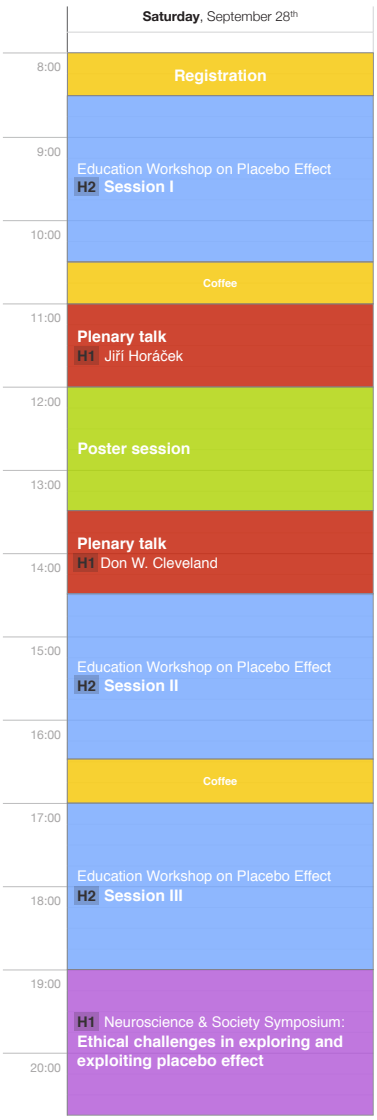
Book of Abstracts

www.sinapsa.org/SiNC13

Faculty of Medicine, University of Ljubljana, Slovenia
27—29 September 2013

Contents

Schedule at a glance



SNC'13

SiNAPSA Neuroscience Conference '13

Ljubljana, Slovenia, September 27-29, 2013

SiNAPSA Neuroscience Conference '13 Programme

www.sinapsa.org/SiNC13

Faculty of Medicine, University of Ljubljana, Slovenia
27—29 September 2013

SiNAPSA Neuroscience Conference ’13 Programme

Friday, 27 September

8:00—19:00 **Registration** | Foyer 24

8:30—10:30 **Young Neuroscientists Forum Ljubljana ‘13** | Hall II 53

8:30 **Neural stem cells-enriched tubulization improves anatomical and functional restoration of the severed rat sciatic nerve**
Stefano Frausin

8:45 **Early exposure to enriched environment reverses learning deficits and improves hippocampal neuron survival in rats with selective cholinergic lesion**
Pela Bisatti

9:00 **Effects of cognitive remediation during 14-day bed rest on walking performance of older adult men**
Uroš Marušič

9:15 **Cognitive emotion regulation of aversive emotional responses and their prediction recruits a common regulatory system**
Satja Mulej Bratec

9:30 **Tract-specific and global white matter alterations in healthy ageing**
Rok Berlot

9:45 **Characterization of cognitive deficits in rats with selective cholinergic, noradrenergic and dopaminergic lesions**
Elena Di Martino

10:00 **The role of corticogenesis-regulating genes during brain repair and regeneration after ischemia**
Dunja Gorup

10:15 **Neurophysiology model of the human lumbar cord separated from brain control by traumatic injury**
Simon M. Danner

10:30—11:00 **Opening of the SNC’13** | Hall I

11:00—12:00 AOŽ Memorial lecture | Hall I 28
Integrating network structure and function in the human brain
Olaf Sporns

12:00—13:30 **Poster session A & Lunch break** | Poster exhibition area
Cellular Neuroscience A
Clinical neuroscience A
Cognitive neuroscience A
Neuroscience methods A
Molecular neuroscience A
Systems Neuroscience A

14:30—16:30 Translational neuroscience | Hall I
Odvisnost: bolezen možganov? (Lundbeckov satelitski simpozij)
Chair: Andrej Kastelic

14:35 **Dogajanje v možganih ob stiku z alkoholom**
Zvezdan Pirtošek

15:00 **Ali odvisnosti od alkohola v možganih poteka na uniformen način**
Maja Rus Makovec

15:25 **Kaj nevroznanstvena razlaga pomeni za vsakodnevno delo s pacienti s sindromom odvisnosti od alkohola**
Maja Bundalo Bočić

15:50 **Zmanjševanje škode pri odvisnostih**
Andrej Kastelic

16:30—17:00 **Coffee break** (sponsored by Lundbeck) | Poster exhibition area

17:00—19:00 Symposium | Hall II 36
Lumbar cord contribution in the postural and locomotor control studied in animal and human model
Chair: Milan R. Dimitrijević

17:00 **The acute phase of spinal cord injury: Electrophysiological insights from an in vitro model**
Andrea Nistri

17:30 **Neural mechanisms underlying control of posture and locomotion in animal models of different complexity**
Tatiana G. Deliagina

18:00 **Central pattern generator of the human lumbar cord deprived of brain control**
Karen Minassian

18:30 **Modification of segmental reflex activity by postural motor tasks**
Ursula Hofstoetter

17:00—19:00 Symposium | Hall III 39
Cognitive control in health and disease
Chair: Grega Repovš

17:00 **Advancements in the dual mechanisms framework of cognitive control**
Todd Braver

17:30 **Cognitive and affective control: insights from study of schizophrenia**
Deanna M. Barch

18:00 **Cognitive control in Parkinson disease: insights from deep brain stimulation of the subthalamic nucleus**
Tammara Hershey

18:30 **Functional networks of the brain underlying flexible cognitive control**
Grega Repovš

19:00—20:30 **Guided tour of the Old town** 25

19:30—00:00 **YNFL'13 Social** | Klub 300 25

Saturday, 28 September

8:00—19:00 **Registration** | Foyer 24

8:30—10:30 Symposium | Hall III 41
New vistas in neuropeptide research
Chair: Ronald See

8:30 **Novel mass spectrometry imaging of neuropeptides and applications to Parkinson's disease**
Per Andren

9:00 **Regulation of peptide discharge from single vesicles: pre- and postfusion role of SNAREs**
Robert Zorec

9:30 **Role of hypothalamus and steroidogenic factor 1 in body weight regulation**
Gregor Majdič

10:00 **Oxytocin reduces cocaine seeking and restores cocaine-induced decreases in glutamate receptor function**
Ronald See

8:30—10:30 **Educational workshop on placebo effect** | Hall II 22
Session I: Introduction to the placebo effect

8:30 **Definition, research methods, and overview of the workshop**
Maja Bresjanac

9:00 **General mechanisms across (patho)physiological conditions**
Fabrizio Benedetti

10:30—11:00 **Coffee break** (sponsored by Droga Kolinska d. d.) | Poster exhibition area

11:00—12:00 Plenary talk | Hall I 29
From infection hypothesis of schizophrenia to brain imaging: all make sense now?
Jiří Horáček

12:00—13:30 **Poster session B & Lunch break** | Poster exhibition area
Cellular neuroscience B
Clinical neuroscience B
Cognitive neuroscience B
Neuroscience methods B
Molecular neuroscience B
Systems neuroscience B

13:30—14:30 Plenary talk | Hall I 29
Engineering therapies for neurodegenerative disease: ALS, Huntington's and beyond
Don W. Cleveland

14:30—16:30 Symposium | Hall III 43
Transmissible spongiform encephalopathies – from cause to cure
Chair: Vladka Čurin Šerbec

14:30 **Prions**
Giuseppe Legname

15:00 **Insights into molecular structures of human prion proteins with inherited mutations by NMR**
Janez Plavec

15:30 **Surveillance of Creutzfeldt-Jakob disease in Slovenia since 1987 to 2013**
Mara Popović

16:00 **Diagnostics and therapy of prion diseases - some new challenges**
Vladka Čurin Šerbec

14:30—16:30 **Educational workshop on placebo effect** | Hall II 22
Session II: Mechanisms in specific conditions

14:30 **Pain**
Elisa Carlino

15:00 **Parkinson disease**
Elisa Frisaldi

15:30 **Depression**
Bettina Doering

16:00 **Physical performance**
Antonella Pollo

16:30—17:00 **Coffee break** (sponsored by Droga Kolinska d. d.) | Poster exhibition area

17:00—19:00 Symposium | Hall III 45
Botulinum toxin type A and pain
Chairs: Zvezdan Pirtošek, Maja Relja

17:00 **Botulinum toxin for the treatment of pain**
Dirk Dressler

17:25 **Behavioural evidence for central origin of the antinociceptive action of botulinum toxin type A**
Lidija Bach-Rojecky

17:50 **Immunohistochemical evidence of central antinociceptive action of botulinum toxin type A**
Ivica Matak

18:15 **The effect of botulinum toxin type A on neurogenic dural inflmation: a clue to mechasnis of its action in migraine**
Boris Filipović

18:40 **What we do not understand about botulinum toxin?**
Zdravko Lacković

17:00—19:00 **Educational workshop on placebo effect** | Hall II 28
Session III: Clinical and ethical implications

17:00 **Use of placebo in clinical trials**
Paul Enck

17:40 **Use of placebo in clinical practice**
Zvezdan Pirtošek

18:20 **Ethical guidelines on the use of placebo in clinical research and practice**
Jože Trontelj

19:00—20:30 Neuroscience and society | Hall I
Ethical challenges in exploring and exploiting the response to placebo

21:00—00:00 **SNC'13 Social** | CD Club, Cankarjev dom 25

Sunday, 29 September

8:00—17:00 **Registration** | Foyer 24

8:30—10:30 Symposium | Hall I 47
Neurosurgeons meet neuroscientists
Chair: Andrej Vranič

8:30 **Cortical removal vs. cortical preservation: why do we need both?**
Andrej Vranič

9:00 **The soul, the pineal gland and the neurosurgeon. Does modern neurosurgery give us some knowledge of the soul?**
Anne-Laure Boch

9:30 **Glioblastoma multiforme - between surgery and genetics**
Boštjan Matos

10:00 **Invasive brain surgery and implantable devices for treatment of psychiatric conditions: old debate but with new technologies?**
Frederic Gilbert

10:30—11:00 **Coffee break** (sponsored by Droga Kolinska d. d.) | Poster exhibition area

11:00—12:00 Plenary talk | Hall I 30
How placebos, words and rituals change the patient's brain
Fabrizio Benedetti

12:00—13:30 **Poster session C & Lunch break** | Poster exhibition area
Cellular neuroscience C
Clinical neuroscience C
Cognitive neuroscience C
Neuroscience methods C
Molecular neuroscience C
Systems neuroscience C

13:30—14:30 Plenary talk | Hall I 30
Developmental dynamics of radial vulnerability of the cerebral compartments in preterm infants and neonates
Ivica Kostović

14:30—16:30 Symposium | Hall I 49

Hypoxic brain damage, neuroprotection and long-term outcome with regard to quality of life

Chairs: Neil Marlow, Metka Derganc

14:30 **The EPICure studies: changing outcomes for extremely preterm children**
Neil Marlow

15:10 **Reduction in brain volume in young adults with perinatal hypoxic-ischaemic encephalopathy**
Tina Bregant

15:30 **Therapeutic hypothermia – 8-year experience**
Metka Derganc

15:50 **Outcome of hypoxic-ischaemic encephalopathy (HIE) in late adolescence: insights on cognitive outcome from neuropsychology, DTI and resting state fMRI**
David Gosar

16:10 **Amplitude-integrated EEG versus conventional EEG use in NICU/NSCU**
David Neubauer

16:30—16:45 **Closing of the SiNAPSA Neuroscience Conference '13** | Hall I
with announcement of the best poster award

Poster sessions

Friday, 27 September

* YNFL'13

* YNFL'13

Saturday, 28 September

* YNFL'13

* YNFL'13

Sunday, 29 September

* YNFL'13

* YNFL'13

SNC'13

SiNAPSA Neuroscience Conference '13

Ljubljana, Slovenia, September 27-29, 2013

Educational Workshop on Placebo Effect

www.sinapsa.org/SiNC13/workshop

Faculty of Medicine, University of Ljubljana, Slovenia
27—29 September 2013

Saturday, 28 September

8:30—10:30 **Educational workshop on placebo effect** | Hall II
Session I: Introduction to the placebo effect

8:30 **Definition, research methods, and overview of the workshop**
Maja Bresjanac

9:00 **General mechanisms across (patho)physiological conditions**
Fabrizio Benedetti

10:30—11:00 **Coffee break** (sponsored by Droga Kolinska d. d.) | Poster exhibition area

12:00—13:30 **Lunch break**

14:30—16:30 **Educational workshop on placebo effect** | Hall II
Session II: Mechanisms in specific conditions

14:30 **Pain**
Elisa Carlino

15:00 **Parkinson disease**
Elisa Frisaldi

15:30 **Depression**
Bettina Doering

16:00 **Physical performance**
Antonella Pollo

16:30—17:00 **Coffee break** (sponsored by Droga Kolinska d. d.) | Poster exhibition area

17:00—19:00 **Educational workshop on placebo effect** | Hall II
Session III: Clinical and ethical implications

17:00 **Use of placebo in clinical trials**
Paul Enck

17:40 **Use of placebo in clinical practice**
Zvezdan Pirtošek

18:20 **Ethical guidelines on the use of placebo in clinical research and practice**
Jože Trontelj

19:00—20:30 Neuroscience and society | Hall I
Ethical challenges in exploring and exploiting the response to placebo

SNC'13

SiNAPSA Neuroscience Conference '13

Ljubljana, Slovenia, September 27-29, 2013

General Information

www.sinapsa.org/SiNC13

Faculty of Medicine, University of Ljubljana, Slovenia
27—29 September 2013

General Information

Venue
Faculty of Medicine, University of Ljubljana
Korytkova 2, SI-1000 Ljubljana, Slovenia

Contact E-mail
For general queries, please write to: snc13@sinapsa.org

Registration and Information Desk
For further information about registration, please contact the Registration Office:
Tel.: +386 1 2417 136
Fax: +386 1 2417 296
e-mail: registration@cd-cc.si

The Registration Desk will be located in the Foyer of Faculty of Medicine and open as follows:
Thursday, 26 September, 17:00 – 19:00
Friday, 27 September, 8:00 – 19:00
Saturday, 28 September, 8:00 – 19:00
Sunday, 29 September, 8:00 – 17:00

Information for Poster Presenters
There are no strict requirements regarding poster size. The poster boards allow posters up to 120 cm tall and 90 cm wide.
Presenters are advised to mount their posters on Friday morning and leave them up until the closing of the SNC'13.
The presenters are requested to be present and available for questions and discussion at the specified time-slot:
A - Friday 12:00-13:30; B - Saturday 12:00-13:30; C - Sunday 12:00-13:30.

Information for Speakers
For oral presentations a computer projection system will be provided in the lecture hall. To ensure smooth and timely progression of the sessions, presentations should be submitted in advance of the relevant symposium.
Presenters can either send the presentation by e-mail to snc13@sinapsa.org, or submit it on a suitable electronic medium (CD, USB drive) either at the time of registration or on the day of the symposium, but no later than 15 minutes before the start of the session. Presenters should name the presentation file by their last name. Using the computer available in the lecture hall is a preferred method of presentation. If a presenter plans to use his/her own laptop, they should notify the organizers in advance of the session. Advance requests are required also for slide or video projection.

Internet
At the Faculty of Medicine the wireless internet is avaliable for registered users through Eduroam (https://www.eduroam.org/).
Participants can also use the public computers located in the foyer which also have internet access.

Conference Identification Badge
A conference identification badge will be included in the conference material provided upon registration. There will be no admittance to the Scientific Sessions without the conference badge.

Attendance Certificate
A Certificate of Attendance will be issued to all registered participants.

CME Certificate
Members of the Slovenian Medical Chamber will receive 20 CME (Continuing Medical Education) credits.

Coffee Breaks

During breaks, refreshments will be available free of charge to participants wearing congress badges.

Lunch Breaks

During lunch breaks, sandwiches will be available for purchase at the “Mandibula” café inside the Faculty of Medicine. You can also preorder lunch boxes (5 EUR) and lunch menus (8 EUR) at the registration desk. Lunch boxes will be available in the foyer. Lunch will be served at the “Štorklja” restraurant (next door from the Faculty of Medicine).

Social Programme

Guided Tour of the Old Town

Friday, September 27, 19:00 - 20:30

Join us for a pleasant short guided walk around the Old town of Ljubljana. Please register for the tour at the registration desk.
The tour will depart at 19:00 from the conference venue (Faculty of Medicine).

YNFL Social

Friday, September 27, 19:30 - 00:00

Shortly after the closing of Friday’s Programme an arranged transport will take the YNFL participants (all SNC’13 registered undergraduate and graduate students) to one of Ljubljana’s well known bowling places, Klub 300. The party there will start off with a welcome drink and continue with “cosmic bowling” offering special effects and “red pin” awards. After the bowling we will continue in a reserved space of the Club with some food, drinks and music.
Some national and international senior neuroscientists will also join us during bowling. At the end of this social event, arranged transport will take us back to the center of Ljubljana.
Please register at the registration desk.

SNC’13 Social

Saturday, September 28, 21:00 - 00:00

Join us at the CD Club (Cankarjev dom Cultural and Congress Centre, Erjavčeva street 10, www.cd-cc.si) for a relaxing evening with food, drinks, live music and a beautiful view over Ljubljana.
Group departure at 20:30 from the Conference venue (30-min walk) and from Central Hotel (15-min walk).

Committees and Organisation

SiNAPSA Neuroscience Conference '13 was organised by
SiNAPSA, Slovenian Neuroscience Association and
Faculty of Medicine, University of Ljubljana

SNC'13 Programme Committee
Prof. Maja Bresjanac (Chair)
Institute of Pathophysiology, Faculty of Medicine, University of Ljubljana, Slovenia
Prof. David Neubauer
Department of Pediatric Neurology, University Medical Centre Ljubljana, Slovenia
Assoc. Prof. Peter Pregelj
University Psychiatric Hospital Ljubljana, Slovenia
Dr. Boris Rogelj
Department of Biotechnology, Jožef Stefan Institute, Ljubljana, Slovenia
Prof. David B. Vodušek
Department of Neurology, University Medical Centre Ljubljana, Slovenia

SNC'13 Organising Committee
Assist. Prof. Blaž Koritnik (Chair)
Institute of Clinical Neurophysiology, University Medical Centre Ljubljana, Slovenia
Dr. Jure Bon
Psychiatric Hospital Begunje, Slovenia
Mateja Drolec Novak
Institute of Pathophysiology, Faculty of Medicine, University of Ljubljana, Slovenia
Judita Jeran
Institute of Clinical Neurophysiology, University Medical Centre Ljubljana, Slovenia
Assoc. Prof. Grega Repovš
Department of Psychology, Faculty of Arts, University of Ljubljana, Slovenia
Martina Starc
Department of Psychology, Faculty of Arts, University of Ljubljana, Slovenia

YNFL'13 Programme Organising Committee
Dr. Nadja Jarc (Chair)
Department of Vascular Neurology and Intensive Therapy, University Medical Centre Ljubljana, Slovenia
Simon Brezovar
Department of Neurology, University Medical Centre Ljubljana, Slovenia
Dr. Matej Markota
Department of Psychiatry, Harvard Medical School, Boston, USA
Miha Pelko
Institute for Adaptive and Neural Computation, School of Informatics, University of Edinburgh, UK
Klara Tostovršnik
Faculty of Medicine, University of Ljubljana, Slovenia

Principal sponsor
Lundbeck

Conference was supported by
Janssen, Genzyme, Apta Medica, Krka, Droga Kolinska, City of Ljubljana

SNC'13

SiNAPSA Neuroscience Conference '13

Ljubljana, Slovenia, September 27-29, 2013

Abstracts

SNC'13 Plenary and Special Lectures

www.sinapsa.org/SiNC13

Faculty of Medicine, University of Ljubljana, Slovenia
27—29 September 2013

Friday, September 27th, 11:00
[AOŽ Memorial Lecture]

Integrating network structure and function in the human brain

Olaf Sporns

Indiana University Bloomington, USA

Recent advances in network science have greatly increased our understanding of the structure and function of many networked systems, ranging from transportation networks, to social networks, the internet, ecosystems, and biochemical and gene transcription pathways.

Network approaches are also increasingly applied to the brain, at several levels of scale from cells to entire brain systems. This lecture will focus on network approaches to understanding the large-scale connectivity of the human brain, the "human connectome".

Early studies in this field have focused on mapping brain network topology and identifying some of its characteristic features, including small world attributes, modularity and hubs. More recently, the emphasis has shifted towards linking brain network topology to brain dynamics, the patterns of functional interactions that unfold during both rest and task conditions.

In my talk I will give an overview of recent work characterizing the structure of complex brain networks, with particular emphasis on studies demonstrating how the brain's structural topology constrains and shapes its capacity to process and integrate information.

Sporns O (2011) Networks of the Brain. MIT Press.
Sporns O (2012) Discovering the Human Connectome. MIT Press.

More information at www.sinapsa.org/SiNC13/AOZ.

Friday, September 27th, 13:30
[Plenary Lecture]

The motor and non-motor functions of the basal ganglia: evidence from studies of Parkinson's disease

Marjan Jahanshahi

University College London, The National Hospital for Neurology and Neurosurgery, Queen Square, London, UK

Traditionally, the basal ganglia were considered purely motor structures. However, in recognition of the fact that the greatest connectivity of the basal ganglia is with the non-motor areas of the frontal cortex such as the dorsolateral prefrontal cortex, the anterior cingulate and the orbitofrontal cortex, there has been increasing appreciation of the role of these subcortical structures in non-motor associative and limbic functions. Furthermore, accidental lesions of the basal ganglia in man are most frequently associated with non-motor behavioural symptoms such as abulia and apathy. In Parkinson's disease, the most typical movement disorder associated with basal ganglia dysfunction, motor symptoms such as bradykinesia (slowness of movement), akinesia (poverty of action), tremor and rigidity as well as non-motor symptoms such as executive dysfunction and cognitive decline, depression, anxiety and apathy are amongst the core features of the illness.

In this talk, I will first illustrate involvement of the basal ganglia in several key motor functions namely, selection and inhibition, timing, and procedural learning with examples of our research findings in patients with Parkinson's disease. Second, I will provide examples of the role of the basal ganglia in non-motor functions such as cognition and learning from research results showing deficits on cognitive tasks that involve executive processing or probabilistic incremental learning in Parkinson's disease, and also consider the effects of levodopa medication or deep brain stimulation of the subthalamic nucleus on these tasks. Finally, I will discuss limbic-motor interactions that mediate motivational modulation of movement speed in Parkinson's disease and will present data showing that prospect of monetary reward, avoidance of aversive stimuli, or provision of external stimuli all influence speed of movement initiation and execution in this disorder. This evidence establishes the role of the basal ganglia and their frontal connections in a host of motor, cognitive and limbic functions.

Saturday, September 28th, 11:00
[Plenary Lecture]

From infection hypothesis of schizophrenia to brain imaging: all make sense now?

Jiří Horáček

Prague Psychiatric Center, Czech Republic
Third Faculty of Medicine, Charles University, Prague, Czech Republic

Evidence from both animal and human studies implicates the essential role of immune system in the pathophysiology of a number of neuropsychiatric disorders with known or suspected developmental origins, including schizophrenia. Our previous results showed significantly increased plasma levels of IL-6, IL-10 and TNF-alpha level in first episode schizophrenia patients. These immunological mechanisms would mediate the relationship between genetic vulnerability and environmental factors. Both perinatal and postnatal candidate infections appear to be associated with the immunological dysbalance and an elevated risk of schizophrenia.

An emerging literature from epidemiologic, clinical, and preclinical studies has provided evidence that perinatal exposure to infection contributes to the etiology of these disorders. The postnatal infection of latent toxoplasmosis is associated with an increased incidence of schizophrenia with an odds ratio of 2.73, and 2.54 for first episode patients.

To address the question of interaction between genetic vulnerability and immunological dysbalance with infection etiology we studied the influence of seropositivity for latent toxoplasmosis on brain morphometry in schizophrenia patients investigated by magnetic resonance imaging. An optimized voxel-based morphometry of magnetic resonance imaging was analyzed by analysis of variance with diagnosis and seropositivity as factors. Grey matter (GM) volume was reduced in schizophrenia patients compared with controls in the cortical regions, hippocampus and in the caudate. In the schizophrenia sample we found a significant reduction of GM volume in T. gondii positive comparing with T. gondii-negative patients bilaterally in the caudate, median cingulate, thalamus and occipital cortex and in the left cerebellar hemispheres. T. gondii-positive and -negative controls did not differ in any cluster. Among participants seropositive to T. gondii the reduction of GM in the schizophrenia subjects was located in the same regions when comparing the entire sample ($p < 0.05$, FWE corrected).
Our study is the first to document that latent toxoplasmosis is connected with the reduction of GM in schizophrenia. T. gondii can affect gray matter by several mechanisms including kynurenine metabolites and dopamine overactivity.

Acknowledgments: This work was supported by grant NT/13843 and NT/13897 from the Ministry of Education, Youth and Sports of the Czech Republic.

Saturday, September 28th, 13:30
[Plenary Lecture]

Engineering therapies for neurodegenerative disease: ALS, Huntington's and beyond

Don W. Cleveland

The Ludwig Institute and Department of Cellular and Molecular Medicine, University of California at San Diego, USA

The genes whose mutation is now known to cause the major neurodegenerative diseases are widely expressed, including superoxide dismutase (SOD1) whose mutation causes an inherited form of the fatal, adult motor neuron disease ALS. Mutation in SOD1 mutant causes ALS through an acquired toxicity unrelated to dismutase activity. Use of cell type-selective mutant gene silencing has demonstrated that toxicity requires mutant damage within both motor neurons and their neighbors, with mutant SOD1 within motor neurons and oligodendrocytes driving disease onset, while damage within neighboring astrocytes and microglia accelerates disease progression. Slowed disease progression has been achieved by a clinically feasible infusion of DNA antisense oligonucleotides (ASOs) that direct destruction of SOD1 mRNA widely within the non-human primate nervous system. Additionally, disease progression can be slowed in a clinical feasible approach by reducing mutant SOD1 expression within astrocytes with a single peripheral administration of a replication defective viral delivery vector (AAV9) encoding an shRNA to target SOD1 mRNA destruction.

The landscape of disease mechanism in ALS was reset with discovery that the largest genetic cause of ALS is dominant, hexanucleotide expansion within intron 1 of the C9orf72 gene. Hexanucleotide-containing RNA foci that may sequester one or more RNA binding proteins are shown to accumulate intranuclearly in multiple cell types inside and outside of the nervous system. Proof of principle for therapy development has been achieved by identification of antisense oligonucleotides complementary to the C9orf72 pre-mRNA that selectively target degradation of C9orf72 RNAs containing the expansion.

Finally, ASO infusion to target catalytic degradation of specific mRNAs may prove to be a broadly applicable therapeutic approach. Indeed, polyglutamine expansion in the widely expressed huntingtin protein is the sole cause of Huntington's disease (HD). Infusion of ASOs targeting huntingtin mRNA effectively lowers huntingtin levels in the primary brain regions affected in HD. Transient infusion of ASOs not delays disease progression, but mediates a sustained reversal of disease phenotype that persists for much longer than the huntingtin reduction, findings that establish a feasible therapeutic strategy for sustained HD disease reversal from a "Huntingtin holiday" produced by transient therapy.

Sunday, September 29th, 11:00
[Plenary Lecture]

How placebos, words and rituals change the patient's brain

Fabrizio Benedetti

Department of Neuroscience, University of Turin Medical School and
National Institute of Neuroscience, Turin, Italy

Although placebos have long been considered a nuisance in clinical research, today they represent an active and productive field of research and, because of the involvement of many mechanisms, the study of the placebo effect can actually be viewed as a melting pot of concepts and ideas for neuroscience. Indeed, there exists not a single but many placebo effects, with different mechanisms and in different systems, medical conditions, and therapeutic interventions. For example, brain mechanisms of expectation, anxiety, and reward are all involved, as well as a variety of learning phenomena, such as Pavlovian conditioning, cognitive and social learning. There is also some experimental evidence of different genetic variants in placebo responsiveness. The most productive models to better understand the neurobiology of the placebo effect are pain and Parkinson's disease. In these medical conditions, the neural networks that are involved have been identified: that is, opioid, cannabinoid, cholecystokinin, dopamine modulatory networks in pain and part of the basal ganglia circuitry in Parkinson's disease. Important clinical implications emerge from these recent advances in placebo research. First, as the placebo effect is basically a psychosocial context effect, these data indicate that different social stimuli, such as words and therapeutic rituals, may change the chemistry and circuitry of the patient's brain. Second, the mechanisms that are activated by placebos are the same as those activated by drugs, which suggests a cognitive/affective interference with drug action. Third, if prefrontal functioning is impaired, placebo responses are reduced or totally lacking, as occurs in dementia of the Alzheimer's type.

Sunday, September 29th, 13:30
[Plenary Lecture]

Developmental dynamics of radial vulnerability of the cerebral compartments in preterm infants and neonates

Ivica Kostović

University of Zagreb, Croatia

Neurogenetic events (proliferation, migration, axonaL growth, dendritic differentiation, synaptogenesis etc.) in the fetal cerebrum take place in transient, cytoarchitectonically defined, laminar compartments which are stratified along radial axis of the cerebral wall (ventriculepia). Neuroimaging techniques offer opportunity to visualize transient compartments in vivo and track their dynamic reorganization during perinatal period. In order to explain radial vulnerability we shall discuss: 1. the nature of neurogenetic processes within the given compartments, 2. radial extent of lesion, 3. complexity of cellular targets (neurons and dendrites, glia, progenitor cells, growing axons, extracellular matrix-ECM and 4. developmental "windows" of vulnerability. Growing evidence indicates that cellular elements, namely growing axons and subplate neurons and ECM determine radial vulnerability of the preterm cerebral wall. In early preterm (up to 28 postconceptial week – PCW) hypoxic-ischaemic lesions predominantly damage periventricular fibres (callosum and crossroads of pathways), subplate neurons and ECM. After 28 PCW the vulnerable are long corticocortical pathways at the interface between sagittal strata and subplate. In the newborn, radial vulnerability shifts towards gyral white matter, subplate remnant and neurons-dendrites of the cortical plate. In conclusion, developmental vulnerability changes along radial axis in relation to growing axonal strata and deep to superficial differentiation of neurons in subplate and cortical plate. These spatial and temporal patterns of vulnerability will determine cognitive, neurological and behavioural impairments after perinatal lesions. The most important translational result of our concept is that MR properties at borders between different compartments of the cerebral wall may have prognostic significance for outcome after perinatal lesion.

SNC'13

SiNAPSA Neuroscience Conference '13

Ljubljana, Slovenia, September 27-29, 2013

Abstracts

SNC'13 Thematic Symposia

www.sinapsa.org/SiNC13

Faculty of Medicine, University of Ljubljana, Slovenia
27—29 September 2013

Friday, September 27th, 14:30
[Symposium: Normal cognition and cognitive decline – can imaging white matter complete the picture?]

Networks, cognition and early cognitive decline

Michael O'Sullivan

Department of Clinical Neuroscience, Institute of Psychiatry, King's College London, UK

Much of our early understanding of connections, distributed networks and the role that they play in cognition came from either experimental lesions in animals or rare clinical cases (disconnection syndromes). Dr O'Sullivan will explain how non-invasive imaging techniques have built rapidly on this historical background. With a focus on memory and cognitive control, he will describe recent findings linking change within specific connections to distinct aspects of early decline. Description of some remaining key challenges will set the scene for the talks that follow.

Friday, September 27th, 15:00
[Symposium: Normal cognition and cognitive decline – can imaging white matter complete the picture?]

Localised white matter damage and global network properties in ageing

Rok Berlot

Department of Clinical Neuroscience, Institute of Psychiatry, King's College London, UK
Laboratory for Cognitive Neuroscience, Department of Neurology, University Medical Centre Ljubljana, Slovenia

Brain connectivity has been extensively investigated at various spatial scales. While microstructural changes of specific white matter tracts have been linked to different aspects of cognitive decline, their role within large-scale structural and functional networks has not been examined extensively. Mr Berlot will give an overview of recent work investigating localised damage in the context of whole-brain networks and present findings relating structural integrity of white matter tracts to large-scale network properties in ageing.

Friday, September 27th, 15:30
[Symposium: Normal cognition and cognitive decline – can imaging white matter complete the picture?]

Neuromodulation in cognitive ageing

Nicola Jane Ray

Department of Clinical Neuroscience, Institute of Psychiatry, King's College London, UK

Age-related pathologies affect not only information processing networks (for example, for memory) but also modulatory networks that affect many cognitive processes. One example is the cholinergic system, which innervates cortical sites involved in a multitude of cognitive processes and is also the current target of treatments in Alzheimer's disease. Modulatory systems may also be important in resilience and reorganisation of network functions after injury. Dr Ray will present some early evidence that supports this contention and discuss the potential importance in the context of rehabilitation and recovery.

Friday, September 27th, 16:00
[Symposium: Normal cognition and cognitive decline – can imaging white matter complete the picture?]

Structural network abnormalities and cognitive impairment in cerebral small vessel disease

Andrew J. Lawrence

Stroke and Dementia Research Centre, St George's University of London, UK

Graph analysis of brain networks, derived from in-vivo MRI, is a relatively recent technique used to cast light on the organisational principles of the brain in health and disease. Its results have particular relevance for the mechanisms of cognitive impairment in SVD-stroke. Dr Lawrence will give an overview of the technique and present findings from its application to baseline diffusion tractography and cognitive data from the St George's Cognition and Neuroimaging in Stroke (SCANS) study.

Friday, September 27th, 14:30
[Symposium: Movement disorders - from bench to bedside]

Facial bradykinesia in Parkinson's disease and atypical parkinsonism

Matteo Bologna

Sapienza University of Rome, Italy

Clinical observations suggest that reduced spontaneous and emotional facial expressions are features of facial bradykinesia in Parkinson's disease (PD). In atypical parkinsonism, facial bradykinesia may be associated with additional dystonic features. Experimental studies evaluating spontaneous and emotional facial movements in PD demonstrate that patients have reduction in spontaneous blinking and emotional facial expression. Regarding voluntary movements, these are smaller in amplitude and slower in velocity in orofacial region. In contrast, movements of the upper face, such as voluntary blinking, are of normal velocity and amplitude but impaired in terms of switching between the closing and opening phases. In progressive supranuclear palsy (PSP), voluntary blinking is not only characterised by a severely impaired switching between the closing and opening phases, but it is also slow in comparison with PD. In summary, facial bradykinesia of PD includes abnormalities of spontaneous, emotional and voluntary facial movements. In PSP, spontaneous and voluntary facial movements are abnormal but experimental studies on emotional facial movements are lacking. The differences in facial bradykinesia between PD and PSP patients may arise from different anatomical involvement in two diseases. In PD, facial bradykinesia is primarily depended on basal ganglia dysfunction whereas in PSP, it is a consequence of a widespread degeneration involving not only the basal ganglia, but also cortical and brainstem structures. Experimental data on facial bradykinesia in other atypical parkinsonism, including multiple system atrophy and corticobasal degeneration are limited.

Friday, September 27th, 14:55
[Symposium: Movement disorders - from bench to bedside]

The cerebellum in dystonia - help or hindrance?

Mark J Edwards

Sobell Department of Motor Neurosciences and Movement Disorders, Institute of Neurology Queen Square, London, UK

Dystonia has historically been considered a disorder of the basal ganglia. I will critically examine the evidence for a role of the cerebellum in the pathophysiology of dystonia, by linking information available from both clinical and experimental studies: work detailing cerebellar connectivity in primates, data that suggests a role for the cerebellum in the genesis of dystonia in murine models, clinical observation in humans with structural lesions and heredodegenerative disorders of the cerebellum and imaging studies of patients with dystonia. The typical electrophysiological findings in dystonia are the converse to those found in cerebellar lesions. However, certain subtypes of dystonia mirror cerebellar patterns of increased cortical inhibition. Furthermore, altered cerebellar function can be demonstrated in adult onset focal dystonia with impaired cerebellar inhibition of motor cortex and abnormal eyeblink classical conditioning. We propose that abnormal, likely compensatory activity of the cerebellum is an important factor within pathophysiological models of dystonia. Work in this exciting area has only just begun but it is likely that the cerebellum will have a key place within future models of dystonia.

Friday, September 27th, 15:20
[Symposium: Movement disorders - from bench to bedside]

Secondary and primary dystonia: pathophysiological differences

Maja Kojović

Department of Neurology, University Medical Centre Ljubljana, Slovenia
Institute of Neurology, University College London, UK

Primary dystonia is thought to be a disorder of the basal ganglia (BG) because the symptoms resemble those of patients who have anatomical lesions in the same regions of brain (secondary dystonia). However, these two groups of patients respond differently to therapy suggesting differences in pathophysiological mechanisms. Pathophysiological deficits of primary dystonia include reduced inhibition at many levels of the motor system, increased plasticity and decreased eye blink classical conditioning (EBCC) which is a marker of cerebellar involvement. We compared electrophysiological features between primary and secondary dystonia, using transcranial magnetic stimulation of motor cortex and EBCC paradigm, to test whether dystonia symptoms share the same underlying mechanism. Eleven patients with hemidystonia caused by unilateral brain lesion were tested over both hemispheres and compared to ten patients with primary segmental dystonia and ten healthy participants. Patients with primary dystonia had increased cortical plasticity and reduced EBCC. On the contrary, secondary dystonia patients had normal cortical plasticity on both affected and non-affected side and normal EBCC, while intracortical inhibition was reduced on the affected side only. We demonstrate that abnormally enhanced cortical plasticity is not required for clinical expression of dystonia. Normal EBCC in secondary dystonia suggests the absence of functional cerebellar involvement in this form of dystonia whereas reduced intracortical inhibition on the side of the lesion may result from abnormal BG output or be a consequence of maintaining an abnormal dystonic posture. The conclusion is that dystonia is a motor symptom that reflects different possible pathophysiological states into which the motor system can be pushed through variety of insults.

Friday, September 27th, 15:45
[Symposium: Movement disorders - from bench to bedside]

Sensory attenuation in functional movement disorders

Isabel Pareés

Sobell Department of Motor Neurosciences and Movement Disorders, Institute of Neurology, University College London, UK

Functional movement disorders (FMD) are quantifiably different from abnormal movement seen in organic disorders, mainly because those resemble movements that are made voluntarily. However, patients with FMD experience the abnormal movement as involuntary or not self-triggered. It has been suggested that a lack of agency for the movement is the reason for such experience. In this study we measure sensory attenuation of self-produced stimuli, a phenomenon which has been proposed to be an implicit measure of the sense of agency, and that it has been previously demonstrated to be impaired in patient with delusions. We predicted that patients with FMD have a similar impairment to delusional patients.

Fourteen patients with FMD and 14 healthy controls were assessed in a force-match task. There were two conditions: participants had to match a reference force, either by pressing directly on themselves (self condition), or by using a robot to produce the pressure (external condition). Higher levels of force generated attempting to match the reference force when the force is self-generated compared to the external condition would be consistent with sensory attenuation.

Healthy controls consistently overestimated the force required when it was self-generated. However, patients were significantly more accurate than healthy controls in estimating the forces in the self-condition. This is consistent with patients having significantly less attenuation.

Our study suggests that a dysfunction of the sensory attenuation mechanism is present in patients with FMD. This might contribute to explain why they do not report the abnormal movements as self-triggered.

Friday, September 27th, 16:10
[Symposium: Movement disorders - from bench to bedside]

Tremor in inflammatory neuropathies: cerebellar learning distinguishes patients with and without tremor

Petra Schwingenschuh

Department of Neurology, Medical University of Graz, Austria

Tremor is a common feature of inflammatory neuropathies, particularly those associated with IgM paraproteinaemia. The pathophysiology of this tremor is unclear, and although the cerebellum has been proposed to play a role, perhaps by causing mistimed motor output due to delayed and dispersed sensory feedback from the limbs, evidence for this is limited. There is little or no information about what drives the development of tremor in only a proportion of those with inflammatory neuropathy, or about the pathophysiological basis on which to develop treatments for this disabling symptom.

Here we directly compared patients with inflammatory neuropathy and tremor, patients with inflammatory neuropathy without tremor and healthy controls on a test of cerebellar associative learning (eyeblink classical conditioning), a test of sensorimotor integration (short afferent inhibition) and a test of associative plasticity (paired associative stimulation). We also recorded tremor in the arms using accelerometry and surface EMG.

We found impaired responses to eyeblink classical conditioning and paired associative stimulation in patients with neuropathy and tremor compared with both neuropathy patients without tremor and healthy controls. Short afferent inhibition was normal in all groups.

Our data strongly suggest impairment of cerebellar function that is linked to the production of tremor in a proportion of patients with inflammatory neuropathy.

Friday, September 27th, 17:00
[Symposium: Lumbar cord contribution in the postural and locomotor control studied in animal and human model]

The acute phase of spinal cord injury: Electrophysiological insights from an in vitro model

Andrea Nistri

Neuroscience Department, International School for Advanced Studies (SISSA), Trieste, Italy

Shortly after an acute lesion to the spinal cord, complex cellular mechanisms amplify the initial damage to affect initially-spared areas with consequent onset of chronic disability. The precise pathological processes underlying such events are incompletely understood and are not readily clarified with in vivo animal models that cannot provide direct and repeated access to lesioned circuits. This realization has prompted the use of in vitro preparations of the rodent spinal cord that retain the intrinsic ability to produce locomotor-like discharges from lumbar ventral roots and, thus, offer the opportunity to study the still unclear process of lesion progression in relation to the operation of locomotor circuits at various times after lesion. Furthermore, these models enable a detailed analysis to understand the type and topography of damaged cells. Molecular biology techniques can, therefore, be applied to unravel the mechanisms of damage and to devise pharmacological tools to counteract them. In particular, using the rat spinal cord in vitro, we have set up methods that reliably produce discrete lesions by short application of the glutamate agonist kainate. The neuronal loss arises slowly via a non-apoptotic cell death mechanism termed parthanatos. Parthanatos is thought to be caused by mitochondrial damage and exhaustion of cell energy stores as a consequence of hyperactivation of enzymatic systems brought into action to repair DNA damage. Locomotor network activity is irreversibly destroyed by kainate in a virtually all-or-none manner and with little relation to the actual neuronal loss. This observation suggests that destruction of a highly-vulnerable cell population is the process responsible for the loss of locomotion function. A different in vitro lesion model based on temporary hypoxic challenge to the spinal cord together with toxic radicals primarily damages white matter cells (through conventional apoptosis) with deficit (without full suppression) of locomotor network function, while neurons are less vulnerable. Thus, distinct methods to damage the spinal cord induce a differential outcome in terms of lesioned cells and locomotor function. This unexpected finding suggests that pharmacological agents for early neuroprotection should be designed to target selective biochemical pathways leading to cell death that depends on the nature of the initial lesion. This notion highlights the complexity of setting up neuroprotective strategies to improve the outcome of spinal cord injury.

Friday, September 27th, 17:30
[Symposium: Lumbar cord contribution in the postural and locomotor control studied in animal and human model]

Neural mechanisms underlying control of posture and locomotion in animal models of different complexity

Tatiana G. Deliagina

Department of Neuroscience, Karolinska Institute, Stockholm, Sweden

Control of body posture and locomotion are evolutionary old and vital motor functions based on in-born neural mechanisms. We study locomotor and postural mechanisms, as well as their interaction, by using animal models of different complexity: a lower vertebrate (lamprey) and higher vertebrates (rabbit and cat).

It is known that spinal mechanisms are able to generate different modes of forward locomotion. We have found that

(i) the spinal cord of the lamprey and cat can generate locomotion in different directions. In the cat, the spinal cord contains a mechanism (VCM) generating the vertical component of step, and mechanisms (HCMs) generating the horizontal component of step in the specific directions (forward, backward, leftward, etc.). HCMs receive sensory input signaling limb motion in stance; reaching the extreme position triggers a limb transfer in the opposite direction. VCM and HCMs are also used for postural corrections during standing. Postural perturbation activates VCM and a specific HCM generating a corrective step in a particular direction. The VCM and a specific HCM can be activated by supraspinal commands. We have shown that mesencephalic locomotor region (MLR) activates VCM and HCM necessary for forward stepping. Thus, MLR can be considered as a command center for forward locomotion.

(ii) The spinal cord (in both lamprey and rabbit) contains the networks generating spinal postural reflexes, which contribute to body stabilization in intact animals.

(iii) Perturbations of body orientation during forward locomotion cause postural reactions, which are well incorporated into the basic locomotor pattern. We found a number of limb and trunk mechanisms contributing to postural control during locomotion. They are: a limb transfer mechanism (stabilizing the limb position relative to trunk at the moment of foot landing); limb load compensating reflexes (operating during stance); a limb stance configuration mechanism (counteracting to abduction/adduction of the limb during stance), and a trunk configuration mechanism (straightening the trunk in response to its bending). We have shown that basic neuronal mechanisms underlying interactions of postural and locomotor systems reside in the brainstem, cerebellum, and spinal cord.

Friday, September 27th, 18:00
[Symposium: Lumbar cord contribution in the postural and locomotor control studied in animal and human model]

Central pattern generator of the human lumbar cord deprived of brain control

Karen Minassian

Medical University of Vienna, Austria

Across species, unperturbed locomotion is characterized by muscle activations with a stereotyped spatiotemporal pattern of one basic movement cycle and the successive duplications of this pattern. In spite of the encephalization and the erect, bipedal mode of walking, independent observations imply that rhythmic lower limb motor patterns can be generated in humans by similar spinal neural circuits as in other vertebrates. However, little is known about the organization of these so-called central pattern generators (CPGs) or locomotor rhythm and pattern generating networks in humans. The present study bases on previous work demonstrating that the human lumbar spinal cord isolated from brain control due to traumatic spinal cord injury (SCI) can generate rhythmic, locomotor-like activity in response to sustained epidural spinal cord stimulation of certain frequencies. In the supine position the electromyographically recorded rhythmic activities of the lower limb muscles consist of a series of stimulus time-related compound muscle action potentials (CMAPs), each initiated in posterior root afferents. The rhythmic modulations of these posterior-root muscle (PRM) reflexes result in the overall patterns. The relation between individual stimuli and responses, as well as the CMAP characteristics of these responses, allow for the identification of mechanisms beyond the information gained from the overall electromyographic patterns.

Here, electromyographic activities of quadriceps, hamstrings, tibialis anterior and triceps surae, bilaterally in response to epidural stimulation at 20 Hz–40 Hz were analyzed in 10 individuals with motor complete post-traumatic SCI. Forty 10-seconds segments of rhythmical activities involving all four muscle groups of one side were detected in 7 subjects and analyzed. The EMG profiles (shape of the rectified, data-reduced EMG activity of a muscle group averaged across all complete cycles) and their phases of bursting and suppressed activities were identified. Latencies of PRM reflexes, composing these rhythmic activities, were calculated.

In all 10-s segments, rhythmic activities of all muscle groups had the same cycle frequency. In-between muscles, rhythmic activity occurred either synchronized or alternating, within phases resembling flexion or extension. No other phase-relations were observed. Within different patterns of rhythmic activities, a given muscle group could be controlled either as 'flexor' or 'extensor'. PRM reflexes constituting bursts during the extension phases had monosynaptic latencies. These responses were suppressed during flexion and were replaced by delayed, oligosynaptic PRM reflexes in quadriceps, tibialis anterior and triceps surae.

The human model of the lumbar spinal cord as well as the results of the study demonstrate similarities and differences with the animal experimental CPG-model. Complete anatomic transection of the human spinal cord after traumatic injury is rare. Small-diameter, slow conducting translesional fibers can remain after injury and their influence upon segmental reflex activity can be assessed electrophysi-

ologically. Rhythmic peripheral feedback from the lower limbs cannot be excluded, yet in the supine position, afferent information essential for rhythm generation (hip extension angle and axial limb load) is minimal. The EMG profiles of rhythmic activities with their peaks either in the flexion or extension phase can be explained by a plurisegmental control and the conceptual CPG model of half-centers. The phasic modulation of the monosynaptic reflex gain and the putative presynaptic control of primary afferents are further similarities with animal experimental results. Yet, the conceptualization of the human locomotor generating networks under the influence of tonic epidural stimulation as a 'half-center model' would require an asymmetrical organization, with a more indirect control of the functional flexors. Obviously, the flexion-extension patterns as generated by the human lumbar networks are different than the more complex patterns produced during active human over-ground stepping, that requires additional control mechanisms from supraspinal centers as well as from periphery.

Friday, September 27th, 18:30
[Symposium: Lumbar cord contribution in the postural and locomotor control studied in animal and human model]

Modification of segmental reflex activity by postural motor tasks

Ursula Hofstoetter

Center of Medical Physics and Biomedical Engineering, Medical University of Vienna, Austria

The maintenance of body posture in humans during the execution of postural and volitional tasks relies on dynamically adjusted, continuous motor coordination. The goal of the present study was to test the underlying sensory-motor control mechanisms by assessing task-dependent modifications of short-latency spinal reflexes associated with tonic and phasic motor activities. The originality of the study lies in analyzing monosynaptic spinal reflexes of several lumbar spinal cord segments in healthy adult subjects simultaneously elicited by electrical posterior root-stimulation and in testing their modifications during the execution of well controlled and coordinated postural and volitional multi- and single joint (i.e., multi- and oligosegmental) movements.

A novel, non-invasive method of transcutaneous spinal cord stimulation was used to simultaneously elicit monosynaptic posterior root-muscle (PRM) reflexes – named according to the sites of their initiation and their detection by surface electromyography – in multiple thigh and leg muscle groups bilaterally in subjects with intact nervous system functions (Minassian et al., 2007; Hofstoetter et al., 2008). PRM reflexes were used to assess the modification of synaptic transmission at several segmental levels simultaneously with the subjects (i) in upright standing position, performing unilateral dorsal and plantar flexion while standing on the contralateral lower limb as well as while leaning forward and backward at the ankle; and (ii) in supine position, isometrically lifting one of the extended lower limbs at the hip; and just before the execution of a fast withdrawal movement, i.e., during the preparatory phase of the movement.

We have demonstrated that PRM reflexes were modulated in the flexor and extensor muscle groups of the lower limbs to meet the functional requirements of the motor tasks and at the same time to counteract perturbation of equilibrium. In particular, the excitability of motoneurons associated with muscles that were quiescent during a specific task was inhibited. Moreover, modifications of motornuclei excitability took place even before the execution of the motor tasks.

The presented approach opens a new avenue for non-invasively investigating how motor control is triggered and maintained by spinal cord networks in subjects with intact or altered nervous system functions. Expanding the knowledge about the interaction between segmental reflex organization and automatic postural capacities will be crucial in designing new and adjusting already available rehabilitation strategies for restoration of locomotor functions in people with neurological disorders. Moreover, it will help advancing our understanding of how to maintain intact motor control functions and prevent postural disturbances.

Hofstoetter US, Minassian K, Hofer C, Mayr W, Rattay F, Dimitrijevic MR (2008). Modification of reflex responses to lumbar posterior root stimulation by motor tasks in healthy subjects. Artif Organs 32, 644-648.
Minassian K, Persy I, Rattay F, Dimitrijevic MR, Hofer C, Kern H (2007). Posterior root-muscle reflexes elicited by transcutaneous stimulation of the human lumbosacral cord. Muscle Nerve 35, 327-336.

Friday, September 27th, 17:00
[Symposium: Cognitive control in health and disease]

Advancements in the dual mechanisms framework of cognitive control

Todd Braver

Department of Psychology, Washington University in Saint Louis, USA

Research in my lab has focused on the neural mechanisms of cognitive control: the ability to regulate thoughts and actions in an intelligent, goal-directed manner. We have argued that such mechanisms, which involve a network of brain regions centered on the lateral prefrontal cortex, are highly flexible, and can operate in both a proactive and reactive mode. The proactive mode of control is future-oriented, preparatory and sustained in nature, while the reactive mode is transient, stimulus-driven, and frequently engaged by the presence of interference. I will present some recent work highlighting this theoretical approach, its utility for understanding individual differences and cognitive impairment in different populations, as well as some new directions it has taken us in understanding how motivation interacts with cognitive control.

Friday, September 27th, 17:30
[Symposium: Cognitive control in health and disease]

Cognitive and affective control: insights from study of schizophrenia

Deanna M. Barch

Departments of Psychology, Psychiatry and Radiology, Washington University in Saint Louis, USA

Schizophrenia is a complex psychiatric syndrome presenting with a heterogeneous set of symptoms that include cognitive and motivational abnormalities as well as psychotic symptoms. Clinicians have long recognized that abnormalities in cognitive function, affective processing and motivated behavior are a key component of this illness, with major implications for understanding functional impairment. This presentation overviews evidence that these deficits may reflect, at least in part, impairments in the ability to actively maintain and utilize internal representations of emotional experiences, previous rewards, and motivational goals in order to drive current and future behavior in a way that would normally allow individuals to obtain desired outcome. We refer to the mechanisms that support this anticipatory use of context and goals as proactive control. Prior research suggest that proactive control is supported by interactions between the dorsolateral prefrontal cortex and neurotransmitter systems such as dopamine, GABA and glutamate. We discuss the evidence for impairments in proactive control in schizophrenia and the evidence for associated impairments in dorsolateral prefrontal cortex and dopamine function in this illness. Further, we describe evidence suggesting that such proactive control impairments may be important for understanding affective and motivational impairments in schizophrenia as well as cognitive impairments.

Keywords: schizophrenia, proactive control, dorsolateral prefrontal cortex, motivation, cognitive control

Friday, September 27th, 18:00
[Symposium: Cognitive control in health and disease]

Cognitive control in Parkinson disease: insights from deep brain stimulation of the subthalamic nucleus

Tammara Hershey

Departments of Psychiatry and Radiology, Washington University School of Medicine, Saint Louis, USA

The basal ganglia, and the subthalamic nucleus (STN) in particular, is thought to contribute to aspects of cognitive control, particularly the selection of wanted and suppression of unwanted motor patterns according to explicit rules (i.e., response inhibition). Deep brain stimulation of the STN (STN DBS) in individuals with Parkinson disease (PD) provides a unique window into understanding this relationship. We have used information about the anatomical organization of the STN and novel imaging approaches to functionally map the STN region with respect to its role in cognitive control. Results from our lab and others suggest that the ventral subthalamic nucleus region is involved in the balance between appropriate selection and inhibition of prepotent responses in cognitive paradigms, but that a wide area of the subthalamic nucleus region is involved in PD motor symptoms. These findings highlight the role of the ventral subthalamic nucleus region in response inhibition and suggest an approach for the clinical optimization of deep brain stimulation of the subthalamic nucleus for both motor and cognitive functions.

Friday, September 27th, 18:30
[Symposium: Cognitive control in health and disease]

Functional networks of the brain underlying flexible cognitive control

Grega Repovš

Department of Psychology, Faculty of Arts, University of Ljubljana, Slovenia

To be able to generate goal directed behaviour, a cognitive system needs to be able to form and maintain ad hoc functional networks of regions that efficiently exchange and collaborate in processing the relevant information, generating a virtual workspace supporting the performance of the task at hand. Previous research using activation analyses identified key cognitive control networks that enable setting up a task set, maintaining its activity and adjust its function based on ongoing feedback. Recently, resting state and task-based functional connectivity analyses have been employed to study the dynamics of the integration between and within the control networks and its possible breakdown in schizophrenia. The studies have revealed dynamic adjustment of connectivity both within fronto-parietal network as well as with other cognitive control networks and the rest of the brain. The changes in connectivity strength robustly reflected task difficulty, whereas the particular shifts in whole-brain connectivity reflected the specifics of the task demands. Exploration of whole-brain functional connectivity further revealed prefrontal regions that are closely connected with the rest of the brain (i.e. hubs), for which the strength of their connectivity correlates with cognitive control and fluid intelligence, and the pattern of their dysconnectivity correlates with schizophrenia symptom severity. These findings highlight the importance of the study of functional brain integration and provide exciting insights into the mechanisms underlying flexible cognitive control.

Keywords: cognitive control, functional connectivity, fronto-parietal network, fluid intelligence

Saturday, September 28th, 08:30
[Symposium: New vistas in neuropeptide research]

Novel mass spectrometry imaging of neuropeptides and applications to Parkinson's disease

Per Andren

Uppsala University, Sweden

Neuropeptidomics is the technological approach for detailed analysis of endogenous peptides from the brain and the central nervous system. MALDI mass spectrometry imaging (MSI) or nano-liquid chromatography electrospray ionization (nanoLC-ESI) MS are powerful tools utilized for thorough analytical imaging and profiling of a large number of neuropeptides and small proteins. We have developed an approach using targeted sequence collections for identifying endogenous peptides from the brain. This approach enables a fast, specific, and sensitive identification of endogenous peptides. The sequence collections were used to identify novel peptides from brain tissue, and a number of previously uncharacterized peptides and potentially bioactive neuropeptides were identified. Further, maintaining the biochemical, molecular and structural sample integrity is essential for correct sample comparisons. We present novel software and protocols for the quantification of neuropeptides and drugs directly in tissue sections using MSI. Parkinson disease (PD) is characterized by progressive loss of dopaminergic neurons in the substantia nigra pars compacta projecting to the striatum. The information regarding the expression of neuropeptides in PD is limited. Here, we have elucidated brain neuropeptide mechanisms in experimental PD using the unilateral 6-hydroxydopamine and MPTP model to degenerate dopamine neurons. The analysis demonstrated several differentially expressed peptides in the PD model, including peptides from precursors such as secretogranin-1, somatostatin, prodynorphin, and cholecystokinin. Disease-related biotransformation of precursors into individual peptides was observed in the experimental PD models. Several previously unreported and potentially biologically active peptides were also identified from the striatal samples. This study provides further evidence that neuropeptides take part in mediating the central nervous system failure associated with PD.

Saturday, September 28th, 09:00
[Symposium: New vistas in neuropeptide research]

Regulation of peptide discharge from single vesicles: pre- and postfusion role of SNAREs

Robert Zorec

Faculty of Medicine, University of Ljubljana, Slovenia

Exocytosis is a multistage process involving a merger between the vesicle and the plasma membranes, leading to the formation of a fusion pore, a channel, through which secretions are released from the vesicle to the cell exterior. A stimulus may influence the pore by either dilating it completely (full-fusion exocytosis) or mediating a reversible closure (transient exocytosis). In neurons, these transitions are short-lived and not accessible for experimentation. However, in some neuroendocrine cells, initial fusion pores may reopen several hundred times, indicating their stability. Moreover, these pores are too narrow to pass luminal molecules, especially peptides, to the extracellular space, termed release-unproductive. However, on stimulation, their diameter dilates, initiating the release of cargo without de novo fusion pore formation. To explain the stability of the initial narrow fusion pores, anisotropic membrane constituents with non-axisymmetrical shape were proposed to accumulate in the fusion pore membrane. Although the nature of these is unclear, they may consist of lipids and proteins, including SNAREs, which may facilitate and regulate the pre- and post-fusional stages of exocytosis.

Saturday, September 28th, 09:30
[Symposium: New vistas in neuropeptide research]

Role of hypothalamus and steroidogenic factor 1 in body weight regulation

Gregor Majdič

Faculty of Veterinary Medicine, University of Ljubljana, Slovenia

Body weight regulation is one of the main homeostatic processes in an organism ensuring long-term survival of the individual. The main body weight regulation center in the brain is believed to be the hypothalamus. The hypothalamus receives direct inputs from the periphery, mainly in the arcuate nucleus, in the form of metabolic hormones such as leptin, insulin, ghrelin and others. The hypothalamus processes received information, and relays information about energy status either directly or through other, higher brain centers, back to the periphery. Within the hypothalamus, the arcuate, paraventricular, dorsomedial and ventromedial nuclei, and lateral hypothalamic area, are thought to be the most important regulators of energy balance. Many studies have revealed major roles in the regulation of energy balance for neuropeptide Y, agouti related peptide (AgRP), melanocortin (α-MSH) and cocaine and amphetamine related transcript (CART), which are all produced in the arcuate nucleus and are transported mainly into the paraventricular nucleus. Beside these, many other genes, encoding for other neuropeptides or for transcription factors, are involved in the regulation of energy balance. Steroidogenic factor 1 (SF-1) is a transcription factor, member of nuclear receptor superfamily, specifically expressed in the ventromedial hypothalamic nucleus (VMH). Mice lacking SF-1 have disorganized VMH and develop late onset obesity. Although the expression of NPY, AgRP, α-MSH and CART is not altered in SF-1 KO mice in arcuate and paraventricular nuclei, the cytoarchitecture of cells and fibers expressing these neuropeptides is altered in the whole region of mediobasal hypothalamus. Furthermore, recent studies have shown that the same SF-1 expressing cells in the VMH might regulate both fear response and energy balance, suggesting that these cells could be an important link between stress and regulation of energy balance/food intake.

Saturday, September 28th, 10:00
[Symposium: New vistas in neuropeptide research]

Oxytocin reduces cocaine seeking and restores cocaine-induced decreases in glutamate receptor function

Ronald See

Faculty of Medicine, University of Tabuk, Saudi Arabia
Department of Neurosciences, Medical University of South Carolina, Charleston SC, USA

Recent findings suggest that central oxytocin may be a critical modulator of natural and drug reward. However, the role of oxytocin has not been well studied in a valid model of drug addiction, and the effects of oxytocin on key neural regulators of the addiction circuitry have not been examined.

Here, we assessed acute oxytocin modulation of cocaine seeking during cocaine self-administration and reinstatement of cocaine seeking in rats after acute, systemic oxytocin treatment.

Male Sprague Dawley rats self-administered intravenous cocaine, paired with light+tone conditioned cues. Rats received oxytocin (0.1, 0.3, 1, 3 mg/kg, IP) or vehicle prior to cocaine self-administration sessions in a counterbalanced manner. Another set of rats received oxytocin or vehicle prior to discrete reinstatement trials for conditioned cue-induced or cocaine-primed reinstatement of cocaine seeking. In additional experiments, rats underwent the same cocaine self-administration regimen or received paired saline vehicle infusions and tissue was then obtained from a number of brain regions previously implicated in cocaine seeking. Western blotting techniques were used to measure several key receptors and signaling molecules across various brain regions.

Oxytocin reduced cocaine seeking and intake during self-administration and dose-dependently reduced cocaine seeking induced by cocaine-conditioned cues or a cocaine prime. In addition, oxytocin selectively reversed cocaine-induced decreases in pt-GluR1 and pt-ERK.

These data suggest that increased oxytocin reduces the primary and secondary reward properties of cocaine and may act as an anti-relapse medication through modification of glutamatergic regulators of cocaine seeking.

Saturday, September 28th, 14:30
[Symposium: Transmissible spongiform encephalopathies – from cause to cure]

Prions

Giuseppe Legname

SISSA, Trieste, Italy

Prion disorders are group of neurodegenerative diseases with unique etiology. In fact, they can be sporadic, genetic or infectious. The causative agent for these maladies is a misfolded protein isoform, the prion, of the endogenous physiological cellular prion protein.
Several decades of studies have indicated that the unique features of the prion are responsible for the distinct neuropathological and biochemical outcomes in animals and patients affected.
In this seminar, I will present an overview of landmark achievements in the field of prion biology and disease.

Saturday, September 28th, 15:00
[Symposium: Transmissible spongiform encephalopathies – from cause to cure]

Insights into molecular structures of human prion proteins with inherited mutations by NMR

Gregor Ilc[1,2], Gabriele Giachin[3], Ivana Biljan[1,4], Giuseppe Legname[4,5,6], Janez Plavec[1,3,7]

[1]Slovenian NMR Centre, National Institute of Chemistry, Ljubljana, Slovenia
[2]EN-FIST Centre of Excellence, Ljubljana, Slovenia
[3]Laboratory of Prion Biology, Neurobiology Sector, Scuola Internazionale Superiore di Studi Avanzati (SISSA), Trieste, Italy
[4]Department of Chemistry, Faculty of Science, University of Zagreb, Croatia
[5]Italian Institute of Technology, SISSA Unit, Trieste, Italy
[6]ELETTRA Laboratory, Sincrotrone Trieste S.C.p.A., Trieste, Italy
[7]Faculty of Chemistry and Chemical Technology University of Ljubljana, Slovenia

Understanding mechanisms by which cellular prion protein (PrPC) misfolds and leads to disease may benefit from detailed analysis of 3D structures. Our recent studies utilizing heteronuclear Nuclear Magnetic Resonance spectroscopy in solution have focused on structural characterization of different human PrPC variants that are linked to genetic prion diseases. High-resolution structures of Q212P, V210I and E219K mutants exhibit unique structural features that are caused by a single amino acid substitution and suggest molecular mechanisms of early events of the conformational conversion of PrPC to its pathological form, PrPSc.

Structural details of human prion protein HuPrP(90-231) carrying V210I mutation were analyzed under acidic and neutral pH conditions. While nearly complete assignment was obtained for V210I mutant at pH 5.5, amide protons are involved in fast exchange with solvent at pH 7.2 which renders observation of some amino acids residues from unstructured N-terminal region. Significant pH-related local structural differences were observed in the α2−α3 interhelical region, at the interface of the β1−α1 loop, in helices α1 and α3, and in the β2−α2 loop region. The detailed analysis of interactions suggests that spontaneous misfolding of PrPC may occur under acidic-pH conditions in endosomal compartments.

Saturday, September 28th, 15:30
[Symposium: Transmissible spongiform encephalopathies – from cause to cure]

Surveillance of Creutzfeldt-Jakob disease in Slovenia since 1987 to 2013

Mara Popović[1], Nuška Čakš[2], Gorazd Stokin[3], Aleš Kogoj[3], Alenka Kraigher[2]

[1]Institute of Pathology, Faculty of Medicine, University of Ljubljana, Slovenia
[2]National Institute of Public Health of Republic of Slovenia, Ljubljana, Slovenia
[3]University Psychiatric Hospital Ljubljana, Slovenia

The epidemics of bovine spongiform encephalopathy and transmission of this disease to humans in eighties and nineties of the last century provoked the consecutive surveillance projects of Creutzfeld-Jakob disease (CJD) to be established in Europe and other part of the developed world, named EURO-CJD, with the aim to find each case of human form of BSE, variant CJD (vCJD). Slovenia was included in one of the first EURO-CJD surveillance projects in 1994, and now is in the twentieth year of successful collaboration. During that time the Prion laboratory was founded at the Faculty of Medicine University of Ljubljana, enabling us to use fresh brain tissue of the patients deceased due to CJD for research and diagnostic purposes. Incidence of CJD increased considerably from 0,5 in the period 1987 to 1995 to 2,3 in the period 2001 to 2013, when the notification of the clinically suspected CJD cases and autopsy have become mandatory. In 2007 the expert group for CJD surveillance in Slovenia was established at the Institute of Public Health of Slovenia, composed of a neurologist, a psychiatrist, two epidemiologists and a neuropathologist. 84 notifications of clinically suspected CJD cases have been achieved since 2001. Out of that, 36 cases were confirmed and 24 were disproved by autopsy, 2 cases were disproved by clinicians, in 9 cases the autopsy failed to be performed, and 13 patients with clinically suspected CJD are still alive. All definite CJD cases are of sporadic type. Only one case of genetic prion disease, Gerstmann-Straussler-Scheinker's syndrome, clinically presented as spinocerebellar degeneration was recognized. Mean age of definite CJD cases was 68 years, female to male ratio is 1,6, and mean duration of illness was 6 months. Gene analysis revealed no mutation in PRNP of definite CJD cases, and the polymorphic codon 129 came out to be MM in 64 % of cases, MV in 14 % of cases and VV in 8 % of cases. In 14 % of cases gene analysis has not been performed yet. No case of vCJD has been found in Slovenia, so far.

Saturday, September 28th, 16:00
[Symposium: Transmissible spongiform encephalopathies – from cause to cure]

Diagnostics and therapy of prion diseases - some new challenges

Vladka Čurin Šerbec

Centre for the Production of Diagnostic Reagents and for Research, Blood Transfusion Centre of Slovenia, Ljubljana, Slovenia

Although scrapie in sheep has been known for centuries, the importance of prion diseases only became widely recognized in the last decades with the epidemics of bovine spongiform encephalopathy (BSE), the consequent appearance of a new variant of Creutzfeldt-Jakob disease (vCJD) in humans and its possible transmission by blood. According to »protein-only hypothesis«, prion diseases are caused by incorrectly folded cellular prion protein (PrPC), called prion (PrPSc). Despite significant efforts, neither etiology nor immunology of prion diseases is well understood at the moment. No significant humoral or cellular immune response has been observed in patients with sporadic or acquired prion diseases. B- and T-cell tolerance are the main obstacles for an effective immune response to the incorrectly folded self-protein or to PrP of other mammals; sequence similarity among them is typically higher than 85%. The development of reliable premortem diagnostic tools as well as a potential anti-TSE passive or active vaccine thus represent a major problem. The knowledge, obtained in prion research, seems to be also useful in other neurodegenerative diseases, which represent an important issue.

In the presented work, the PrPSc-specific IgG mAb will be described, which recognizes a new, recently discovered fragment in TSE infected brain, PrP226* (1,6). On the basis of this mAb a diagnostic test for postmortem BSE diagnostics without proteinase K digestion of the brain sample was developed in the past (1,2). The study of importance of PrP226* for diagnostics is in progress. As a new challenge in prion research, anti-idiotypic mAbs were prepared as a possible way to exercise an active vaccine, by using a panel of mAbs for stringent selection (3) and an overview of the immunogenicity of the prion peptides was done (4). To examine a passive vaccine, scFv fragment of PrPSc-specific mAb was prepared in humanised form and it was linked to a peptide which enables crossing of the blood-brain barrier (5,7,8).

1. Čurin Šerbec, V., Bresjanac, M., Popović, M., Pretnar Hartman, K., Galvani, V., Rupreht, R., Černilec, M., Vranac, T., Hafner, I., Jerala, R. (2004) Monoclonal antibody against a peptide of human prion protein discriminates between Creutzfeldt-Jakob's disease-affected and normal brain tissue. J. Biol. Chem. 279 (5), 3694-3698.
2. Vranac, T., Pretnar Hartman, K., Popović, M., Venturini, A., Žerovnik, E., Čurin Šerbec, V. (2006) A single prion potein peptide can elicit a panel of isoform specific monoclonal antibodies. Peptides 27 (11), 2695-2705.
3. Colja Venturini, A., Bresjanac, M., Vranac, T., Koren, S., Narat, M., Popović, M., Čurin Šerbec, V. (2009) Anti-idiotypic antibodies: a new approach in prion research. BMC Immunology 10, article 16, on line.
4. Ghielmetti, M., Vranac, T., Čurin Šerbec, V. (2009) Prion protein peptides as vaccines. Mini-Reviews of Medicinal Chemistry 9, 470-480.
5. Škrlj, N., Čurin Šerbec, V., Dolinar, M. (2010) Single-chain Fv antibody fragments retain binding properties of the monoclonal antibody raised against peptide P1 of the human prion protein. Appl Biochem. Biotechnol., 6, (160), 1808-1821.
6. Kosmač, M., Koren, S., Giachin, G., Stoilova, T., Gennaro, R., Legname, G., Čurin Šerbec, V. (2011) Epitope mapping of a PrPSc-specific monoclonal antibody: Identification of a novel C-terminally truncated prion fragment. Mol. Immunol., 48 (5), 746-750.
7. Škrlj, N., Vranac, T., Popović, M., Čurin Šerbec, V., Dolinar, M. (2011) Specific binding of the pathogenic prion isoform: Development and characterisation of a humanized single-chain variable antibody fragment. PlosOne, 6 (1), art.no.e15783 (9 pages).
8. Škrlj, N., Drevenšek, G., Hudoklin, S., Romih, R., Čurin Šerbec, V., Dolinar, M. (2013), Cell-penetrating peptide penetratin enables brain delivery of the PrPSc-specific single-chain antibody fragment. Appl. Biochem. Biotechnol., 169, 159-169.

Saturday, September 28th, 17:00
[Symposium: Botulinum toxin type A and pain]

Botulinum toxin for the treatment of pain

Dirk Dressler

Department of Neurology, Hannover Medical School, Germany

Botulinum toxin (BT) can induce a well controllable paresis. It also seems to have intrinsic analgesic effects. With these features BT has been used to treat a considerable number of pain conditions.
In muscular pain, BT can be helpful in dystonia, spasticity, bruxism with temporomandibular joint dysfunction and in special pain conditions including piriformis syndrome and scalenus syndrome. Its use in myogelosis, tension type headache and fibromyalgia is controversial.
In non-muscular pain BT has gained an international drug registration for the treatment of chronic migraine. Peripheral non-muscular pain including polyneuropathic pain and trigeminal pain may or may not respond to BT.

Saturday, September 28th, 17:25
[Symposium: Botulinum toxin type A and pain]

Behavioural evidence for central origin of the antinociceptive action of botulinum toxin type A

Lidija Bach-Rojecky

Department of Pharmacology, Faculty of Pharmacy and Biochemistry, Univesity of Zagreb, Croatia

During the last several years antinociceptive effect of botulinum toxin type A (BTX-A) was investigated both, in animal models and in humans. In series of experiments we demonstrated that BTX-A's antinociceptive action might be of central origin, contrary to usual assumption. BTX-A reduced inflammatory hyperalgesia, but not local edema or protein extravasation induced by the carrageenan and capsaicin injections into the rat hindpaw (Bach-Rojecky et al., 2008). The antinociceptive activity of BTX-A was obtained with lower doses and with faster onset after intrathecal than after peripheral injection. Studies of rat "mirror pain" (muscular hyperalgesia) and streptozotocin-induced polyneuropathy demonstrated bilateral effects following unilateral BTX-A injection (Bach-Rojecky and Lacković, 2009; Bach-Rojecky et al., 2010). In the model of acidic saline-induced bilateral muscle hyperalgesia, BTX-A injection into the distally cut sciatic nerve was still able to reduce contralateral pain, thus excluding the involvement of peripheral nerve endings in the antinociceptive action of the toxin (Bach-Rojecky and Lacković, 2009). In this model, the effect of peripheral BTX-A was prevented by colchicine-induced blockade of axonal transport in the sciatic nerve, suggesting that retrograde axonal transport of BTX-A was necessary for its antinociceptive action. Recently we provided first insights into the mechanism of BTX-A's central antinociceptive activity. We demonstrated prevention of BTX-A effects on formalin-induced and experimental neuropathic pain and c-Fos expression by opioid antagonists thus suggesting that the central antinociceptive action of BTX-A might be associated with the activity of endogenous opioid system (involving μ-opioid receptor).

Saturday, September 28th, 17:50
[Symposium: Botulinum toxin type A and pain]

Immunohistochemical evidence of central antinociceptive action of botulinum toxin type A

Ivica Matak[1], Lidija Bach-Rojecky[2], Boris Filipović[1], Peter Riederer[3], Zdravko Lacković[1]

[1]Laboratory of Molecular Neuropharmacology, Department of Pharmacology, University of Zagreb School of Medicine, Croatia
[2]Department of Pharmacology, University of Zagreb School of Pharmacy, Croatia
[3]Department of Psychiatry, Psychosomatics and Psychotherapy, University of Würzburg, Germany

Botulinum toxin A (BTX-A) has been approved for treatment of movement disorders and migraine. Widely assumed peripheral mechanism of action has been questioned by recent studies which demonstrated the axonal transport in facial nerve and within central nerves. Findings in our laboratory suggested a central antinociceptive activity following axonal transport in sciatic nerve.

To characterize the axonal transport of BTX-A, toxin's enzymatic activity in CNS was assessed using immunofluorescent detection of its cleaved substrate synaptosomal-associated protein 25 (SNAP-25) following injections into the rat whisker pad, hind-paw, intramuscular injection into the gastrocnemius and intraneural injections into the sciatic nerve. Intraneural colchicine was employed to prevent the axonal transport in sciatic nerve.

Following whisker pad BTX-A injection, cleaved SNAP-25 has been observed in medullary dorsal horn. Cleaved SNAP-25 following subcutaneous, intramuscular and intraneural toxin injection in rat hind limbs has been observed in corresponding segments of ipsilateral dorsal and ventral horn. Central SNAP-25 cleavage following BTX-A injection into the sciatic nerve was prevented by colchicine.

Our results suggest that the axonal transport of BTX-A in spinal and trigeminal sensory neurons commonly occurs after peripheral applications. Toxin's central enzymatic activity after its axonal transport is most likely modulating the nociceptive transmission between primary afferents and second order neurons.

Acknowledgements: Antibody to cleaved SNAP-25 was a kind gift from Ornella Rossetto (University of Padua, Italy).

Sources of funding: Croatian Ministry of Science, Education and Sport and Deutscher Academischer Austauch Dienst.

Saturday, September 28th, 18:15
[Symposium: Botulinum toxin type A and pain]

The effect of botulinum toxin type A on neurogenic dural inflmation: a clue to mechasnis of its action in migraine

Boris Filipović, Ivica Matak, Zdravko Lacković

Laboratory of Molecular Neuropharmacology, Department of Pharmacology and Croatian Brain Research Institute, University of Zagreb School of Medicine, Croatia

Migraine is a common neurological condition affecting over 10 per cent of the population. Recently Botulinum toxin type A (BTX-A) was approved for treatment of migraine but the mechanism was not clear.

Trigeminovascular of migraine is a dominant hypothesis about its pathophysiology. Basically it connects pain with release of vasodilatatory neuropeptides (CGRP, substance P) from peripheral sensory nerve endings innervating dural and cranial blood vessels. Classical animal model of migraine is neurogenic dural extravasation (sterile inflammation, DNI) induced by electrical stimulation of rat trigeminal ganglion. Recently we found DNI associated with peripheral trigeminal nerve injury, application of formalin in trigeminal area or Freud adjuvant induced maxillo-mandibular joint pain. The mechanism of action of antimigraine drugs is to prevent release of vasadilatator neuropeptides from peripheral sensory nerve endings, and consequently prevent vasodilatation.
In comparison to strong DNI evoked by pain in trigeminal regions, smaller but significant DNI was observed following the occipital nerve constriction. However DNI was not observed in the sciatic nerve injury.

Thus DNI seems to be specifically associated with to trigeminal area and adjacent occipital area. In line with trigeminovascular theory we found that BTX-A, known to prevent release of different neurotransmitters, prevents DNI induced by trigeminal pain. This seems to be the best explanation of beneficial effect of BTX-A in migraine.

Saturday, September 28th, 18:40
[Symposium: Botulinum toxin type A and pain]

What we do not understand about botulinum toxin?

Zdravko Lacković

Laboratory of molecular Neuropharmacology, Department of Pharmacology and
Croatian Brain Research Institute, University of Zagreb School of Medicine, Croatia

For therapeutic and cosmetic reasons botulinum toxin type A (BTX-A) is nowadays used every year by millions of people. It is estimated that only in the United States each year for cosmetic reasons about 5 million people receives botulinum toxin It cleaves SNAP 25 one of the SNARE proteins required for vesicle exocytosis. Accordingly flaccid paralysis is a hallmark of botulism poisoning. Small intramuscular doses are for years used in neurology and oculistic and other disciplines. However in the last period clinically increasing number of pain condition shoved beneficial effect of botulinum toxin, Best known and accepted example is migraine. Classically it was believed that it acts only at peripheral nerve endings. Last years in Zagreb Laboratory of Molecular Pharmacology iit was for discovered that botulinum toxin administered peripherally is transported along sensory neurons to sensory centres in the central nervous system. Associated with that new antinociceptive activities of toxin were discovered (e.g., painful neuropathy due to diabetes or physical damage, the pain centre of origin). Particularly interesting are the findings that the toxin reduces pain in the trigeminal area and associated neuronal inflammation of the meninges as reported here by our PhD candidate Boris Filipović. Those discoveries changes the assertions in textbooks of pharmacology, microbiology and others that botulinum toxin has only peripheral effects - and raises new questions about the safety or new clinical possibilities of this neurotoxin. Moreover continuation of this research can add to our understanding of pain phenomenon's like supersensitivity and alodinija. Report from our PhD candidate Ivica Matak partially at this symposium partially answers this question. Finally new discovery on association between botulinum toxin and opioid receptors in the brain, reported here by Lidija Bach Rojecky provide first indication about central mechanism of botulinum toxin action. Is this sufficient? Definitively not and more we know more new questions emerge.

Sunday, September 29th, 08:30
[Symposium: Neurosurgeons meet neuroscientists]

Cortical removal vs. cortical preservation: why do we need both?

Andrej Vranič

Clinical Department of Neurosurgery, University Medical Centre Ljubljana, Slovenia

The purpose of the presentation will be to describe cortical resection in order to treat epileptogenic foci, as well as techniques of cortical preservation when performing tumor excision.

About 30% of patients with epilepsy are resistant to drug therapy; many of them are potential candidates for surgical treatment. Selection of patients is based on precise identification of the epileptogenic area. Invasive monitoring with subdural surface electrodes positioning or deep electrodes implantation is usually required. More and more surgery is performed on pediatric patients. Most frequently performed surgical procedures are partial temporal lobe resection in adults, and focal resection or hemispherotomy in children. A recent randomized controlled trial demonstrated early surgery for patients with temporal lobe epilepsy being superior to medical therapy. Complications are generally temporary, and surgery is generally associated with improvement in depression. Although the enduring benefits of surgery has been demonstrated, epilepsy surgery continues to be underutilized.

The aim of brain tumor surgery is not only total lesion removal, but also a functionally unaffected patient. Several techniques have been developed in order to facilitate cortical preservation. Next to imaging procedures, pre- and intraoperative functional techniques are of utmost importance, allowing us to discern eloquent cortical areas before or during surgery. The only way the language area of the brain can be identified is awake surgery. Our experience in introducing awake surgery will be discussed.

Sunday, September 29th, 09:00
[Symposium: Neurosurgeons meet neuroscientists]

The soul, the pineal gland and the neurosurgeon. Does modern neurosurgery give us some knowledge of the soul?

Anne-Laure Boch

Service de Neurochirurgie, Hôpital Pitié- Salpêtrière, Paris, France

According to French philosopher René Descartes (1596-1650), human soul is not only lodged in the body like "a pilot in a ship", but tightly bound to it. Its very seat is the pineal gland, right in the middle of the head. By opening the skull with his trepan, modern neurosurgeon often visits this secrete cabin. The daily inspection of the soul's apartment should give him a pertinent point of view on this serious matter. How does the neurosurgeon consider the soul, mind, and spirit? Do neuroscience and neurosurgery – the medical technique that is issued from neuroscience – have some knowledge of the soul question? Are they able to construct…or only deconstruct, in a field which is traditionally seen as philosophy and religion's preserve?

Sunday, September 29th, 09:30
[Symposium: Neurosurgeons meet neuroscientists]

Glioblastoma multiforme - between surgery and genetics

Boštjan Matos

Clinical Department of Neurosurgery, University Medical Centre Ljubljana, Slovenia

Glioblastoma multiforme is the most common and most aggressive primary brain tumor. The standard treatment for newly diagnosed glioblastoma is gross total removal, if possible, followed by chemo- and radiotherapy. Despite maximum treatment, majority of patient only have a median survival time of 15 months. In contrast to many other malignancies, there have only been small improvements in the glioblastoma patients prognosis over recent decades. A better understanding of the molecular biology of glioblastomas has enabled the development of various bio-markers that have diagnostic, prognostic and predictive values. The purpose of this presentation is to provide up-to-date overview of current identified molecular alterations which lead to more individualized treatment approaches in glioblastoma.

Sunday, September 29th, 10:00
[Symposium: Neurosurgeons meet neuroscientists]

Invasive brain surgery and implantable devices for treatment of psychiatric conditions: old debate but with new technologies?

Frederic Gilbert

ARC Centre of Excellence for Electromaterials Science, University of Tasmania, Hobart, Australia

The history of psychiatry accounts for many changes in the ways medicine has explained psychiatric condition aetiologies; and consequently, has modified the ways some disorders have been treated. Recently, there has been growing interest in using invasive brain surgery, involving implantable devices as a last recourse to alleviate the symptoms of patients suffering from different types of psychiatric conditions (i.e. Treatment Resistance Depression, Obsessive Compulsive disorder, Alzheimer, etc.), even though the origin of these conditions is still far from being fully understood. The purpose of this presentation is to explore the new ethical issues of using novel invasive and implantable technologies to treat psychiatric conditions.

Sunday, September 29th, 14:30
[Symposium: Hypoxic brain damage, neuroprotection and long-term outcome with regard to quality of life]

The EPICure studies: changing outcomes for extremely preterm children

Neil Marlow

UCL Institute for Women's Health, London, UK

Caring for babies of extremely low gestational age is challenging with high mortality and morbidity among survivors. It is important to monitor the outcomes for such babies to help with counselling and practice. We have carried out 2 prospective national cohort studies: EPICure – children born 22-25 weeks of gestation in 1995 across the British Isles – and EPICure2 – children born 22-26 weeks across England in 2006. In this presentation I will describe outcomes at 3 years for babies born before 27 completed weeks of gestation in England during 2006, and evaluate changes in outcome since 1995 born between 22 and 25 weeks of gestation.

1031 surviving babies of mothers resident in England of <27 completed weeks gestational age in 2006. Evaluation was blinded to neonatal course (n=576) or from routine local assessments carried out at around 2 years of age (n=191). Outcomes for 584 children born at 22-25 weeks of gestation were compared to those of 260 surviving children of mothers resident in England born in 1995.
Main outcome measures were: survival to three years, disability (using consensus definitions), and developmental scores (normal population values: mean 100 (standard deviation: 15)). Multiple imputation was used to account for the high proportion of missing data in the 2006 cohort.

Of the 576 children evaluated following birth in 2006, overall 13% were categorised with severe and 12% with moderate impairment. The prevalence of neurodevelopmental impairment increased with gestational age from 45% at 22-23 weeks, 30% at 24 weeks, 25% at 25 weeks and to 20% at 26 weeks. Cerebral palsy was found in 83 (14%) of survivors. Mean developmental quotients were lower than those of the general population and showed a direct relationship with gestational age from 80 (standard deviation: 21) at 22-23 weeks, 87 (19) at 24 weeks, 88 (19) at 25 weeks, and 91 (18) at 26 weeks. There were no significant changes to these results following imputation. Comparing imputed outcomes between the 2006 and 1995 cohorts, the proportion of survivors born between 22 and 25 weeks of gestation with severe disability, using 1995 definitions, was unchanged (19%). Fewer survivors had shunted hydrocephalus or seizures. Considering all babies admitted for neonatal care, survival increased by 13% and survival without disability increased by 11% (6% to 16%).

Both survival and impairment in early childhood are closely related to gestational age for births <27 weeks. Following multiple imputation to account for the high proportion of missing values we estimate that a higher proportion of admissions for neonatal care now survive without disability, particularly at 24 and 25 weeks.

1. Costeloe K.L., Hennessy E.M., Haider S., Stacey F., Marlow N., Draper E.S. Short term outcomes after extreme preterm birth in England: comparison of two birth cohorts in 1995 and 2006 (the EPICure studies). BMJ 2012; 345; e7976
2. Moore T., Hennessy E.M., Myles J., Johnson S.J., Draper E.S., Costeloe K.L., Marlow N. Neurological and developmental outcome in extremely preterm children born in England in 1995 and 2006: the EPICure studies. BMJ 2012; 345:e7961

Sunday, September 29th, 15:10
[Symposium: Hypoxic brain damage, neuroprotection and long-term outcome with regard to quality of life]

Reduction in brain volume in young adults with perinatal hypoxic-ischaemic encephalopathy

Tina Bregant[1], Milan Rados[2], Lana Vasung[2], Metka Derganc[3], Alan C. Evans[4], David Neubauer[1], Ivica Kostovic[2]

[1]Department of Paediatric Neurology, University Children's Hospital, University Medical Centre Ljubljana, Slovenia
[2]Croatian Institute for Brain Research, School of Medicine, University of Zagreb, Croatia
[3]Department of Paediatric Surgery and Intensive Care, University Medical Centre, Ljubljana, Slovenia
[4]McConnell Brain Imaging Centre, Montreal Neurological Institute, Canada

A severe form of perinatal hypoxic-ischaemic encephalopathy (HIE) carries a high risk of perinatal death and severe neurological sequellae while in moderate and mild HIE only discrete cognitive disorders may occur. Imaging biomarkers for long term outcome in children with perinatal HIE are not known.

The purpose was to compare total brain volumes and region-specific cortical measurements between young adults with mild-moderate perinatal HIE and a healthy control group of the same age. Childhood survivors of HIE are at increased risk of cognitive, behavioural and memory problems even in the absence of gross motor problems.

MR imaging (3T Magnetom Trio Tim, Siemens) was performed in a cohort of 14 young adults (9 males, 5 females, mean age 22.1±0.7 years) with a history of mild or moderate perinatal HIE defined by Sarnat and Sarnat criteria. The control group consisted of healthy participants (9 males, 5 females, mean age 22.8±0.7 years) without a history of perinatal HIE.
Automated volumetric analysis was done after the automatic processing of MR images using a fully automated CIVET pipeline. We measured gyrification indexes, total brain volume, volume of white and grey matter, and cerebrospinal fluid. We also measured volumes, thickness and area of the cerebral cortex in the frontal, parietal, temporal, occipital lobe, and of the cingulated and parahippocampal gyrus, isthmus cinguli, and insula.
Adolescents were neurologically examined and interviewed, health-related quality of life was assessed by SF-36v2 questionnaire, Rosenberg self-esteem inventory and Unwholesome behaviour questionnaire.

The HIE patient group showed smaller absolute volumetric data. Statistically significant ($p<0.05$) reductions of gyrification index in the right hemisphere, of cortical areas in the right temporal lobe and parahippocampal gyrus, of cortical volumes in the right temporal lobe and of cortical thickness in the right isthmus of the cingulate gyrus were found. Comparison between the healthy group and the HIE group of the same gender showed statistically significant changes only in the male HIE patients, where a significant reduction was found also in whole brain volume, left parietal and temporal cortical areas and left temporal lobe cortical volume.
Adolescents with HIE reported higher morbidity yet a good quality of life: for adolescents with HIE M=81.9 (SD=11.2) and for healthy adolescents M=75.3 (SD=11.5); $p=0.112$. Adolescents with HIE did not distinguish from healthy adolescents in self-esteem ($p=0.68$) and unwholesome behaviours, except for over-eating ($p=0.01$). In group of HIE professional support was given in 50.0%, while healthy group did not receive any.

Our analysis of total brain volumes and region-specific corticometric parameters suggested greater vulnerability of males to the deleterious effects of mild and moderate perinatal HIE, with predilection changes in the temporal lobes and parahippocampal gyrus, being more pronounced in the right hemisphere.
Despite higher morbidity and deleterious effects of HIE on brain development the adolescents with perinatal hypoxia have a good quality of life which suggests development of compensatory strategies. Adequate family functioning with a school support and well coordinated health care can help children to cope with sequellae of mild to moderate HIE.

Sunday, September 29th, 15:30
[Symposium: Hypoxic brain damage, neuroprotection and long-term outcome with regard to quality of life]

Therapeutic hypothermia – 8-year experience

Metka Derganc

Department of Paediatric Surgery and Intesive Care, University Children's Hospital, University Medical Centre Ljubljana, Slovenia

In 2005, 3 large RCTs of therapeutic hypothermia (TH) in the newborn showed better neurodevelopmental outcome at 18 months of age in cooled newborns with moderate and severe hypoxic encephalopathy compared to normothermia. In 2006, NICHD therefore recommended that TH be introduced as a routine method in the NICUs, provided that the protocol of the original studies be used , follow-up performed and register established.

TH was introduced in the NICU/PICU, University Medical Centre Ljubljana in 2006. A team consisting of paediatric intensivists, neurologists and psychologists was formed.
Whole body hypothermia was achieved by first using manually controlled device (Thecoterm), immediately followed by servo-controlled device (Criticool). TOBY protocol was implemented, with integrated amplitude EEG (aEEG) (Brainz) used among entry criteria and throughout 72 h of hypothermia. Ultrasound and Doppler were done before cooling. MRI was done between 4-7days of life and changes were described according to existing protocols. Infants were examined according to Amiel Tison at 1 month of age. Vision and hearing were checked. Fourty-six newborns were treated with TH, 4 infants/46 died (9%). Developmental outcome (Bayley III) was performed at 18 months of age in 31 children. Severe developmental delay, CP and epilepsy was found in 5/31 (16%), Bayley cognitive score <70 was found in 3/31(10%), 19/31 (61%) had Bayley cognitive score >71, 4 were lost to follow up. Although these results compare favourably to single center results in the USA (Perlman 2011), we feel that to improve these results, we need to add to TH another neuroprotective treatment which is being studied clinically: inhaled xenon, erythropoietin or allopurinol.

Sunday, September 29th, 15:50
[Symposium: Hypoxic brain damage, neuroprotection and long-term outcome with regard to quality of life]

Outcome of hypoxic-ischaemic encephalopathy (HIE) in late adolescence: insights on cognitive outcome from neuropsychology, DTI and resting state fMRI

David Gosar

University Children's Hospital, University Medical Centre Ljubljana, Slovenia

Adolescents who have experienced moderate neonatal hypoxia-ischemia (HIE) have been shown to have specific cognitive deficits, including reductions in verbal fluency, poorer working memory and reduced speed of information processing (Viggedal et al., 2002; Lindström et al., 2006; Mañeru et al. 2001). In adolescents with moderate neonatal HIE a previous study has such deficits in executive functioning and poorer verbal fluency with reduction of white-matter in the corpus callosum (Mañeru et al., 2003). Later studies on the outcome of hypothermia in preschool children with HIE have produced similar findings, showing a connection between cognitive outcome and measures of white matter integrity obtained by diffusion tensor imaging (DTI). In our study we also sought to confirm the impact of white-matter damage on the cognitive function of adolescents with mild and moderate neonatal HIE. Consistent with previous work we hypothesized that adolescents with moderate HIE would show reduced speed of information processing compared to their neurotypical peers. Furthermore, we predicted that the degree of impairment would correlate with the reduction of white matter integrity, as assessed fractional anisiotropy (FA).

Our study included 33 participants with mild or moderate HIE (mean age 18y 5m, SD 1y; 14 females) and 32 neurotypical adolescents (mean age 17y 10mo, SD 1y, 14 females). Both groups completed a comprehensive neuropychological battery measuring short-term memory, inhibition, speed of information processing and long-term visual and verbal memory. Fourteen participants also underwent structural MRI and DTI. Among them ten also had a resting-state fMRI scan.

After controlling for age, gender and maternal education we found a significant effect of HIE on speed of information processing ($F(2, 64) = 3.51$, $p < .037$, $\eta 2 = .115$), but not other neuropsychological measures. Using tract-based spatial statistics (TBSS) we were also able to confirm a correlation between the degree of impairment in this cognitive domain and fractional anisotropy in several white-matter tracts, including the the genu, body and splenium of the corpus callosum, parts of the inferior and superior longitudinal fasciculus and other white matter tracts.

Based on our results we concluded that the long-term cognitive sequelae of moderate HIE do indeed include reduced speed of information processing and are in part mediated by reduced integrity of major white-matter tracts.

Sunday, September 29th, 16:10
[Symposium: Hypoxic brain damage, neuroprotection and long-term outcome with regard to quality of life]

Amplitude-integrated EEG versus conventional EEG use in NICU/NSCU

David Neubaer

Department of Paediatric Neurology, University Children's Hospital, University Medical Centre Ljubljana, Slovenia

The aim is to present pros and cons of the use of amplitude-integrated versus conventional/classical electroencaphalograpy in the neonatal intensive and special care units.
The author presents historical data on amplitude-integrated EEG (aEEG) as well as on conventional EEG (cEEG) and compares these with the development of both methods in his own laboratory. Then follows a short discusssion on pros and cons regarding the use of both methods in NICU and the decsision-making of the most appropriate use of one or another. The statistical data of recording EEG in NICU are discussed and the most often categories of newborns with neurologcal impairments are shown. The examples of each of these categories are presented. At the end also some characteristical examples and pitfalls in aEEG reading are given and the algoprithm of both procedure use is proposed.
Both techniques are very much valuable in the standard of care of ill neonates at the intensive care units and, if the proper guidelines of the effectiveness and use of both, are applied, the management of severely neurologically-ill newborns can be much improved.

SNC'13

SiNAPSA Neuroscience Conference '13

Ljubljana, Slovenia, September 27-29, 2013

Abstracts

Young Neuroscientists Forum Ljubljana '13

www.sinapsa.org/SiNC13/YNFL13

Faculty of Medicine, University of Ljubljana, Slovenia
27 September 2013

Friday, September 27th, 08:30
[Young Neuroscientists Forum Ljubljana '13]

Neural stem cells-enriched tubulization improves anatomical and functional restoration of the severed rat sciatic nerve

Stefano Frausin[1], Lucia Verga Falzacappa[1], Serena Viventi[1], Pela Bisatti[1], Roberta Turrini[2], Alessandro Melatini[2], Ruggero Mele[2], Giampiero Leanza[1]

[1]B.R.A.I.N. Lab for Neurogenesis and Repair, Department of Life Sciences, University of Trieste, Italy
[2]A.O.S. Maria degli Angeli, Pordenone, Italy

Reconstruction of the severed peripheral nerve entails direct suturing or, in case of extensive gap, tubulization of the nerve using adequate biocompatible conduits. Loading tubules with growth-promoting factors or cells may speed-up and/or optimize nerve repair, however, only relatively scant evidence is available.

Here, this possibility has been investigated after the formation of a 5-mm gap and tubulization of the rat sciatic nerve with a cell-compatible, biodegradable PLCL (poly DL-lactide-e-caprolactone, Neurolac®) copolyestere tube filled with either cultured Human Umbilical Mesenchymal Stem Cells (HUMSCs), human neural progenitors or their conditioned medium. The study included also animals subjected to direct suturing of the transected nerve, animals with gap only and animals with gap and unloaded PLCL tube. Starting from one week up to 5 months post-surgery, behavioural tests were administered weekly, followed by histochemical and tract-tracing analyses to assess the anatomical and functional condition of the treated nerve, with respect to the intact contralateral side.

The results showed a remarkable nerve integrity and a better functional recovery in the animals implanted with the cell- or medium-loaded tube, compared to the other groups. Thus, tubulization associated with local supply of growth-promoting factors may represent a viable strategy for optimizing functional restoration of the peripheral nerve, but further analyses are needed before its clinical use.

Keywords: sciatic nerve, tubulization, stem cells

Friday, September 27th, 08:45
[Young Neuroscientists Forum Ljubljana '13]

Early exposure to enriched environment reverses learning deficits and improves hippocampal neuron survival in rats with selective cholinergic lesion

Pela Bisatti, Marino Coradazzi, Lucia Verga Falzacappa, Giampiero Leanza

B.R.A.I.N. Laboratory for Neurogenesis and Repair, Department of Life Sciences, University of Trieste, Italy

Cholinergic loss induces severe cognitive deficits and affects neuron proliferation in the hippocampal dentate gyrus (DG). Conversely, exposure to an enriched environment (EE), is known to enhance neurogenesis, in addition to improving learning abilities, suggesting a relationship between these features. However, this issue has never been addressed in developing animals. Here, the effects of early exposure to EE upon spatial learning and on survival of newborn cells in DG were investigated in rats with a selective cholinergic lesion.

Two litters of rats were used. In each litter, half of the animals underwent immunotoxic or sham-lesions at post-natal day 4. Groups of randomly selected lesioned and control animals were caged in a specially designed EE whereas the remaining rats were maintained under standard (i.e. non-enriched) conditions. At 3 months of age, all animals were tested in a Water Maze task to evaluate possible differences in their spatial learning abilities. One month before sacrifice, all rats were treated with BrdU to assess the survival of newborn neurons in DG.

Lesioned animals caged in standard conditions exhibited mild, but significant working memory deficits, whereas lesioned animals exposed to the EE performed as efficiently as controls. EE exposure enhanced survival of newly generated neurons both in control and in lesioned rats, but did not lead to any behavioural improvements in the former group.

Thus, compensatory mechanisms associated with prolonged EE exposure may enhance survival of newly generated cells in DG, and prevent the mild cognitive deficits induced by an early cholinergic depletion.

Keywords: hippocampal lesion, neurogenesis, working memory, water maze

Friday, September 27th, 09:00
[Young Neuroscientists Forum Ljubljana '13]

Effects of cognitive remediation during 14-day bed rest on walking performance of older adult men

Uroš Marušič[1,3], Voyko Kavcic[2], Mitja Gerževič[1], Matej Plevnik[1], Romain Meeusen[3], Boštjan Šimunič[1], Rado Pišot[1]

[1]Institute for Kinesiology Research, Science and Research Centre, University of Primorska, Koper, Slovenia
[2]Institute of Gerontology, Wayne State University, Detroit, MI, USA
[3]Department of Human Physiology, Faculty of Physical Education and Physical Therapy, Vrije Universiteit Brussel, Brussels, Belgium

Prolonged immobilization or inactivity which follows sports injuries and surgery could lead to serious motor dysfunction preventing a quick recovery and causing elevated costs for a national health care system. Therefore, it is important to develop interventions to reduce the deterioration of the motor output during immobilization or inactivity. We tested the effectiveness of cognitive training in attenuating motor decline (i.e., walking proficiency) during prolonged immobilization by performing a cognitive-based intervention during bed rest (BR).

Fifteen older adult men age 53 - 65 years participated in a 14 days BR study; half of them underwent 12 daily sessions of 50 minutes of cognitive training in which participants had to solve virtual mazes and the other half watched documentaries at the same time. A day before and after BR walking performance was measured with Optogait system in two conditions: normal speed and normal speed with dual task, with walking performance measured in terms of dual task cost [(walking with dual task – walking)/walking X 100].

Results showed that older adult men who underwent cognitive training during 14 days BR did not show any dual task costs in double support, stride, walking speed, and cadence during normal walking pace as compared to those without cognitive training.

Our results unequivocally show that cognitive intervention with spatial navigation training can attenuate decline in walking performance evident after prolonged immobilization. Preventive effects of virtual maze navigation most likely reflect the transfer of cognitive training on executive functions and/or preserved motor control.

Keywords: bed rest, cognitive training, virtual maze navigation, walking performance

Friday, September 27th, 09:15
[Young Neuroscientists Forum Ljubljana '13]

Cognitive emotion regulation of aversive emotional responses and their prediction recruits a common regulatory system

Satja Mulej Bratec[1,2,5], Xiyao Xie[1,2,6], Marie-Luise Brandi[1,2,5], Verena Krupp[2], Afra Wohlschläger[1,2,5], Valentin Riedl[1,2,3], Christian Sorg[1,2,4]

[1]Department of Neuroradiology,
[2]TUM-NIC Neuroimaging Center,
[3]Department of Nuclear Medicine,
[4]Department of Psychiatry, Technische Universität München, Munich, Germany
[5]Graduate School of Systemic Neurosciences,
[6]Department of Psychology, Ludwig-Maximilians- Universität München, Munich, Germany

Cognitive emotion regulation (CER) such as self-distancing is a powerful species-unique way of modulating aversive emotions and conditioned fear. However, whether CER can directly affect both aversive emotional responses and their prediction by recruiting the same regulatory system is yet unknown.

The CER's behavioural and neural effects on aversive emotional responses and their prediction were investigated with the use of model-based functional magnetic resonance imaging (fMRI). The visual presentation of aversive stimuli was combined with a classical conditioning paradigm and varying conditioned – unconditioned stimulus (CS-US) contingencies. On each trial, a cue (CS) was presented, after which an aversive picture (US) followed on a proportion of trials (CS+ trials; otherwise a blank screen was presented: CS- trials). Participant's task was to predict the occurrence of the US. Importantly, CER by self-distancing was employed in half of the experiment, while in the other half, participants were instructed to passively observe the stimuli. Conditioning was modelled by the Rescorla-Wagner model, resulting in learning parameters of aversive prediction and aversive prediction error.

Self-distancing reduced both aversive prediction- and aversive emotional response-related activity in the brain, suppressing activity in emotional areas such as amygdala, insula and striatum. Furthermore, a common regulatory system including the right dorsolateral prefrontal cortex and the angular gyrus was recruited both when participants regulated their predictions of or emotional responses to aversive pictures.

Our data demonstrate that cognitive emotion regulation recruits a common emotion regulation system in order to modulate both current aversive emotional responses and associated neural learning effects.

Keywords: emotion regulation, classical conditioning, prediction

Friday, September 27th, 09:30
[Young Neuroscientists Forum Ljubljana '13]

Tract-specific and global white matter alterations in healthy ageing

Rok Berlot[1,2], Claudia Metzler-Baddeley[3], Derek K Jones[3], Michael J O'Sullivan[1]

[1]Department of Clinical Neuroscience, Institute of Psychiatry, King's College London, United Kingdom
[2]Department of Neurology, University Medical Centre Ljubljana, Slovenia
[3]Cardiff University Brain Research Imaging Centre, School of Psychology, and the Neuroscience and Mental Health Research Institute, Cardiff University, United Kingdom

Healthy ageing is characterised by degradation of white matter microstructure which in turn relates to decline in cognitive function. Diffusion MRI studies often describe either alterations at a global scale or report age associations for individual tracts. It remains unclear to what extent individual tract age alterations are driven by a global process.

39 healthy elderly participants (aged 53-93 yrs.) underwent diffusion MRI scanning. Three temporal pathways were reconstructed by tractography: fornix, parahippocampal cingulum (PHC) and uncinate fasciculus (UF). Mean values of fractional anisotropy (FA) and mean diffusivity (MD) were estimated for each tract and for whole brain white matter. Tract-specific measures were correlated with age and linear regression modelling was used to assess the contribution of mean white matter structural alterations.

Fornix FA was correlated negatively with increasing age. Left and right UF displayed significant positive correlation with age for MD. Left PHC showed a significant decrease in FA and increase in MD with age. When mean white matter measures were included in a regression model, only fornix FA and MD of right UF demonstrated a contribution of age independent of global microstructure.

Our study demonstrates that microstructural alterations in temporal association tracts accompanying ageing partly reflect global alterations in white matter. However, the fornix and right UF exhibit additional age-related structural variation independent of global change.

Keywords: ageing, white matter, diffusion MRI, tractography

Friday, September 27th, 09:45
[Young Neuroscientists Forum Ljubljana '13]

Characterization of cognitive deficits in rats with selective cholinergic, noradrenergic and dopaminergic lesions

Elena Di Martino, Margherita Riggi, Andrea Valeri, Roberta Pintus, Giampiero Leanza

B.R.A.I.N. Lab for Neurogenesis and Repair, Department of Life Sciences, University of Trieste, Italy

Besides classic motor symptoms associated to the loss of nigrostriatal neurons, cognitive deficits and dementia are now emerging as important non-motor features of Parkinson's disease (PD). Noradrenergic (NA), cholinergic (ACh) and dopaminergic (DA) neurons in the Locus Coeruleus (LC), Basal Forebrain (BF) and Ventral Tegmental Area (VTA), respectively, degenerate early in PD and appear to be involved in its non-motor manifestations, however their role has so far been much less studied.

Here, we sought to address this issue in the rat, by producing selective immuno- and neurotoxic lesions, either single or combined, in order to investigate the occurrence of possible interactions between transmitter systems in the production of cognitive deficits. Starting from 12 weeks post-surgery, the animals were tested in the Morris Water Maze (MWM) and the Radial Arm Water Maze (RAWM) tasks, specifically designed to evaluate reference and working memory abilities.

All animals with single lesions did not show significant impairments in the reference memory task compared to control. By contrast, significant working memory deficits were exhibited by the single-lesioned animals, being seen more pronounced in the double- and particularly severe in triple-lesioned animals.

The results suggest that monoaminergic neuron systems may functionally interact for sustaining normal cognitive abilities, their dysfunction being possibly responsible for several of the non-motor symptoms of PD.

Keywords: PD, monoamines, cognition

Friday, September 27th, 10:00
[Young Neuroscientists Forum Ljubljana '13]

The role of corticogenesis-regulating genes during brain repair and regeneration after ischemia

Dunja Gorup[1], Srečko Gajović[1], Marta Rosario[2]

[1]Croatian Institute for Brain Research, School of Medicine, University of Zagreb, Croatia
[2]Institute for Cell and Neurobiology, Charite Universitätsmedizin, Berlin, Germany

The neocortex is responsible for higher brain functions such as sensation, motor control and memory.

During development, generation of the 6 cortical layers is regulated by a handful of transcription factors. We hypothesized that these same molecules are involved not only in development, but also in the adult brain during repair and renovation following damage.
To test this, we have used the ischemic lesion model (MCAO, medial cerebral artery occlusion) in wild type mice and in mice lacking the Toll-like Receptor 2 (TLR2). TLR2 has been shown to be crucial for triggering the inflammatory response, enabling us to address the influence of inflammation on adult neurogenesis following lesion.

Induction of developmental genes was analyzed in control and stroke model wild type and TLR2 KO animals at different times following brain lesion.

We have observed changes in the levels of active serine/threonine kinase JNK2. In addition, we see alterations in the expression patterns of developmentally regulated transcription factors including CTIP2 and SATB2 in lesioned brains. There is de novo expression of the developmentally regulated transcription factor CTIP-2 and P-JNK 2 weeks after MCAO, while IHC has shown that endogenous neuronal stem cells that are activated after the lesion are positive for CTIP-2.

IHC with anti-SATB2 antibody has shown a change in expression after the lesion, compared to the expression in sham operated animals.

Our data suggests that there is an activation of corticogenesis regulating transcription factors following the ischemic lesion. In addition, inflammation appears to modulate this activation.

Keywords: corticogenesis, inflammation, MCAO

Friday, September 27th, 10:15
[Young Neuroscientists Forum Ljubljana '13]

Neurophysiology model of the human lumbar cord separated from brain control by traumatic injury

Simon M. Danner[1,2], W. Barry McKay[3], Karen Minassian[2], Ursula S. Hofstoetter[2], Winfried Mayr[2], Frank Rattay[1], Milan R. Dimitrijević[4,5]

[1]Institute for Analysis and Scientific Computing, Vienna University of Technology, Austria
[2]Center for Medical Physics and Biomedical Engineering, Medical University of Vienna, Austria
[3]Hulse Spinal Cord Injury Lab, Crawford Research Institute, Shepherd Center, Atlanta, USA
[4]Department of Physical Medicine and Rehabilitation, Baylor College of Medicine, Houston, USA
[5]Foundation for Movement Recovery, Oslo, Norway

In animals, the research model for spinal cord injury is well defined by controlled, experimentally set lesions. With the most severe damage, spinal neural networks can be studied in the absence of supraspinal or peripheral inputs. In contrast, traumatic spinal injuries in human and the resulting pathological processes produce highly individualized models of supraspinal control over the spinal cord below the lesion. Previously, it has been shown that clinically motor-complete injuries in humans can retain residual brain influence over spinal cord function below the lesion evidenced through neurophysiological examination.

Fifteen clinically paralyzed subjects participated in this study of epidural spinal cord stimulation effects on spasticity control. Neurophysiological examination showed that three subjects retained the ability to volitionally induce task-appropriate electromyographic activity by the attempt of a single joint movement although no muscle contraction was clinically evident. Eight of the remaining subjects were able to diffusely activate muscles below the lesion in response to reinforcement maneuvers. This type of response was repeatable over 3 trials in 3 subjects. The remaining 4 subjects showed no clinical or subclinical signs of suprasegmental control.

These results suggest that this residual supraspinal influence modified the excitability of the neural networks caudal to the lesion, potentially contributing to the diversity of effects seen in interventions targeting the lumbar spinal cord after injury. Further, these findings highlight the importance of the use of neurophysiological assessment to characterize the lesions within the human research model of the lumbar spinal cord when studying the effects of interventional strategies.

Keywords: spinal cord injury, human, models

SNC'13

SiNAPSA Neuroscience Conference '13

Ljubljana, Slovenia, September 27-29, 2013

Abstracts

SNC'13 Posters

www.sinapsa.org/SiNC13

Faculty of Medicine, University of Ljubljana, Slovenia
27—29 September 2013

CEL-A01 Friday, September 27th, 12:00 [Poster section: Cellular neuroscience A]

Neural stem cells-enriched tubulization improves anatomical and functional restoration of the severed rat sciatic nerve

Stefano Frausin[1], Lucia Verga Falzacappa[1], Serena Viventi[1], Pela Bisatti[1], Roberta Turrini[2], Alessandro Melatini[2], Ruggero Mele[2], Giampiero Leanza[1]

[1]B.R.A.I.N. Lab for Neurogenesis and Repair, Department of Life Sciences, University of Trieste, Italy
[2]A.O.S. Maria degli Angeli, Pordenone, Italy

Reconstruction of the severed peripheral nerve entails direct suturing or, in case of extensive gap, tubulization of the nerve using adequate biocompatible conduits. Loading tubules with growth-promoting factors or cells may speed-up and/or optimize nerve repair, however, only relatively scant evidence is available.

Here, this possibility has been investigated after the formation of a 5-mm gap and tubulization of the rat sciatic nerve with a cell-compatible, biodegradable PLCL (poly DL-lactide-e-caprolactone, Neurolac®) copolyestere tube filled with either cultured Human Umbilical Mesenchymal Stem Cells (HUMSCs), human neural progenitors or their conditioned medium. The study included also animals subjected to direct suturing of the transected nerve, animals with gap only and animals with gap and unloaded PLCL tube. Starting from one week up to 5 months post-surgery, behavioural tests were administered weekly, followed by histochemical and tract-tracing analyses to assess the anatomical and functional condition of the treated nerve, with respect to the intact contralateral side.

The results showed a remarkable nerve integrity and a better functional recovery in the animals implanted with the cell- or medium-loaded tube, compared to the other groups. Thus, tubulization associated with local supply of growth-promoting factors may represent a viable strategy for optimizing functional restoration of the peripheral nerve, but further analyses are needed before its clinical use.

Keywords: sciatic nerve, tubulization, stem cells

CEL-A02 Friday, September 27th, 12:00 [Poster section: Cellular neuroscience A]

Mitochondrial membrane hyperpolarization following normoxia/hypoxia in glucose-deprived mouse astrocytes in culture

Andrej Korenić[1], Manuela Jaklin[2], Myriam Peters[2], Johannes Boltze[2 3], Pavle Andjus[1], Lidija Radenović[1]

[1]Centre for Laser Microscopy, Department of Physiology and Biochemistry, Faculty of Biology, University of Belgrade, Serbia
[2]Fraunhofer Institute for Cell Therapy and Immunology, Leipzig, Germany
[3]Translational Centre for Regenerative Medicine, University of Leipzig, Germany

Astrocytes, the physiological supporters of neurons, are known to tolerate long periods of oxygen-glucose deprivation (OGD), however this time frame has not been taken into account when compared to neuronal injury. In fact, changes in mitochondrial membrane potential (Δψm), as the indicator of the cellular redox state, after long exposures to OGD have not been investigated yet.

Therefore, we have here exposed primary mouse astrocyte cultures to the effect of varying relatively longer durations of hypoxia (oxygen deprivation), glucose deprivation (GD) or OGD, and to various combinations of these treatments. Changes of Δψm were investigated within one hour of reperfusion by applying JC-1, a fluorescent probe that enters the mitochondrial matrix in a potential-dependent manner, thus shifting its emission from green to red.

Our results indicated that, in contrast to ineffectiveness of hypoxia, GD contributed to a more negative Δψm. When the two treatments were combined, the hyperpolarization level during the reperfusion phase was related to lowering of glucose in the culture medium several hours prior to hypoxic treatment. When the effect was not initially observed after hypoxia in low glucose, subsequent chemical hypoxia induced by NaN3 still caused hyperpolarization during the reperfusion phase. However, when GD preceded hypoxia, those two treatments showed significant interaction towards an increased hyperpolarization.

These findings can help to understand how astrocytes cope with the changes in availability of oxygen and glucose, the two main substrates of the electron transport chain and how do such changes reflect on maintaining Δψm during reperfusion.

Keywords: astrocytes, hypoxia, glucose deprivation, mitochondrial hyperpolarization

CEL-A03 Friday, September 27th, 12:00 [Poster section: Cellular neuroscience A]

The effects of prolonged exposure of recombinant GABA-A receptors in cell culture to alcohol and gabapentin

Marina Morić, Boris Kuzman, Marina Malešević, Dubravka Švob Štrac

Laboratory for Molecular Neuropharmacology, Division of Molecular Medicine, Ruđer Bošković Institute, Zagreb, Croatia

Prolonged exposure of GABA-A receptors to alcohol triggers adaptive changes often associated with the development of alcoholism. Anticonvulsant drug gabapentin, structural analogue of GABA, has shown some promise in the treatment of alcoholism and alcohol withdrawal. Despite the therapeutic efficacy of gabapentin, its precise molecular and cellular mechanisms of action are still unclear. Recent reports also suggested potential neuroprotective and antioxidant effects of gabapentin. Hence, the aim of this study was to investigate the protective action of gabapentin on the well-known neurotoxic effects of chronic alcohol consumption and withdrawal.

We chronically exposed the human embryonic kidney (HEK) 293 cells, stably expressing alpha1beta2gamma2S subtype of GABA-A receptors, to alcohol (100 microM), either alone or in combination with 1 microM gabapentin.

The results demonstrated that cytotoxic effect of prolonged alcohol treatment (96h) on HEK cells was reduced by alcohol withdrawal (24h) and simultaneous gabapentin treatment. Prolonged alcohol treatment induced an increase in the number of central benzodiazepine binding sites and allosteric uncoupling between GABA-A receptor binding sites, which were counteracted by alcohol withdrawal. Gabapentin did not affect the number of benzodiazepine binding sites, but restored normal functional interactions between GABA and benzodiazepine binding sites.

The results suggest that long-term alcohol exposure induces changes of recombinant GABA-A receptors similar to chronic benzodiazepines, which also induce dependence. These findings also support the hypothesis of GABA-A receptor involvement in the actions of gabapentin. Further studies should investigate whether functional coupling of GABA-A receptor binding sites underlies the protective effect of gabapentin against the alcohol cytotoxicity.

Keywords: alcohol, long-term treatment, withdrawal, recombinant GABA-A receptors, HEK 293 cells, gabapentin

CEL-A04 Friday, September 27th, 12:00 [Poster section: Cellular neuroscience A]

Neuroprotection and brain accessibility of epigallocatechin gallate, cyanidin-3-glucoside, quercetin and nicotine

Katja Pirc[1], Lea Pogačnik[1], Mihaela Skrt[1], Nataša P. Ulrih[1,2], Inês Pamela[3], Alexandra Brito[3], Dora Brites[3], Rui F.M. Silva[3]

[1]Department of Food Science and Technology, Biotechnical Faculty, University of Ljubljana, Slovenia
[2]Centre of Excellence for Integrated Approaches in Chemistry and Biology of Proteins, Ljubljana, Slovenia
[3]Research Institute for Medicines and Pharmaceutical Sciences, Faculty of Pharmacy, University of Lisbon, Portugal

Blood–brain barrier (BBB) is a main obstacle to consider for the bioactive compounds prone to act in brain cells. Our aim was to evaluate the neuroprotection and brain accessibility abilities of epigallocatechin gallate (EGCG), cyanidin 3-glucoside (C3G), quercetin (Q) and nicotine (N).

Primary cultures of rat cortical neurons exposed to 1 and 50μM solutions of selected compounds for 24h were stimulated with 150μM H2O2 for a further 24h period. Necrotic-like cell death was determined by PI staining and apoptosis by evaluation of nuclear morphology. Solutions of the selected compounds were placed on the upper chamber of a dual-system formed by semipermeable inserts covered with confluent monolayers of a human brain endothelial cell line and the concentrations on the lower and upper chambers were followed by HPLC/DAD.

Both concentrations of EGCG and N were able to reduce neuronal necrotic-like death by ~40% ($p<0.05$). For Q and C3G, only 1μM was protective ($p<0.05$). EGCG reduced neuronal apoptosis by ~30% ($p<0.01$ and $p<0.05$ for 1 and 50μM respectively) and N by ~60% ($p<0.01$, both concentrations); only the 1μM Q solution was neuroprotective (~60%, $p<0.01$). Although it seems that Q doesn't reach the lower chamber, BBB is crossed fast by EGCG (50.6% in 1h), slowly by C3G (only 8.5% in 6h) and moderately by N (20% in 6h).

In conclusion, EGCG and N revealed to be the most promising compounds with both the capability to reach the brain and to protect neurons from oxidative damage.

Work funded by FCT, Portugal; Slovene Research Agency

Keywords: neuroprotection, blood–brain barrier, polyphenols, nicotine, necrosis, apoptosis

CEL-B01 Saturday, September 28th, 12:00 [Poster section: Cellular neuroscience B]

Erythropoietin is not neuroprotective after excitotoxic brain injury

Primož Gradišek[1], Maja Bresjanac[2]

[1]Centre for Intensive Therapy, Clinical Departement of Anesthesiology and Intensive Therapy, University Medical Centre Ljubljana, Slovenia
[2]Institute of Pathophysiology, Faculty of Medicine, University of Ljubljana, Slovenia

Traumatic brain injury triggers excitotoxic secondary brain injury. Hypoxia and ischemia up-regulates the expression of erythropoietin (EPO) and its receptors. EPO attenuates microglial activation, modulates cellular death and neurogenesis. EPO enhances neuroprotection after hypoxia/ischemia. However, the potential of EPO to protect neurons against excitotoxic injury has not been established.

We investigated whether recombinant human erythropoietin (rhEPO) reduces parenchymal damage of the brain and inflammatory response after experimental excitotoxic injury.

Quinolinic acid (QA) was stereotaxically injected into one side of the striatum of 20 young adult Wistar rats. rhEPO in dose of 5000 IE/kg was systemically administered to 5 animals (first series) at 30 minutes, 8 and 20 hours after QA injection; however 5 animals in second series received rhEPO only once, at 1 hour after QA injection. The rest of the animals in first (n=5) and second (n=5) series received saline. The effects of rhEPO on the structural damage and cellular response after injury were examined using MRI and immunohistochemical staining (expression of the astrocytes – GFAP; neurons – NeuN, TH, MAP2 and DARPP; microglia – OX42) at 24 hours (n=10) and 8 days (n=10) following QA injection.

The extent and intensity of the structural brain damage, neuronal loss and the inflammatory response were not reduced in the rhEPO-treated animals, compared to saline-treated animals. Extent of QA-induced injury was not related either to dose of rhEPO or to the time from the injury.

Systemically administered rhEPO did not provide neuroprotection in a quinolinic acid-induced animal model of excitotoxic brain injury.

Keywords: erythropoietin, quinolinic acid, immunohistochemistry

CEL-B02 Saturday, September 28th, 12:00 [Poster section: Cellular neuroscience B]

Myosin II, but not microtubule motors, controls outer radial glial cell mitotic behavior in developing human neocortex

Bridget E. LaMonica, Jan H. Lui, Arnold R. Kriegstein

Eli and Edythe Broad Center of Regeneration Medicine and Stem Cell Research, University of California, San Francisco, USA

Evolutionary expansion of the neocortex, thought to underlie the enhanced cognitive abilities of humans, is partially attributed to increased proliferation of neurogenic progenitor cells called outer radial glia (oRG) during development. oRG cells are direct progeny of ventricular radial glial (vRG) cells, the primary neural stem cells present in all mammals. The division mode of oRG cells is highly unique. The soma rapidly translocates a distance of several cell diameters along the basal fiber towards the cortical plate immediately prior to cytokinesis, a process called mitotic somal translocation (MST). MST contrasts with vRG cell interkinetic nuclear migration, a less rapid mitotic behavior that is highly dependent on microtubule but not actomyosin motors. Whether the highly stereotypical mitotic behavior of oRG cells is mechanistically similar to, and possibly evolutionarily derived from, that of vRG cells is unknown.

Here, we show that non-muscle myosin II (NM-II), but not microtubule motors, controls mitotic somal translocation (MST). We find that intracellular calcium levels transiently increase during MST, and that chelation of extracellular calcium with EGTA specifically inhibits MST but not mitosis.

Our results suggest that the MST is driven by influx of calcium through plasma membrane calcium channels, resulting in myosin light chain kinase-dependent NM-II phosphorylation and subsequent actin polymerization. We propose that this mechanism for progenitor cell translocation complements canonical neuronal migration and was utilized in evolution to deliver newborn neurons closer to the cortical plate in species with large brains.

Keywords: Radial glia, neocortex, neurogenesis, evolution, stem cells

Glial activation and oxidative stress in the ALS SOD1 G93A transgenic rat model

Stefan Stamenković[1], Vesna Selaković[2], Lidija Radenović[1], Pavle R. Andjus[1]

[1]Center for Laser Microscopy, Institute for Physiology and Biochemistry, Faculty of Biology, University of Belgrade, Serbia
[2]Institute for Medical Research, Military Medical Academy, Belgrade, Serbia

Amyotrophic lateral sclerosis (ALS) is a progressive and fatal neurodegenerative disorder characterized by death of neurons in cerebral cortex, brain stem and spinal cord. Most ALS cases are sporadic, while only 10% occurs in familial forms, among which 20% are caused by mutations in the Cu, Zn-superoxide dismutase (SOD1). One of the most important and well characterized pathological mechanisms in ALS is the neuroinflammatory reaction mainly governed by activated microglia and astrocytes. It was proposed that the mutant SOD1 released in the extracellular space activates these glial cells leading to neuroinflammation and increased reactive oxygen species production.

Therefore, we decided to check for markers of glial activation and oxidative stress in the brain stem and hippocampus of the rat transgenic SOD1G93A model of ALS.

Immunohistochemistry with markers of microglia, astrocytes, and neurons, and anti-SOD1 antibody, showed strong glial activation in these regions and revealed the existence of pronounced intracellular aggregations of SOD1 in neurons and both types of glial cells as well. Examination of oxidative stress parameters by spectrophotometric biochemical assays detected increased presence of reactive oxygen and nitrogen species, increased index of lipid peroxidation, decreased SOD1 and increased Mn SOD (SOD2) activity, in both hippocampus and brainstem. Finally, investigations on primary cortical astrocytes culture with ROS production indicators, MitoSox red and H2DCDFA, showed increased ROS production in astrocytes from ALS compared to control animals.

These results redefine oxidative stress not just as a consequence, but also as a cause and essential pathogenic mechanisms of neuroinflammation that ends in neurodegeneration.

Keywords: ALS, ROS, SOD1 G93A

Progressive motoneuronal degeneration and motor disfunction in SOD1G93A mice: effects of implanted mesenchymal stem cells from human umbilical cord (HUMSCS)

Serena Viventi[1], Miriana Quattromani[1], Lucia Verga Falzacappa[1], Stefano Frausin[1], Pela Bisatti[1], Alberto Tommasini[2], Erica Valencic[2], Giampiero Leanza[1]

[1]B.R.A.I.N. Lab for Neurogenesis and Repair, Department of Life Sciences, University of Trieste, Italy
[2]Scientific Research Institute and Hospital for Pediatrics "Burlo Garofolo", Trieste, Italy

Transplantation of Mesenchymal Stem Cells from the Human Umbilical Cord (HUMSCs) has recently emerged as a promising strategy for the treatment of disorders such as Amyotrophic Lateral Sclerosis (ALS), a disease characterized by progressive loss of motor neurons in cortex, brainstem, and spinal cord. However, extensive pre-clinical characterization of these cells is necessary, prior to their clinical use. Here, the functional properties of HUMSCs were investigated following implantation in SOD1G93A mice, a well-known ALS model.

HUMSCs, cultured and primed using a neuron-conditioned medium, were implanted into the lateral ventricle of newborn (post-natal day 4) SOD1G93A mice. The distribution of grafted HUMSCs and their effects on disease onset and progression, motor performance, and motoneuron numbers and morphology, were assessed relative to control sham- or non-transplanted and wild-type mice.

HUMSCs transplantation significantly delayed the appearance of the severe functional impairments typically exhibited by these animals at 4-6 months of age and extended their lifespan by about 30-40%, as opposed to non-transplanted mice. Grafted cells were found in the walls of the lateral ventricles and central canal but not in the brain or the spinal parenchyma, suggesting that production and release of locally acting factors with protective and/or antiinflammatory properties, rather than replacement of degenerating neurons, are likely responsible for the observed restorative effects.

Keywords: ALS, SOD1G93A mice, HUMSCs

CEL-C01 Sunday, September 29th, 12:00 [Poster section: Cellular neuroscience C]

Fusion pore properties of gliotransmitter vesicles in isolated astrocytes

Alenka Guček[1], Jernej Jorgačevski[1,2], Priyanka Singh[1], Claudia Geisler[3], Alexander Egner[3], Robert Zorec[1,2]

[1]Laboratory of Neuroendocrinology-Molecular Cell Physiology, Faculty of Medicine, University of Ljubljana, Slovenia
[2]Celica Biomedical Center, Ljubljana, Slovenia
[3]Department of Optical Nanoscopy, Laser-Laboratory Göttingen, Germany

Bidirectional communication between neurons and astrocytes, the most abundant type of glial cells, has become a subject of numerous studies, embodying astrocytes as an important partner in synaptic modulation. Astrocytes exhibit Ca2+-based cytosolic excitability, which modulates the release of gliotransmitters, which bind to surrounding cells. Non-vesicular and vesicular-based mechanisms of gliotransmitter release appear to co-exist in astrocytes; however the lack of understanding of the basic properties of secretion in astrocytes requires an additional insight into regulated exocytosis for different types of gliotransmitter vesicles.

To evaluate the morphology of distinct vesicle types we used high resolution stimulated emission depletion microscopy (STED) and structured illumination microscopy (SIM), whereas the interaction of vesicle and the plasma membranes (one of the late stages of exocytosis) was monitored directly by cell-attached patch-clamp measurements of membrane capacitance (Cm), a parameter linearly related to the surface area of the plasma membrane, in isolated astrocytes.

Preliminary results show, that in astrocytes discrete steps in membrane capacitance reflect unitary exo-endocytic events of single vesicle interactions with the plasma membrane. For the first time we demonstrate direct real-time measurements of predominantly reversible capacitance steps, reflecting transient exocytosis, and irreversible capacitance steps, reflecting full-fusion exocytosis, in cultured astrocytes. The amplitude of these events reflects the size of interacting vesicles. By assuming the specific capacitance of 10 fF/μm2 and spherical morphology the diameter of vesicles were from 40 nm to 800 nm, similar to the ones measured by STED and SIM microscopies.

Keywords: astrocyte, gliotransmitter, STED microscopy, cell-attached

CEL-C02 Sunday, September 29th, 12:00 [Poster section: Cellular neuroscience C]

Study of putamen neuronal activity before a multisensory task

P. Montes-Lourido, A. F. Vicente, M. A. Bermudez, M. C. Romero, R. Perez, F. Gonzalez

Department of Physiology, University of Santiago de Compostela, Spain

The putamen is part of the basal ganglia and its function is mainly related to motor coordination. However the hypothesis of this work assumes that neural activity into the putamen nucleus is to be modulated by the different components of the task, the presence or absence of a stimulus enhancer, motor act, and the presence of the reward.

In our study we used a visual stimulus (silhouette of a white square) as enhancer of another visual stimulus (abstract image). We used four abstract images: two images meant 'Yes' and were associated with obtaining reward and two images meant 'No' and were associated with no reward. The 'Enhancer' indicated the existence of double reward in Images 'Yes' and more waiting between trials if it presented before the images 'No'. We recorded the activity of neurons in the putamen of a monkey (Maccaca mulatta) trained to perform this visuomotor task that requires the execution of a movement and retention of a move to the presentation of different images. We used an ANOVA statistical test to study neuronal activity during task execution.

Of all the recorded neurons, 8% increased their activity after the presentation of the 'Enhancer' (ANOVA, $p<0.05$), 61% increased their activity around the lever down (ANOVA, $p<0.05$) and 31% increased their activity after the presentation of the reward (ANOVA, $p<0.05$).

These results indicate that the putamen is related to stimulus processing relevant to the task, with the motor action and reward processing.

Keywords: putamen, enhancer, neuronal

CEL-C03 Sunday, September 29th, 12:00 [Poster section: Cellular neuroscience C]

Architectural study of single astrocytic vesicle at nanometer scale

Priyanka Singh[1], Jernej Jorgačevski[1,2], Marko Kreft[1,2,3], Randy F. Stout[4,5], Maja Potokar[1,2], Vladimir Parpura[4,6], Robert Zorec[1,2]

[1]Institute of Pathophysiology, Faculty of Medicine, University of Ljubljana, Slovenia
[2]Celica Biomedical Center, Ljubljana, Slovenia
[3]Biotechnology Faculty, University of Ljubljana, Slovenia
[4]Department of Neurobiology, Center for Glial Biology in Medicine, University of Alabama, Birmingham, USA
[5]The Dominick P. Purpura Department of Neuroscience, Albert Einstein College of Medicine, New York, USA
[6]Department of Biotechnology, University of Rijeka, Croatia

Astrocytes are glial cells which provide important metabolic support to neurons, actively tune synaptic activity and influence brain microcirculation. One of the key processes which sustain astrocyte communication with neighbouring cells is regulated exocytosis mediating the release of gliotransmitters, delivery of membrane transporters, channels and other molecules to the plasma membrane. The fusion of vesicle with the plasma membrane is thought to be associated with SNARE complexes. Sb2, one of the SNARE members, is present on a secretory vesicle. However, there is a debate on how many Sb2 molecules are involved in the fusion between vesicle and plasma membrane in astrocytes. To visualize these events, one should have the appropriate markers and microscope which can image the cells beyond the diffraction limit.

We generated a pH-sensitive indicator yellow synaptopHluorin (YSpH) as a marker for Sb2 and as a functional readout for monitoring the properties of fusion pores. In an acidic environment YSpH is non-fluorescent and becomes fluorescent upon alkalinization, permitting the study of fusion of vesicles with the membrane during gliotransmitter release. We selected one of the super-resolution technique i.e., structured illumination microscopy (SIM) having twice better resolution than confocal laser scanning microscopy (CLSM).

Our preliminary results, obtained by CLSM (with the resolution limit of about 200 nm) and SIM (with the resolution limit of about 120 nm) show that YSpH efficiently reports the fusion pore establishment in astrocytes and reveals the configuration of Sb2 on single vesicle in astrocytes.

Keywords: astrocytes, vesicles, synaptopHluorin, structured illumination microscopy

CEL-C04 Sunday, September 29th, 12:00 [Poster section: Cellular neuroscience C]

Is glioblastoma growth and malignant phenotype supported or suppressed by umbilical cord blood-derived MSCs in vitro?

Monika Witusik-Perkowska[1], Magdalena Zakrzewska[1], Malgorzata Szybka[1], Colin P. McGuckin[2], Nico Forraz[2], Dariusz J. Jaskolski[3], Wielislaw Papierz[4], Pawel P. Liberski[1]

[1]Department of Molecular Pathology and Neuropathology, Medical University of Lodz, Poland
[2]Cell Therapy Research Institute, Lyon, France
[3]Department of Neurosurgery and Oncology of the Central Nervous System, Medical University of Lodz, Poland
[4]Department of Pathomorphology, Medical University of Lodz, Poland

Understanding the nature of interactions between tumour and normal cells may shed new light on the process of tumour pathogenesis and progression or even create a base for searching for new therapeutic approaches.

The aim of the present study was to investigate the effects of human umbilical cord blood derived mesenchymal stem cells (hUCB-MSCs) on glioblastoma cell growth and phenotype in vitro.

Co-cultures of hUCB-MSCs and glioblastoma-derived cells were performed in a transwell system. Analyses focused on assessment of expression of glioma-associated genes (IL-13Rα2, Fra-1, EphA2) and putative tumour stem cell markers (e.g. SOX2, Bmi-1, Msi-1, nestin). Gene expression at mRNA level was evaluated by real-time PCR and protein analysis was performed by immunofluorescence method. Additionally, the presented experimental model was exploited for evaluation of proliferation ability of glioblastoma-derived cells co-cultured with hUCB-MSCs.

The obtained results showed that the presence of hUCB-MSCs can alter the characteristics of glioblastoma cells in vitro with regard to examined tumour-associated antigens expression and tumour stem cell markers level. However, comparative analysis did not result in consistent findings for all tested glioblastoma samples. The observed contradictions may be caused by heterogeneous nature of glioblastoma, thus further research is needed to elucidate this phenomenon.

Acknowledgements:
The study was supported by the Foundation for Polish Science; PARENT/BRIDGE grant (POMOST/2011-3/13) and grant of Medical University of Lodz (502-03/1-034-04/502-14-048)

Keywords: glioblastoma, hUCB-MSCs, cell culture, TSCs, glioma-associated antigens

CLI-A01 Friday, September 27th, 12:00 [Poster section: Clinical neuroscience A]

Motor-cortex excitability and cognitive profiles after different rehabilitation programs in PD patients with freezing of gait

Pierpaolo Busan[1], Susanna Mezzarobba[2], Mauro Catalan[2], Monica Belfiore[1], Giulia Sgubin[2], Lorella Pellegrini[2], Airì Gorian[2], Mihaela Banica[2], Gilberto Pizzolato[2], Piero Paolo Battaglini[1]

[1]B.R.A.I.N. Center for Neuroscience, Department of Life Sciences, University of Trieste, Italy
[2]Department of Medical, Surgical and Health Sciences, University of Trieste, Italy

In order to reduce the disruption of gait in Parkinson's disease (PD), we compared the effects of two rehabilitation programs on freezing of gait (FoG) and concomitant impairments.

Seventeen FoG-PD patients were assigned to two groups. The first performed a rehabilitation protocol based on motor imagery (MI), while the second underwent treadmill training (TT). Patients were studied at baseline and at the end of treatments by evaluating severity of FoG, cognitive abilities and cortical excitability. This was done by registering from lower limbs while applying Transcranial Magnetic Stimulation (TMS) over the contralateral motor cortex. Groups were matched for variables such as disease stage and duration. MI allowed a higher reduction of FoG compared to TT.

Neuropsychological testing showed a tendency toward a cognitive decline in both groups. However, MI mainly induced an improvement in semantic recall, while TT mainly avoided a decline in interference inhibition. TMS suggested a tendency toward an increase in motor thresholds, recruitment curves, as well as in short intracortical inhibition, after both treatments. On the other hand, a tendency toward a prolongation in the duration of silent period was observed in both groups, as well as a tendency toward a diminution in intracortical facilitation, especially in the TT group. MI and TT treatment partially differed when considering effects on cognitive functions, while neurophysiologic effects were comparable for a series of indexes.

This could suggest the existence of different mechanisms of action in the two treatments.

Keywords: Freezing of gait, Parkinson's Disease, Transcranial Magnetic Stimulation

CLI-A02 Friday, September 27th, 12:00 [Poster section: Clinical neuroscience A]

Resting heart rate variability and early heart rate recovery. Are they correlated?

Aljoša Danieli[1,4], Lara Lusa[2], Nejka Potočnik[2], Bernard Meglič[1], Anton Grad[3], Fajko F. Bajrović[1,2]

[1]Department of Neurology, University Medical Centre Ljubljana, Slovenia
[2]Medical Faculty, University of Ljubljana, Slovenia
[3]General Hospital Izola, Slovenia
[4]Barsos Medical Centre, Ljubljana, Slovenia

Aerobic endurance training is known to accelerate HRR after exercise in healthy subjects as well as in patients with coronary artery disease. As shown by pharmacological autonomic blockade, HRR early after exercise is dependent primarily on parasympathetic reactivation. Thus, accelerated HRR early after exercise in endurance trained athletes may be attributed to augmented parasympathetic reactivation. In the present cross-sectional study, we tested the hypothesis that the HRR early after submaximal exercise is related to the resting parasympathetic modulation.

Thirty endurance trained athletes (20 males, aged 50 ± 7 years) and thirty sedentary control subjects (20 males, aged 52 ± 6 years) performed a submaximal exercise on a cyclo-ergometer. Pre-exercise resting short-term heart rate variability (HRV) parameters in time and frequency-domains were correlated with HRR during the first 30 seconds, one minute and two minutes after cessation of exercise.

We found that HRR was statistically significantly faster in athletes than in their controls at all examination time points ($p<0.05$). HF, SDNN and RMSSD were statistically significantly higher in athletes than in controls ($p<0,05$), but other resting HRV parameters were not statistically different between groups. HRR correlation after 30 seconds, 1 and 2 minutes of recovery with total power, HF and RMSSD were positive, while the correlation with HFnu and LF/HF was negative for small and positive for larger values. The opposite was true for SDNN.

These findings support the hypothesis that HRR early after submaximal exercise is related to resting parasympathetic modulation in middle-aged subjects.

Keywords: autonomic modulation, endurance training, heart rate recovery, heart rate variability

A population-based study of outpatient antipsychotic prescription trends in Slovenia – preliminary results

Polonca Ferk[1], Brane Leskošek[2], Mojca Kržan[3]

[1]Department of Pharmacology and Experimental Toxicology, Faculty of Medicine, University of Maribor, Slovenia
[2]Institute for Biostatistics and Medical Informatics, Faculty of Medicine, University of Ljubljana, Slovenia
[3]Institute of Pharmacology and Experimental Toxicology, Faculty of Medicine, University of Ljubljana, Slovenia

The number of antipsychotic drugs prescriptions is rising fast worldwide. However, the pharmacotherapy of psychotic patients still remains suboptimal.

The main aim of the present study was to investigate the prevalence rates of antipsychotic prescriptions and to present a snapshot of a trend of outpatient prescribing antipsychotic drugs in Slovenia in the period 2003-2012. The appropriate data were kindly provided by the Health Insurance Institute of Slovenia. Preliminary results of the study are summarized in this abstract.

The results show that in 2003, 82,398 prescriptions of antipsychotic drugs were prescribed to 26,097 outpatient psychotic patients, while in 2012, the number of prescriptions raised to 134,442 in 38,475 patients. In 2003, the most frequently prescribed antipsychotic drug was sulpiride, with the frequency of 37.2 % of all antipsychotic drug prescriptions, in 45.3 % treated psychotic patients. In 2012, the most prescribed antipsychotic drug in Slovenia was quetiapine, with the frequency of 54.2 % of all antipsychotics' prescriptions, in 53.2 % treated psychotic patients.

According to the literature data, the trend of prescribing antipsychotics in Slovenia is rising comparable to other developed countries. With the increasing number of prescriptions of antipsychotics in the last ten years, many pharmacodynamic and pharmacokinetic drug interactions with antipsychotics could be expected and, according to the Stockley's Drug Interactions book and two databases (Lexicomp, payable, and Drugs.com, freely available), at least some of them could be clinically important. Investigating the prevalence of drug interactions with typical as well as with atypical antipsychotics in Slovenia and consequently providing suggestions for improvements in prescribing those drugs are the main part of our research in progress.

Keywords: drug interactions, mental disorders, psychosis, psychiatry, quetiapine

Cortical control of breathing: what can we learn from EEG?

Judita Jeran[1], Aleš Belič[2], Ignac Zidar[1], Janez Zidar[1]

[1]Institute of Clinical Neurophysiology, University Medical Centre Ljubljana, Slovenia
[2]Laboratory of Modelling, Simulation and Control, Faculty of Electrical Engineering, University of Ljubljana, Slovenia

In mammals respiration is controlled by the involuntary system, residing in the brainstem, and a voluntary system residing in the cerebral cortex. Similarly to any other voluntary movement, voluntary breathing is associated with power changes of alpha (8-12 Hz) and beta (13-30 Hz) EEG rhythms over the sensorimotor cortical areas, time locked to the movement onset, i.e., event-related synchronization (ERS) and desynchronization (ERD). It is not known, however, whether similar power changes occur also during automatic breathing.

To establish this, and clarify if breathing-related ERS/ERD is changed in patients with amyotrophic lateral sclerosis (ALS) with signs of respiratory insufficiency, we recorded surface EEG during normal breathing in sitting and supine posture, in 17 ALS patients and 17 healthy controls. EEG was processed with a method of ERS/ERD, and the results were plotted as group averages.

Only in beta frequency band, there was a 7% ERD over the sensorimotor cortex that preceded the onset of inspiration in both, ALS and healthy controls. The ERD peaked 0.25 breathing period after the inspiratory onset and was followed by an ERS. In sitting and supine postures, the groups differed in their beta ERS/ERD over the frontal electrodes where maximal ERD of controls overlapped with maximal ERS of ALS.

Since the participants were distracted from thinking about breathing, the power changes in beta EEG rhythm likely reflect the background breathing-related activity of the sensorimotor cortex.

Keywords: breathing, EEG, ALS

CLI-A05 Friday, September 27th, 12:00 [Poster section: Clinical neuroscience A]

The association of BDNF polymorphisms and cognitive function in patients with Alzheimer's disease and mild cognitive impairment

Matea Nikolac Perković[1], Fran Borovečki[2], Nataša Klepac[3], Sanja Hajnšek[3], Dorotea Muck-Šeler[1], Nela Pivac[1]

[1]Division of Molecular Medicine, Rudjer Boskovic Institute, Zagreb, Croatia
[2]Department for Functional Genomics, Center for Translational and Clinical Research, University Hospital Center Zagreb, University of Zagreb School of Medicine, Croatia
[3]Department of Neurology, University Hospital Center Zagreb, University of Zagreb School of Medicine, Croatia

Brain derived neurotrophic factor (BDNF) is one of the key proteins involved in modulating neuronal survival, differentiation and synaptic plasticity in the brain. The reduction of the BDNF concentration in different brain areas has been associated with dementia and cognitive decline.

The study investigated the association of the five BDNF polymorphisms, rs 6265 (Val66Met), rs11030104, rs7934165, rs1519480 and rs56164415 (C270T), with cognitive impairment. Eighty-two patients with Alzheimer's disease (AD) and 49 patients with mild cognitive impairment (MCI), which presents a high risk condition for AD, were included. Diagnosis of AD was done according to the NINCDS-ADRDA and DSM-IV criteria. Cognitive impairment was evaluated using Mini-Mental Status Examination (MMSE) and Clock Drawing Test (CDT).

After subdividing the subjects according to the different BDNF variants, association between rs1519480 and MMSE scores in patients with AD (F=3.856; P=0.025) and MCI (F=3.270; P=0.047) was found. There was a marginal association of MMSE scores with C270T polymorphism in patients with AD (F=3.697; P=0.058). Similar results were obtained using CDT scores to predicts person's cognitive abilities, showing that AD patients differed significantly (F=4.666; P=0.034) in CDT scores when subdivided according to the rs1519480 genotype, while this association was marginally significant in individuals with MCI (F=3.904; P=0.054). We have also found an association of rs11030104 with CDT scores in AD (F=5.495; P=0.022). Other analysed polymorphisms were not significantly associated with MMSE or CDT scores.

These results reveal that BDNF rs1519480 and rs11030104 polymorphisms were significantly associated with cognitive decline in patients with AD or MCI.

Keywords: BDNF, Alzheimer's disease, MCI, cognition, polymorphisms

CLI-A06 Friday, September 27th, 12:00 [Poster section: Clinical neuroscience A]

Impact of the volume of the resection on outcome in patients who underwent operative treatment of medial temporal lobe epilepsy

Gašper Zupan[1], Bogdan Lorber[2]

[1]Faculty of Medicine, University of Ljubljana, Slovenia
[2]Centre for Adult Epilepsy, Department of Neurology, University Medical Centre Ljubljana, Slovenia

One third of patients with medial temporal lobe epilepsy (mTLE) have refractory form of the disease and they are considered potential candidates for resective operation of epileptogenic zone. The team treating those patients always tries to determine the optimal size of resection in order to benefit and not to harm the patient.

We identified 18 Slovenian patients with mTLE who had appropriate magnetic resonance (MRI) series done after the operation. The procedures were performed in renowned epilepsy centers abroad. Their average age of the operation was 35.8 years and mean follow-up time was 5.5 years ± 2.5. Semi-automatically, we calculated volumes of resections from MRI images with 3D Slicer.

Comparison of the measured volumes with the last available data of seizure freedom expressed in ILAE classification was made. In the time frame of our follow-up, 67% of patients were without any seizures (Class 1) and 78% were Class 1 or just with auras (Class 2). Comparison of volume and outcome shown no correlation (Pearson factor: 0.15, P-value: 0.55).

We concluded that the span of resection is not important in outcome measured by ILAE classifications. Several studies show that resections of hippocampus and other mesial structures in temporal lobe are more crucial than the volume itself. The benefit of removal of neocortical elements is controversial. Our study shows that surgeons do not have to perform extended resection and risk additional neurological damage in order to achieve better result.

Keywords: epilepsy surgery, epilepsy, resection volume, seizures

CLI-A07 Friday, September 27th, 12:00 [Poster section: Clinical neuroscience A]

Seizure and quality-of-life outcome after epilepsy surgery in Slovenia: retrospective study

Črt Zavrnik[1], Bogdan Lorber[2]

[1]Medical Faculty, University of Ljubljana, Slovenia
[2]Division of Neurology, University Medical Centre Ljubljana, Slovenia

Surgical treatment of medically intractable epilepsy is one of the most successful treatments of chronic neurological disorders. Post-operative seizure freedom is reported in 50-80% of patients. Quality-of-life outcome is less frequently studied. At the Divison of Neurology of University Medical Centre Ljubljana, we run the epilepsy surgery program in collaboration with different foreign Epilepsy Centers for more than decade. The goal of this retrospective study is to identify seizure and psychosocial outcome of Slovenian epilepsy patients.

56 Slovenian patients who went under surgery treatment of intractable epilepsy between 2001 and 2012 were involved in this study. All were invited to the interview from March to June, 2013. 28 (50%) responded; for others, data were collected from documentation of their last visit. The mean follow-up of this study was 4.3 ± 3.0 years.

The pathology of excision was mesial temporal sclerosis, cortical dysplasia, gliosis, and other in 58.9%, 12.5%, 19.6% and 9.0%, respectively. Results showed that the rate of seizure freedom (Engel class I) at the time of follow-up was 78.6%. Off medication (and seizure-free) were 14.3% of patients. Higher employment rate and performed car licence exam rate as well as higher frequency of mood disorders and divorce rate are observed since surgery.

Epilepsy surgery leads to improvement of seizure outcome. To emphasize, the results of diagnosis and treatment of Slovenian epilepsy patients are encouraging. Seizure freedom is not only comparable, but also exceeds many other foreign follow-up studies.

Keywords: epilepsy, epilepsy surgery, seizure outcome, quality-of-life

CLI-B01 Saturday, September 28th, 12:00 [Poster section: Clinical neuroscience B]

Tract-specific and global white matter alterations in healthy ageing

Rok Berlot[1,2], Claudia Metzler-Baddeley[3], Derek K Jones[3], Michael J O'Sullivan[1]

[1]Department of Clinical Neuroscience, Institute of Psychiatry, King's College London, UK
[2]Department of Neurology, University Medical Centre Ljubljana, Slovenia
[3]Cardiff University Brain Research Imaging Centre and the Neuroscience and Mental Health Research Institute, Cardiff University, UK

Healthy ageing is characterised by degradation of white matter microstructure which in turn relates to decline in cognitive function. Diffusion MRI studies often describe either alterations at a global scale or report age associations for individual tracts. It remains unclear to what extent individual tract age alterations are driven by a global process.

39 healthy elderly participants (aged 53-93 yrs.) underwent diffusion MRI scanning. Three temporal pathways were reconstructed by tractography: fornix, parahippocampal cingulum (PHC) and uncinate fasciculus (UF). Mean values of fractional anisotropy (FA) and mean diffusivity (MD) were estimated for each tract and for whole brain white matter. Tract-specific measures were correlated with age and linear regression modelling was used to assess the contribution of mean white matter structural alterations.

Fornix FA was correlated negatively with increasing age. Left and right UF displayed significant positive correlation with age for MD. Left PHC showed a significant decrease in FA and increase in MD with age. When mean white matter measures were included in a regression model, only fornix FA and MD of right UF demonstrated a contribution of age independent of global microstructure.

Our study demonstrates that microstructural alterations in temporal association tracts accompanying ageing partly reflect global alterations in white matter. However, the fornix and right UF exhibit additional age-related structural variation independent of global change.

Keywords: ageing, white matter, diffusion MRI, tractography

CLI-B02 Saturday, September 28th, 12:00 [Poster section: Clinical neuroscience B]

Cognitive functioning in patients after out of hospital cardiac arrest: Preliminary data

Barbara Dolenc[1], Ana Ožura[1], Vita Štukovnik[1], Špela Tadel Kocjančič[2], Robert Masten[3], Marko Noč[2]

[1]Division of Neurology, University Medical Centre Ljubljana, Slovenia
[2]Division of Internal Medicine, University Medical Centre Ljubljana, Slovenia
[3]Department of Psychology, Faculty of Arts, University of Ljubljana, Slovenia

Cognitive deficits after out of hospital cardiac arrest (OHCA) are common, however, incompletely described. Executive functions, psycho-motor function and memory are reported to be most frequently affected. The aim of the present study is to examine cognitive functioning in patients after OHCA.

So far, 10 patients 3 months after OHCA were included in our study. We assessed four major cognitive domains: mental speed (SDMT), sustained attention (TAP), learning and memory (CVLT II), executive functions (Controlled oral word association). Subjects' test results were compared with the normative data of the tests.

Sustained attention was impaired in 50% of the patients. Reaction times of responding to simple stimuli were significantly longer. Patients made more errors and omissions that would be expected for their age and education. Psycho-motor speed was severely impaired in 10% of patients. Learning was impaired in 10% of patient, whereas delayed recall of verbal information was preserved in all patients. Verbal fluency was defective in 30% of patients.

Our results revealed that cognitive deficits exist in patients three months after OHCA. Attention seems to be the most impaired component as half of so far examined patients had difficulties sustaining their focus to simple stimuli. This could consequently influence all other cognitive subsystems as well as patients' daily functioning. Although this is only preliminary data, it seems that medical care after OHCA should also promote cognitive rehabilitation. However, this study is still in process, therefore more participants are needed to confirm our conclusions.

Keywords: out of hospital cardiac arrest, cognitive functioning, attention

CLI-B03 Saturday, September 28th, 12:00 [Poster section: Clinical neuroscience B]

Botulinum toxin in cases of occipito-temporal pain

V. Goldobin, E. Klocheva

North-Western State Medical University n.a. I. I. Mechnikov, St. Petersburg, Russia

Occipitotemporal headache may occur due to different causes. One of the variants is connecned with posterior belly of digastric muscle spasm with subsequent irritation of neck vasonervous structures.

We examined 7 women with unilateral occipitotemporal headache. The palpation of digastric muscle posterior belly projection zone increased the pain, MRI of the head observed unilateral contraction of posterior venter of digastric muscle with surrounding structure conflict. The type A botulinum toxin injection was performed into the contracted belly in all these patients. The dosage varied from 30 to 50 units.

The clinical improvement started in 10-14 days after the injection with complete disappearing of symptoms in 3-4 weeks period in all patients.

The contraction of posterior belly of digastric muscle may be the key point of occipitotemporal headache, type A botulinum toxin injection lead to dramatical improvement. The MRI may help to confirm such condition.

Keywords: Botulinum toxin, digastric muscle spasm, headache

CLI-B04 Saturday, September 28th, 12:00 [Poster section: Clinical neuroscience B]

Physical and cognitive performance changes caused by expectation of enhancement

Michael Kecht[1,2], Grega Repovš[3], Dejan Georgiev[4], Jure Bon[4], Barbora Minarikova[2], Mara Bresjanac[1]

[1]Laboratory for Neuronal Plasticity and Regeneration, Institute of Pathophysiology, Faculty of Medicine, University of Ljubljana, Slovenia
[2]Research Platform of Cognitive Science, University of Vienna, Austria
[3]Department of Psychology, Faculty of Arts, University of Ljubljana, Slovenia
[4]Department of Neurology, University Medical Centre Ljubljana, Slovenia

The present study aims to advance the current understanding of placebo effect mechanisms in healthy population by analysing changes in objective measures of physical and cognitive performance induced by expectation of an enhancement effect.

Healthy young volunteers of both genders participated in a study employing short tests of physical (maximal hand grip force, maximal leg extension work) and cognitive (three-stimuli auditory oddball test with silent counting) performance. Subjects scheduled two experimental sessions at least three days apart at the same time of day. During each visit two measurement runs were separated by a brief intermission during which an effervescent tablet of vitamin C dissolved in water was administered and announced either as "a stimulant" or a "control" beverage. During the session EEG, EMG of hand flexors and ECG recordings were collected.

Results showed significant effect of enhancement expectation on total leg workout but not on maximal hand grip force. There was no difference in oddball test performance between runs and sessions, but a significant session x run interaction in EEG measures revealed a decrease in P3 mean amplitude after the "stimulant", however not after the control substance. Neither autonomic nervous tone nor myoelectrical activity of handgrip flexors seemed to be significantly modulated by placebo treatment.

Our results revealed an objectively measured placebo effect on motivation dependent endurance performance but not on core muscle strength or oddball test accuracy. Sustained mental performance with a concurrent reduction in cognitive resource allocation may suggest reliance of subjects on stimulant effect during cognitive task.

Keywords: auditory oddball, placebo effect, EEG, ECG, EMG

CLI-B05 Saturday, September 28th, 12:00 [Poster section: Clinical neuroscience B]

Partial recovery of sight after the surgical decompression of optic chiasm performed 3 days after the onset of total blindness

Andrej Porčnik, Peter Spazzapan, Domagoj Jugović, Borut Prestor

Department of Neurosurgery, University Medical Centre Ljubljana, Slovenia

Lesions occurring in the proximity of optic chiasm often cause visual deficits or even total blindness. It is important to achieve decompression as soon as possible to prevent irreversible damage to the nerve fibers. The treatment of choice of suprasellar tumors is radical surgical removal with transcranial or transsphenoidal approach. However, when immediate intervention due to acute blindness is needed, a transventricular neuroendoscopic approach can be a useful method.

We present a case of a 56-year-old woman whose vision impaired one year before the admission to our department. She had a right sided hemianopsy. Visus was 0.3 on the right and 0.8 on her left eye. Electrophysiological studies (visual evoked potentials) were abnormal on both eyes. Magnetic resonance imaging showed a cystic tumor in the suprasellar region that was compressing the optic chiasm. She refused the operation at that time. Finally she was admitted to our department for total blindness that appeared three days before the admission. Pupils were dilated and non-reactive. Endoscopic transventricular approach was used to resect the cystic tumor and to decompress the optic chiasm. On the left eye vision recovered to 0.7 and visual evoked potentials improved. On the right eye she remained blind with abnormal visual evoked potentials.

When treating suprasellar tumors compressing optic chiasm early decompression of nerve structures in essential. The optimal surgical approach should be individually chosen. The presented case shows that even a few days after the onset of total blindness partial recovery of sight can still be achieved.

Keywords: blindness, neurosurger, suprasellar tumor, transventricular resection

CLI-B06 Saturday, September 28th, 12:00 [Poster section: Clinical neuroscience B]

Comparison of spectral changes in EEG recordings of an epileptic patient before and after the vagal nerve stimulator implantation

Mastaneh Torkamani-Azar[1], Hakan Ekmekci[2], Hulagu Kaptan[3], Ali Okatan[4]

[1]Department of Mechatronics, Faculty of Engineering, KTO Karatay University, Konya, Turkey
[2]Department of Neurology, School of Medicine, Selcuk University, Konya, Turkey
[3]Department of Neurosurgery, School of Medicine, Selcuk University, Konya, Turkey
[4]Department of Computer Engineering, Faculty of Engineering, KTO Karatay University, Konya, Turkey

Implantation of vagus nerve stimulators (VNS) has been shown to decrease the power and frequency of seizures in epileptic patients diagnosed with non-localizable epileptogenic zones (EZ) while MRI findings display a completely normally brain in morphology. This study focuses on using Independent Component Analysis to develop spatial filters for tracking changes in the local cortical regions before and after the VNS surgery.

The subject was a 36-year-old Caucasian man with a 20-year history of partial, subcortical epileptic seizures. Besides his regular myoclonic and tonic-clonic attacks, he experienced two incidents of long, restless epileptic conditions at the ages of 30 and 34. He was diagnosed with intractable epilepsy as MRI scans showed normal focal activities, but his EEG recordings included considerable abnormalities despite taking five antiepileptic medications. He underwent a VNS implant surgery using the Cyberonics VNS Therapy System and reported to experience neither partial nor general seizures after the surgery, although he still continues to experience minimal auditory processing disorder.

In the first phase of this ongoing study, we analyzed EEG recordings taken 31, 21, and 4 months before and 11 days after the VNS implantation surgery with the regular 2-30 Hz IPS and hyperventilation intervals. The 18-channel recordings were analyzed in MATLAB using EEGLAB plugin. The results showed that the maximum channel powers decreased 5dB and that the power of independent components arising from the temporal lobe mitigated considerably after the VNS surgery. This observation can be related to the suppressing effect of the magnetic pulses sent from the stimulator and future recordings will enable us to analyze the causality in more depth.

Keywords: epilepsy, refractory, intractable, VNS, EEG, auditory processing disorder, independent component analysis

CLI-B07 Saturday, September 28th, 12:00 [Poster section: Clinical neuroscience B]

Does the intensive cross-modal training of selective attention contribute to language outcome in young aphasic adults after stroke?

Barbara Starovasnik Žagavec, Nada Žemva

Department for Stroke Rehabilitation, University Rehabilitation Institute of Slovenia, Ljubljana, Slovenia

According to epidemiological studies the average annual incidence rate of stroke in young adults (18-45) is still rising. Despite good outcomes only 40-45% returns to previous work or school activities. Many subtle cognitive deficits persist even in chronic phase of the disease; selective attention deficits have large impact on efficacy in short-term and prospective memory, learning and executive functions.

The purpose of our study was trying to gain patient's insight into different stages in deficits of attention after stroke and following non-fluent aphasia and to strengthen the selective attention cognitive efficacy in specific speech and language tasks.

15 patients approximately 4 months after first stroke episode were included in the 12-week period intensive daily neuropsychological training of selective attention while on complex speech and language rehabilitation for non-fluent aphasia.

Important reduction of the errors made in assessing and rehabilitation of selective attention can be seen in the majority of patients with non-fluent aphasia. Hence, there is also the significant effect found on FAST test results which can be used to indicate the general severity of aphasia and to follow later recovery.
The preliminary results possibly show that speech and language rehabilitation of non-fluent aphasia in young adults after stroke combined with a neuropsychological training of selective attention across a 12-week period reduces omission-type errors and improves the level of insight in the attention deficits in speech and language related skills.

Keywords: selective attention, non-fluent aphasia, rehabilitation, stroke

CLI-C01 Sunday, September 29th, 12:00 [Poster section: Clinical neuroscience C]

Partial volume effects contribute to apparent microstructural alterations in mild cognitive impairment

Rok Berlot[1,2], Claudia Metzler-Baddeley[3], Derek K. Jones[3], Michael J. O'Sullivan[1]

[1]Department of Clinical Neuroscience, Institute of Psychiatry, King's College London, UK
[2]Department of Neurology, University Medical Centre Ljubljana, Slovenia
[3]Cardiff University Brain Research Imaging Centre and the Neuroscience and Mental Healhty Research Institute, Cardiff University, UK

Diffusion MRI is widely used to assess white matter microstructural alterations in neurological disorders. These groups are predisposed to atrophy, which leads to artefacts in estimated values of diffusion metrics through cerebrospinal fluid-based partial volume effects (PVE). Distinguishing changes in morphology from intrinsic microstructure has not been possible with conventional methods of analysis.

25 patients with mild cognitive impairment (MCI) and 20 matched controls underwent diffusion MRI. We corrected for PVE using a post-acquisition voxel-by-voxel approach of free-water elimination. Results of uncorrected and corrected analyses were compared at three spatial levels: individual tracts, mean white matter skeleton (TBSS) and whole brain white matter diffusion histograms.

Individual tracts varied in their susceptibility to PVE. Correction shifted the apparent pattern of tract involvement. Both spurious group differences (fornix MD, left uncinate FA) and masking of true microstructural differences (left and right uncinate MD) were observed as a result of PVE. TBSS was robust for much of the skeleton but with notable localised exceptions (e.g. fornix). Group differences in WM histograms were partly driven by PVE, especially for diffusivity metrics.

Partial volume error contributes both quantitatively to group differences between MCI and controls, and to the apparent spatial pattern of microstructural change.

Keywords: diffusion MRI, partial volume effects, atrophy, mild cognitive impairment

CLI-C02 Sunday, September 29th, 12:00 [Poster section: Clinical neuroscience C]

Processing pseudo-words in patients with mild cognitive impairment in comparison with healthy volunteers: Preliminary data

Christina Manouilidou[1], Barbara Dolenc[2], Tatjana Marvin[3], Katarina Marijanovič[3], Zvezdan Pirtošek[2]

[1]Department of Philology - Linguistics Section, University of Patras, Greece
[2]Laboratory for Cognitive Neuroscience, Department of Neurology, University Medical Centre Ljubljana, Slovenia
[3]Department of General and Comparative Linguistics, University of Ljubljana, Slovenia

The concept of mild cognitive impairment (MCI) was proposed to fill the gap between normal and dementia□type pathological ageing. MCI individuals often demonstrate impairments in language, however, psycholinguistic studies in MCI are scarce. The present study aimed to present data regarding the boundaries of lexical representations in this population.

Six healthy controls and eight MCI patients participated in the study. Materials comprised of 4 groups of pseudo-words (violating grammatical, thematic or aspectual constraints of word formation and unattested possible words without violations), one group of real words and one group of non-words. The words were presented in paper (off-line) and computer (on-line) version. In both versions participants had to indicate if the presented word is part of Slovenian vocabulary.

In off-line task, MCI patients revealed a tendency to accept the pseudo-words with aspectual violations as Slovenian more often. For on-line task, mixed ANOVA revealed a main effect of word type on RT while post-hoc analysis revealed a significant difference in RT for non-words ($p=0.02$). MCI patients accepted more pseudo-words with aspectual violations ($p=0.01$), thematic violations, ($p=0.04$) and blocking ($p<0.001$) in the on-line task than in the off-line.

MCI patients seem to have maintained the ability to detect violations, suggesting the preservation of word formation rules. However, the higher percentages in pseudo-words with aspectual violations suggest that the boundaries of their lexical representations are becoming loose. Patients perform worse under time pressure revealing a reduced processing speed. On-line studies could have the potential for early detection of risk groups for dementia.

Keywords: mild cognitive impairment, language, lexical processing, lexical representations

CLI-C03 Sunday, September 29th, 12:00 [Poster section: Clinical neuroscience C]

Temporal processing in children with long term conductive hearing loss associated with otitis media with effusion

J. Handžić, J. Broz Frajtag, I. Vladika

Department of Ear, Nose and Throat, University of Zagreb, Zagreb University Hospital Center, Croatia

Conductive hearing loss (CHL) in otitis media with effusion (OME) children is the most frequent disease in childhood, which disturbed development of central auditory processing and cognition. The aim of the study was to examine how characteristics of CHL influence temporal cues and speech recognition score (SDS.)

Clinical randomized study included right-handed 48 girls and 95 boys (mean age 6y), tested in age subgroups; 4-7yr, 8-12yr with OME and CHL by audiometry, tympanometry, speech audiometry score (SDS) binaural in free sound field and by headphones separately for left/right ear.

Boys have more OME (66.40%) than girls (33.60%). CHL do not improve with aging for 500Hz, 1000Hz. CHL is highest at girls left ears at 2000Hz and 4000Hz with best improvement with aging. Speech discrimination through left ears of girls (mean threshold, 23.2dB and 100% of speech discrimination, mean, 48.2dB) is poorer than in boy's. Bitemporal processing in free sound field is in on higher level for (SDS threshold, mean20.8dB) (discrimination of 100%,mean 46.2dB) than in boys.

CHL for restrictive frequencies dominantly at age of 4-7yr consequences left temporal and bitemporal processing more in girls than boys

Keywords: conductive hearing loss, temporal processing

CLI-C04 Sunday, September 29th, 12:00 [Poster section: Clinical neuroscience C]

Predicting early lethal outcome after acute ischemic supratentorial stroke using clinical parameters and parameters of quantitative electroencephalography

Anton Kuznietsov

Department of Nervous Diseases, Zaporizhzhya State Medical University, Ukraine

Statistical models to predict the lethal outcome of patients with acute ischemic supratentorial stroke (AISS) have several uses, but no adequate model exist. We therefore developed new model using clinical parameters and parameters of quantitative electroencephalography (QEEG).

One hundred eighteen patients (mean age 67.9±0.8 years) were studied within the first 72 hours of clinical evolution of middle cerebral artery territory ischemic stroke. One hundred seventeen QEEG recordings were obtained. In parietal and occipital regions separately to affected and intact hemisphere the values of absolute spectrum rhythm power and relative spectrum rhytm activity of δ-, θ-, α-, β-ranges in parieto-occipital regions were the QEEG selected variables for development of 14 coefficients. Out of 118 stroke patients, 105 (89.0%) were followed up, 13 (11.0%) - were dead.

Clinical parameters and selected QEEG coefficients performed within the first 72 hours of AISS were estimated as independent variables, then outcome predictions at 21th date of stroke oneset was calculated. Baseline NIHSS score [OR (95% CI) = 1.44 (1.11-1.88), p<0.001] and δ/α ratio values of the affected hemisphere [OR (95% CI) = 1.27 (1.11-1.48), p<0.001] were the best predictors for short-term lethal outcome of AISS [significance level of Hosmer & Lemeshow test p=0.92; AUC (95% CI) = 0.933 (0.871 to 0.971), p<0.05].

The value of δ/α ratio of the affected hemisphere performed within the first 72 hours of AISS and the baseline NIHSS score might be a powerful tool predicting early lethal outcome.

Keywords: stroke, quantitative electroencephalography, prognosis

CLI-C05 Sunday, September 29th, 12:00 [Poster section: Clinical neuroscience C]

Influence of mirror therapy on muscle and skin vasomotor regulation in patients with CRPS

Urška Puh, Sonja Hlebs, Alan Kacin

Department of Physiotherapy, Faculty of Health Sciences, University of Ljubljana, Slovenia

The purpose of the study was to establish the effects of mirror therapy on muscle and skin vasomotor regulation in patients with type I CRPS.

Two patients with CRPS symptoms in the wrist area of the right upper extremity 16 and 6 weeks following wrist fracture participated in 4-week mirror therapy programme (20-30 minutes daily, 5 days/wk) in addition to their conventional physiotherapy. Before and after the mirror therapy in patient 1, NIRS in finger flexors during isometric contractions was measured to detect changes in muscle oxygen consumption and local blood flow occurring with therapy. In patient 2, skin vasomotor tone in the hand was evaluated from the difference in forearm and middle finger temperatures during the initial and final mirror therapy sessions. Descriptive statistics was performed.

In patient 1, NIRS showed significant increases in muscle oxygen consumption and blood flow in both upper extremities, but substantially more on the affected side. In contrast, the exercise-induced decrease in skin vasomotor tone in patient 2 was attenuated on both hands with therapy, which was more pronounced on the affected side.

It seems that mirror therapy has induced upregulation of muscle vasomotor tone and downregulation of skin vasomotor tone in the CRPS affected region. Changes in muscle and skin vasomotor regulation might indicate the positive effects of mirror therapy on autonomic functions which is one of the characteristics in patients with CRPS. The observed effects on local vasomotor regulation need to be investigated on a larger patient sample.

Keywords: complex regional pain syndrome, mirror therapy, upper limb, vasomotor regulation

CLI-C06 Sunday, September 29th, 12:00 [Poster section: Clinical neuroscience C]

Diagnosis of mixed dementia

N. A. Trusova[1], T. A. Makotrova[1], O. S. Levin[1], A. V. Arablinskiy[2]

[1]Department of Neurology, Russian Medical Academy of Postgraduate Education, Moscow, Russia
[2]Clinical Hospital of S. P. Botkin, Moscow, Russia

Mixed dementia (MD), characterized by a combination of Alzheimer's disease (AD) and cerebrovascular disease (CVD), takes the second place in the structure of dementia after AD. But relationships between CVD and AD still remain unclear, which causes difficulties in the diagnosis of MD.

Our Objective was to optimize the diagnosis of MD on the basis of clinical, neuropsychological, neuroimaging data.

We examined 50 patients with dementia (mean age 75.3 years), 20 (40%) had AD, 22 (44%) had MD and 8 (16%) were vascular dementia. All patients underwent neurological, neuropsychological study using special scales, MRI was performed using 1.5 Tesla tomograph.

Patients with MD in contrast to patients with AD at comparable severity of cognitive impairment had pseudobulbar syndrome (55%), frontal disbaziya (50%), postural instability (27%). Patients with MD produced elements of both amnesic and dysexecutive profiles. A direct effect of leukoaraiosis on cognitive profile of patients with MD was found: with an increase in the severity of white matter changes neuropsychological profile acquired more marked dysexecutive character. Neurological disorders in MD correlated with the severity of leukoaraiosis ($p < 0.01$). Patients with MD had cortical-subcortical cerebral microbleeds (75%), which may indicate a combination of amyloid angiopathy in AD with hypertensive
microangiopathy.

Thus, an early development of gait disorders, postural instability, pseudobulbar syndrome, development of dysexecutive cognitive defect in a patient with neuropsychological profile generally characteristic for AD are typical for MD. Identified neuroimaging changes correlate with clinical manifestations, which is an important principle of diagnosis of MD.

Keywords: Alzheimer's disease, mixed dementia, cerebrovascular disease, neuropsychological profile, leukoaraiosis, gait disorders, postural instability, pseudobulbar syndrome

COG-A01 Friday, September 27th, 12:00 [Poster section: Cognitive neuroscience A]

Exploratory study of association between body mass index, 2nd to 4th digit ratio and neuropsychological performance among college students

Tjaša Omerzu, Marina Horvat, Saša Zorjan

Faculty of Arts, University of Maribor, Slovenia

There is growing evidence that obesity (i.e. increased body mass index) is related with many negative medical conditions, among them also poorer performance in a variety of neurocognitive domains including global screening measures and memory tasks (Gunstad, Lhotsky, Wendell, Ferrucci & Zonderman, 2010). One the other hand, association between digit ratio and neurocognitive performance is still unclear, although some studies suggest that lower 2D:4D is related with better performance on cognitive tests measuring spatial ability (Kempel et al., 2005). However, there is lack of research with young population.

Purpose of present exploratory study was to determine whether body mass index (BMI) and 2nd to 4th digit ratio are associated with neuropsychological performance. Sample was consisted of 38 psychology students aged 22 to 46 years (M=25.0; 89.5% women; BMI range 16.6-29.1). Four neuropsychological functions were examined with computerized tasks using programme PEBL; visuo-spatial short term working memory, memory span, psychomotor functioning and spatial ability.

Regression analysis was used to check whether body mass index and digit ratio explain a significant proportion of the variance in neuropsychological performance. The results showed no significant association (p>0.05).

Our findings were not in line with our hypotheses. This can be attributed to several factors, the main one being that there were only a few participants with BMI higher than 25. Other limitations were also our sample size, no data of health status was collected, effect of education. There have been numerous conflicting findings in this field, therefore any certain conclusions are difficult to make.

Keywords: BMI, 2D:4D digit ratio, neuropsychological functioning

COG-A02 Friday, September 27th, 12:00 [Poster section: Cognitive neuroscience A]

ERP correlates of bottom-up and top-down processes of visual attention: comparison of different ocular correction methods

Simon Brezovar[1], Jurij Dreo[1], Grega Repovš[2]

[1]Laboratory for Cognitive Neuroscience, Department of Neurology, University Medical Centre Ljubljana, Slovenia

[2]Department of Psychology, Faculty of Arts, University of Ljubljana, Slovenia

Visual attention is the ability to focus on a single visual stimulus out of many. Models of visual attention have proposed two different sources of attentional control: largely automatic, bottom-up processes independent from cognition or task demands, and effortful, slow, top-down processes. Recent ERP studies into the underlying neural correlates of visual attention have shown task conditions that elicit bottom-up processes to generate P300 component with peak amplitude over parietal sites, whereas task conditions that require top-down processes generate a fronto-central P300 component. An alternative explanation for these findings could be the difference in eye movements during task performance, leading to an artefactual shift in P300 topology.

To assess this possibility, we compared the results when using different methods of removing ocular artefacts (epoch rejection vs. ICA ocular component removal) and computing P300 amplitude (maximum vs. average amplitude). 22 students participated in a visual search task in which they had to report the position of a target stimulus. In bottom-up condition the target stimulus differed from distractors by two features (pop-out search), while in top-down condition it differed by only one feature (serial search). EEG signal was aquired using a 128 channel system and processed offline.

The results revealed a significantly higher frontal P300 amplitude only when using epoch rejection and maximum amplitude. In all other cases no significant differences were observed.

These results support the possibility that previously reported differences in frontal P300 amplitude reflected an ocular artefact rather than actual neuronal signature of top-down vs. bottom-up attentional processing.

Keywords: visual attention, bottom-up processes, top-down processes, P300, ocular rejection method

COG-A03 Friday, September 27th, 12:00 [Poster section: Cognitive neuroscience A]

Towards understanding the importance of redefinition of Placebo effect

Rado Gorjup

Psychology Unit Gaetano Kanizsa, Department of Life Sciences, University of Trieste, Italy

How we define something depends on our current knowledge, common sense, beliefs, values, and also on scientific evidence. However these definitions have a strong impact on perception and construction of our attitudes and belief systems and thusly on our reality.
In other words, our knowledge, our temporary physical, cognitive, behavioral, and emotional capacities will decide what kind of definitions and actions someone accepts, follows, and reinforces, what is true and what is not, what is possible for someone and what is not… it is the subjective interpretation of the perceived situation… It is about what we expect and believe to happen.
Placebo is not an inert entity but instead it has a potential of subjective interpretation, a healing potential of its own, over and above that of any healing potential of the medication per se. Such healing potential is greatly dependent on how strong the interpretation value in being healed is that is created by the doctor. We show how Placebo effect goes beyond the usual "sugar pill" approach by using the evidence based approach - A science of compassionate care!
By introducing the new concept of redefined terms of Placebo phenomenon we clearly show that the human mind (unconscious and conscious) is an inevitable substance involved in the Healing Process. The terms "placebo", "placebo effect", and "placebo response" are replaced with the new unified working definitions which offers new insides in understanding the placebo puzzle.

Keywords: placebo, evidence based medicine, art of healing

COG-A04 Friday, September 27th, 12:00 [Poster section: Cognitive neuroscience A]

Acute neurophysiological effect of epigallocatechin gallate (EGGC)

Andreja Emeršič[1,2], Jurij Dreo[1], Zvezdan Pirtošek[1]

[1]Laboratory for Cognitive Neuroscience, Department of Neurology, University Medical Centre Ljubljana, Slovenia
[2]Entrapharm d.o.o., Ljubljana, Slovenia

Epigallocatechin gallate (EGCG) is the most abundant catechin in green tea extract putatively responsible for majority of the potential health benefits associated with green tea consumption. This polyphenol has been shown to exert neuroprotective effects in cellular and animal models of neurological disorders. EGCG is expected to have a positive influence on the course of Alzheimer´s disease but has not been studied sufficiently in regards to its cognitive and neurophysiological effects. Before assessing potential disease-modifying action of EGCG in patients, we therefore decided to investigate its influence on brain electrical activity in a healthy cohort.

Ten young volunteers (mean age 22 years; 9 right-handed; 5 males) completed the preliminary study in a placebo-controlled, crossover and double-blind fashion. All participants received a single 300 mg dose of EGCG and placebo in counterbalanced order on separate days. They were asked to refrain from caffeinated products, alcohol beverages and green tea at least 24 hours prior to each visit. Following a 90-minute absorption period, EEG was recorded with a 64 channel system during the resting state as well as during visual and auditory oddball task. All EEG analyses were performed off-line. We compared both treatment conditions using EEG measures of general brain function and attentional processing: spectral power in delta, theta, alpha and beta band, P3 amplitude, P3 latency and topographical distribution of P3.

We did not detect any significant differences between placebo and EGCG. Nevertheless there seemed to be a trend toward longer P3 latencies obtained with frequent stimuli after EGCG administration.

Keywords: EGCG, electroencephalography, spectral analysis, event-related potential

COG-A05 Friday, September 27th, 12:00 [Poster section: Cognitive neuroscience A]

Disinhibition as a model of spatial working memory deficits in schizophrenia – preliminary findings

Martina Starc[1], John D. Murray[2], Nicole Santamauro[3], Aleksandar Savic[3], Xiao-Jing Wang[4], Alan Anticevic[3]

[1]Department of Psychology, Faculty of Arts, University of Ljubljana, Slovenia
[2]Department of Neurobiology, Yale University School of Medicine, New Haven, USA
[3]Department of Psychiatry, Yale University School of Medicine, New Haven, USA
[4]Center for Neural Science, New York University, USA

Schizophrenia is characterized by a severe deficit in working memory (WM). A possible neural mechanism of such cognitive deficits is the disruption in excitation-inhibition balance in the prefrontal cortex. A prefrontal network model of spatial WM predicts 2 behavioral consequences of such disinhibition: 1) increased variability of the memory trace over time, reducing the precision of stored information and 2) decreased ability to filter out distractors. We tested these predictions using behavioral data from schizophrenia patients (SCZ, n=9) and healthy matched controls (n=8). Controls also underwent an NMDA antagonist (ketamine) infusion, a pharmacological model of schizophrenia hypothesized to induce disinhibition.

Participants were asked to remember the position of circles. After a 10s delay participants used a high-sensitivity joystick to indicate the remembered location. In a distractor task, an additional circle appeared during the delay that participants ignored. Tasks were also performed in the fMRI scanner where controls underwent an infusion of saline or ketamine.

Findings largely follow model predictions. Compared to controls, SCZ exhibit increased variance and less precision in the delay task but not in the control motor task, showing a specific WM deficit. SCZ also show increased distractibility, especially for distractors at specific spatial locations. A similar pattern of results emerges with ketamine. Controls under ketamine display more variable results compared to baseline and become susceptible to distraction, similar to patient findings.

These preliminary findings show promising support for disinhibition as a neural model of WM deficits in schizophrenia and ketamine as a suitable pharmacological model of these deficits.

Keywords: spatial working memory, excitation-inhibition balance, distraction, ketamine, spiking neural network model

COG-B01 Saturday, September 28th, 12:00 [Poster section: Cognitive neuroscience B]

The association of EEG parameters and autonomic response observed in task performance

S. Tymchenko[1], E. Eismont[2]

[1]Crimea State Medical University named after S. I. Georgievsky, Simferopol, Ukraine
[2]Taurida National V. I. Vernadsky University Simferopol, Ukraine

Spontaneous, intrinsic brain's activity recorded with electroencephalogram (EEG) is used to measure tonic cortical arousal and its alterations are associated with neuropsychiatric disorders. It has been also established that various cardiovascular diseases are associated with typical changes in heart rate variability (HRV) widely used as a marker of autonomic nervous activity.

In order to evaluate possible relationships between the cardiac autonomic control and the integrated central nervous system activity EEG and ECG signals were simultaneously recorded in 15 females (25.8±3.5 y/o) in 6 states: awake with eyes opened (EO), awake with eyes closed (EC), during hyperventilation, math computations, positive and negative emotions. Time-domain indices were derived from the series of consecutive R-R intervals of the ECG to measure HRV and spectral analysis was applied to ECG and EEG recordings.

Both positive (with HFn) and negative (with LFn, LF/HF) correlations were revealed with spectral power densities in the alpha band and its sub-types during EC and EO ($0.49<r<0.69$, $p<0.05$) suggesting positive association with parasympathetic activation and relief from anxiety, state of emotional comfort, whereas time-domain HRV parameters were not significantly altered. Frontal midline theta rhythm was negatively correlated with parasympathetic activation during EC and math computations ($0.50<r<0.57$, $p<0.05$). Furthermore, analyses of EEG and HRV during problem solving show progressively stronger alpha-power suppression and theta-power augmentation accompanied by significant decline in parasympathetic activity.

These results suggest a close relationship between cardiac autonomic function under the specific states, showing certain interactive relationships between the peripheral autonomic activities and integrated central nervous system activity.

Keywords: electroencephalography (EEG), heart rate variability (HRV), autonomic nervous system, power spectral analysis

COG-B02 Saturday, September 28th, 12:00 [Poster section: Cognitive neuroscience B]

Transient processes and synchronization of independent ensembles neurons with human choice after the stimulus

A. V. Zaleshin

Institute of Higher Nervous Activity and Neurophysiology of RAS, Moscow, Russia

Stages of processes of neural activity of the cerebral cortex at which large-scale synchronization is carried out are interesting: at once for a significant volume of the cortex and between ensembles of neurons which are dissimilar in composition and properties. Synchronization automatically does not assume presence of communications between neural ensembles. The processes of neuronal activity of ensembles are nonlinear and depend on coordination with other ensembles. In particular, it is possible to investigate time correlation of rhythms with each other in connection with the external stimulus reflected in behavior. The stimulus can be displayed in two ensembles with a constant delay.
During experiment different variants of synchronization of cortical EEG are recorded. Examinees depending on a choice share on algorithm: on making a casual choice, on generated and not generated algorithm of a choice. Also the differentiation on success of the choice defined by number of accumulated points.
At processing similar synchronization on time parameter of several neural ensembles both to, and after stimulus and the subsequent choice are investigated.
Also of interest are neurons ensembles typically occur at the same time delay before and after the stimulus, but not always synchronized with each other.
Processes can be viewed on the new "stimulus" determining the occurrence of the same neuronal ensemble for some seconds before and after the stimulus.

Keywords: choice, stimulus, transient

COG-B03 Saturday, September 28th, 12:00 [Poster section: Cognitive neuroscience B]

Sensitivity of theta rhythm to 14-day bed rest and cognitive training

Voyko Kavcic[1], Uroš Marušič[2], Saša Pišot[2], Nina Mohorko[2], Rado Pišot[2]

[1]Institute of Gerontology, Wayne State University, Detroit, USA
[2]Institute for Kinesiology Research, Science and Research Centre, University of Primorska, Koper, Slovenia

The theta rhythm is a large EEG signal from the mammalian brain implicated in mnemonic and navigation functions.

With 14-days bed rest (BR) we experimentally induced long term immobilization to evaluate BR effects on spectral composition of baseline EEG recordings with emphasize on theta rhythm. In addition, we also applied cognitive training on 8 of our 14 participants to evaluate if virtual maze navigation can affect anticipated BR induced spectral EEG changes. Fourteen adult men, ages 53 - 65 years, participated in a 14 day BR study: 8 of them underwent 12 daily sessions of 50 minutes cognitive training sessions in which participants had to solve virtual mazes and the other 6 watched documentaries. A day before and after BR we recorded baseline EEG with active 64 channel BrainVision amplifiers. Baseline EEG was decomposed with FFT to 7 different band ranges: delta (2–4 Hz), theta (4–8 Hz), alpha 1 (8–10.5 Hz), alpha 2 (10.5–13 Hz), beta 1 (13–20 Hz), beta 2 (20–30 Hz), and gamma (30-50 Hz).

Results showed that power of theta did not change for older adult men who underwent cognitive training, while for others there was significant increase on theta power, most pronounced over posterior cortices.

Our results unequivocally demonstrate that cognitive intervention with spatial navigation training can attenuate spectral EEG changes after prolonged immobilization. Our results also suggest that cognitive training with virtual maze navigation could be used to prevent the deleterious effects of prolonged hospitalization and/or sedentary life style.

Keywords: EEG, theta rhythm, bed rest (BR), cognitive training, virtual maze navigation

COG-B04 Saturday, September 28th, 12:00 [Poster section: Cognitive neuroscience B]

Two stages of information processing in visual working memory: ERP study

S. Kozlovskiy, A. Korotkova, M. Pyasik

Lomonosov Moscow State University, Russia

We studied brain electrical activity related to memorizing different types of visual information.

Participants in the study were 15 subjects (19-48 years old). Working memory testing consisted of two series, which differed in the level of difficulty (standard 0-back and 1-back tasks), and control task, which included passive observation of the same stimuli.
Presented stimuli were square patterns 9*9, which included white and black squares set in three types of configuration (three types of stimuli, 16 variations each) – schematic faces, letters of Russian alphabet and geometric figures. In each part of the test stimuli were presented in blocks (block of 'faces'. block of 'letters', block of 'figures') of 120 stimuli.
During the tests EEG (21 channels, monopolar) was registered. We calculated averaged ERPs of all subjects for each part of the test and each stimuli type.

The obtained results showed significant differences in ERPs amplitude for the same stimuli type but different memory load for later ERP components (300-500 ms). Differences in ERPs amplitude for different types of stimuli in the same part of the test were found for N200 component.
Thus, it can be concluded that memorizing visual information consists of two stages of information processing. Earlier stage is more stimuli-dependent, whereas later stage is more related to the visual working memory load.

Keywords: visual working memory, event-related potentials

COG-B05 Saturday, September 28th, 12:00 [Poster section: Cognitive neuroscience B]

Electrocortical correlates of temperament

Sanja Tatalović Vorkapić[1], Meri Tadinac[2], Ivana Lučev[3]

[1]Faculty for Teacher Education, University of Rijeka, Croatia
[2]Faculty for Humanities and Social Sciences, University of Zagreb, Croatia
[3]Institute for Migration and Ethnic Studies, Zagreb, Croatia

Numerous research studies have tried to understand the brain-behaviour relationship applying electrophysiological investigations of human personality. As a result, respectable number of explorations was done on the field of biological bases of extraversion and very few on the relationship between temperament and evoked brain potentials. In addition, even though Strelau considered temperament traits were primarily biologically based, there were a small number of psychophysiological studies within the field of temperament.

Taken altogether, the main aim of this study was to investigate the relationship between three temperament dimensions: strength of excitation, strength of inhibition and mobility measured by Pavlov's Temperament Survey (PTS), and amplitudes and latencies of evoked brain potentials (N1, P2, N2, P3 & SW) measured by a simple visual oddball paradigm in two blocks. The participants were female psychology students (N=54) with mean age of 20.

Significant positive correlations were determined between amplitudes of N1-P2-N2-P3 components and strength of excitation and mobility in the first and second block, mostly on parietal electrodes, as well as significant negative correlations of amplitudes of N1-P2-N2-P3 components and strength of inhibition. Expected significant negative correlation between mobility and EP-latencies was not found in this study.

Considering measurement limitations in this research, important future study directions have been given. Various models of personality, specific information processing and different reactions to the easy/hard tasks used in research represent rather significant moderating factors of the relationship between temperament and evoked potentials, which should be taken into consideration in the future studies.

Keywords: Pavlov's typology of temperament, evoked potentials, students

COG-B06 Saturday, September 28th, 12:00 [Poster section: Cognitive neuroscience B]

The effects of intention on cortical excitability: A preliminary TMS study

Ruben Perellón Alfonso[1,2], Stephan Lechner[1,2], Indre Pileckyte[1,2], Jurij Dreo[1], Jure Bon[1], Maja Kojović[1], Nejc Šarabon[3], Blaž Koritnik[1]

[1]Laboratory for Cognitive Neuroscience, Department of Neurology, University Medical Centre Ljubljana, Slovenia
[2]University of Vienna, Austria
[3]S2P, Ljubljana, Slovenia

Transcranial magnetic stimulation (TMS) has been recently used to explore the effects of intention on primary motor cortex (M1) excitability [1, 2]. The results show that intention may influence the amplitude of the motor evoked potentials (MEPs). This effect has been directly linked to cortical inhibitory processes [2].

The present study, now in piloting stage, was designed to explore the relation between cognitive function and motor performance, both in healthy participants and dystonia patients. Three healthy participants have been recorded until now. Subjects were asked to mentally resist or assist a subsequent flexion of the wrist produced by a TMS single pulse to the M1 area. These two conditions were interspersed in a fully randomized fashion, together with a control condition in which a TMS pulse was delivered without previously requiring any mental task. MEP amplitude was recorded at the flexor and extensor carpi radialis muscles (FCR and ECR respectively) using electromyography (EMG). EMG was analyzed for each subject in order to explore the effects of the three different conditions on MEP amplitude.

Statistical analysis of peak to peak MEP amplitudes revealed significant differences between conditions in all subjects, for at least one muscle. However, in the ECR muscle, the same differences between conditions were observed in two subjects, namely, the resist condition exhibited significantly higher amplitudes, as compared to the assist and control conditions. Nevertheless, a larger amount of subjects is needed before asserting any clear tendencies.

If results prove stable, this experimental paradigm could be used to explore the neurophysiological integrity of the cognitive-motor loop in dystonia patients, for whom inhibition is reported to be impaired at a cortical level [3], but has not been thoroughly explored in the relation between cognitive function and motor performance.

[1] Bonnard M. J Cogn Neurosci 2003;15:1207-16.
[2] Bonnard M. Eur J Neurosci 2009;30:913-23.
[3] Hallett M. Neurobiol Dis 2011;42:177-84.

Keywords: intention, inhibition, dystonia, TMS, EEG

COG-C01 Sunday, September 29th, 12:00 [Poster section: Cognitive neuroscience C]

Mindfulness induction improves cognitive, but not physical, performance in non-meditators

Mara Bresjanac[1], Grega Repovš[2], Špela Tevžič[1], Manja Lošdorfer Božič[1], Dejan Georgiev[3], Jure Bon[3]

[1]Laboratory for Neural Plasticity and Regeneration, Institute of Pathophysiology, Faculty of Medicine, University of Ljubljana, Slovenia
[2]Department of Psychology, Faculty of Arts, University of Ljubljana, Slovenia
[3]Neurology Clinic, University Medical Centre Ljubljana, Slovenia

Mindfulness is a psychological state of receptive awareness and attentional control. Although typically achieved through lengthy meditative practice, mindfulness has been employed as an acutely induced state of purposeful and focused attention in an EEG-based brain-computer interface experiment (1), and for manipulating emotional regulation (2). We employed a similar approach to assess acute mindfulness induction (MI) effects on physical and cognitive performance in young, healthy non-meditators.

University students (n=34; 13M) volunteered for a study of MI effects on maximal hand-grip force, maximal leg-extension work in 1 min and a three-stimuli auditory oddball test with silent counting. In each of the two experimental sessions of this randomized, cross-over study, two runs of tests were separated by an intermission presenting one of the two recordings: instructions for attentional control via concentrative meditation techniques (MI), enabling subjects to focus on the immediate task, or the equal length, same narrator, comparable prosody recording of a recent scientific breakthrough (neutral, N). EEG was recorded during the auditory oddball task and event related potential (ERP) P3b characteristics analyzed.

There was no effect of MI on physical performance or mean error of oddball target counts. However, a significant improvement in precision (reduced variance; $p < 0.001$) was found following MI but not the N recording. P3b mean amplitude was maintained after MI but reduced after N. Acute MI facilitated sustained cognitive resource allocation, enabling improved accuracy.

1. J Neural Eng 2011; 8: 025019
2. Emotion 2010; 10: 72

Keywords: auditory oddball, EEG, P3b

The effect of valence on spatial working memory

Martina Starc[1], Alan Anticevic[2], Grega Repovš[1]

[1]Department of Psychology , Faculty of Arts, University of Ljubljana, Slovenia
[2]Department of Psychiatry , Yale University School of Medicine, New Haven, USA

There are well-documented effects of emotional salience on long-term memory and attention, particularly involving negative and highly arousing stimuli. In contrast, effects on working memory (WM) are less well understood. Critically, the majority of studies focus on interfering effects of emotion, whereas its potentially enhancing influence remains uncharacterized. We examined enhancing effects of emotional valence on the precision of spatial WM representations in a task directly adapted from primate physiology experimental work.

30 participants (15 male) were asked to remember the spatial position of circular pictures. After a delay participants used a joystick to move a circle to the correct position, providing a continuous measure of recall accuracy. After the WM task, participants rated the valence and arousal of pictures.

The results revealed a quartic relationship between valence ratings and accuracy of position recall. Highest accuracy was achieved with pictures that were rated as either slightly positive or slightly negative. Accuracy was lowest for highly negative or highly positive pictures with intermediate results for pictures that were rated as neutral.

The results thus support both detrimental and enhancing effects of emotional salience and can be interpreted in the context of the "dual competition" framework [1]. High intensity stimuli divert common resources away from the WM task, while low intensity stimuli provide an "attentional boost" likely to facilitate attentional allocation at encoding but they are not disruptive enough to detrimentally affect task execution.

[1] Pessoa, L. (2009). How do emotion and motivation direct executive control? Trends in Cognitive Sciences, 13(4), 160–166.

Keywords: spatial working memory, emotion cognition interactions, emotional salience, valence effects

Effects of cognitive remediation during 14-day bed rest on walking performance of older adult men

Uroš Marušič[1,3], Voyko Kavcic[2], Mitja Gerževič[1], Matej Plevnik[1], Romain Meeusen[3], Boštjan Šimunič[1], Rado Pišot[1]

[1]Institute for Kinesiology Research, Science and Research Centre, University of Primorska, Koper, Slovenia
[2]Institute of Gerontology, Wayne State University, Detroit, USA
[3]Department of Human Physiology, Faculty of Physical Education and Physical Therapy, Vrije Universiteit Brussel, Belgium

Prolonged immobilization or inactivity which follows sports injuries and surgery could lead to serious motor dysfunction preventing a quick recovery and causing elevated costs for a national health care system. Therefore, it is important to develop interventions to reduce the deterioration of the motor output during immobilization or inactivity.

We tested the effectiveness of cognitive training in attenuating motor decline (i.e., walking proficiency) during prolonged immobilization by performing a cognitive-based intervention during bed rest (BR). Fifteen older adult men age 53 - 65 years participated in a 14 days BR study; half of them underwent 12 daily sessions of 50 minutes of cognitive training in which participants had to solve virtual mazes and the other half watched documentaries at the same time. A day before and after BR walking performance was measured with Optogait system in two conditions: normal speed and normal speed with dual task, with walking performance measured in terms of dual task cost [(walking with dual task – walking)/walking X 100].

Results showed that older adult men who underwent cognitive training during 14 days BR did not show any dual task costs in double support, stride, walking speed, and cadence during normal walking pace as compared to those without cognitive training.

Our results unequivocally show that cognitive intervention with spatial navigation training can attenuate decline in walking performance evident after prolonged immobilization. Preventive effects of virtual maze navigation most likely reflect the transfer of cognitive training on executive functions and/or preserved motor control.

Keywords: bed rest, cognitive training, virtual maze navigation, walking performance

COG-C04 Sunday, September 29th, 12:00 [Poster section: Cognitive neuroscience C]

Cognitive emotion regulation of aversive emotional responses and their prediction recruits a common regulatory system

Satja Mulej Bratec[1,2,5], Xiyao Xie[1,2,6], Marie-Luise Brandi[1,2,5], Verena Krupp[2], Afra Wohlschläger[1,2,5], Valentin Riedl[1,2,3], Christian Sorg[1,2,4]

[1]Department of Neuroradiology,
[2]TUM-NIC Neuroimaging Center,
[3]Department of Nuclear Medicine,
[4]Department of Psychiatry, Technische Universität München, Germany
[5]Graduate School of Systemic Neurosciences,
[6]Department of Psychology, Ludwig-Maximilians- Universität München, Germany

Cognitive emotion regulation (CER) such as self-distancing is a powerful species-unique way of modulating aversive emotions and conditioned fear. However, whether CER can directly affect both aversive emotional responses and their prediction by recruiting the same regulatory system is yet unknown.

The CER's behavioural and neural effects on aversive emotional responses and their prediction were investigated with the use of model-based functional magnetic resonance imaging (fMRI). The visual presentation of aversive stimuli was combined with a classical conditioning paradigm and varying conditioned – unconditioned stimulus (CS-US) contingencies. On each trial, a cue (CS) was presented, after which an aversive picture (US) followed on a proportion of trials (CS+ trials; otherwise a blank screen was presented: CS- trials). Participant's task was to predict the occurrence of the US. Importantly, CER by self-distancing was employed in half of the experiment, while in the other half, participants were instructed to passively observe the stimuli. Conditioning was modelled by the Rescorla-Wagner model, resulting in learning parameters of aversive prediction and aversive prediction error.

Self-distancing reduced both aversive prediction- and aversive emotional response-related activity in the brain, suppressing activity in emotional areas such as amygdala, insula and striatum. Furthermore, a common regulatory system including the right dorsolateral prefrontal cortex and the angular gyrus was recruited both when participants regulated their predictions of or emotional responses to aversive pictures.

Our data demonstrate that cognitive emotion regulation recruits a common emotion regulation system in order to modulate both current aversive emotional responses and associated neural learning effects.

Keywords: emotion regulation, classical conditioning, prediction

COG-C05 Friday, September 27th, 12:00 [Poster section: Cognitive neuroscience A]

P3 topography from different sensory modalities in oddball tasks

Daniel Attia[1,2], Grega Repovš[1], Jurij Dreo[1], Zvezdan Pirtošek[1]

[1]Laboratory for Cognitive Neuroscience, Department of Neurology, University Medical Centre Ljubljana, Slovenia
[2]University of Vienna, Austria
[3]Department of Psychology, Faculty of Arts, University of Ljubljana, Slovenia

The P3 wave is an event-related potential (ERP) component with a latency of 250-500ms. It is considered to be an endogenous potential independent from physical attributes of a stimulus, reflecting attentional, evaluative, categorization and memory processes in response to the stimulus. Specifically, P3 might reflect comparison of the existing neural presentation of the environment with the sensory input and updating in the case of a mismatch [1]. If P3 is indeed independent of the stimulus, that should be reflected in a stable P3 topology across different stimulus modalities [2].

To test this hypothesis 20 healthy subjects completed two sessions of an oddball task using visual and auditory stimuli while 128 channel EEG signal and fMRI signal were acquired on two separate occasions. This is the first study that employs high-resolution EEG while directly comparing P3 topographies obtained in two different stimulus modalities. As such it may provide a better understanding of the basics of the neural P3 generation. As one of the most often used ERP components, detailed understanding of the P3 generation could provide valuable information both for future study designs and interpretation of results in both basic and clinical research.

[1] J. Polich, "Overview of P3a and P3b", in: Detection of change: event-related potential and fMRI findings, J. Polich, Ed. Boston:MA, 2003, pp.83-98
[2] J. Katayama, J. Polich: Stimulus context determines P3a and P3b. Psychophysiology, 35:32, 23–33, 1998

Keywords: P300 topography, modalities, topographical correlation

MET-A01 Friday, September 27th, 12:00 [Poster section: Neuroscience methods A]

Fine control of delivery of neuroactive molecules by optical manipulation techniques

Giulietta Pinato[1,2], Dan Cojoc[2]

[1]University of Nova Gorica, Slovenia
[2]Istituto Officina dei Materiali, Consiglio Nazionale delle Ricerche, Trieste, Italy

Morphological complexity is at the basis of the very high capability of neurons to process electrical as well as chemical information. Mimicking neuronal chemical release characterized by fast and short-distance diffusion of small volumes in confined areas, and delivering controlled amount of molecules to specific compartments is an important issue for a detailed study of neuronal signaling.

Exploiting optical manipulation techniques, in particular optical tweezers and laser micro-dissection, we developed a technique to deliver very precise quantities of soluble compounds to neuronal cells in culture. The technique is based on the encapsulation of small volumes of solutions in the lumen of lipid vesicles. Single vesicles can be then selected and positioned with the optical tweezers near specific compartments of neuronal cells such as somata, dendrites or axons. Vesicles are then broken with UV laser pulses and their content released with micro-metric precision. A quantitative assessment of the encapsulation efficiency allows to estimate the number of molecules released and those reaching different parts of the cells.

This technique was successfully applied to stimulate single neuron firing with KCl in synaptically connected hippocampal primary cultures and to deliver guidance molecules onto growth cones of developing dissociated neurons.

Keywords: optical tweezers, growth cone, vesicle

MET-A02 Friday, September 27th, 12:00 [Poster section: Neuroscience methods A]

Development of novel electrochemical biosensors for detection of neurotransmitters

N. Grgurevič[1], D. Strle[2], M.Trifković[2], G. Majdič[1,3]

[1]Center for Animal Genomics, Veterinary Faculty, University of Ljubljana, Slovenia
[2]Laboratory for microelectronics, Electrical engineering department, University of Ljubljana, Slovenia
[3]Institute of Physiology, Medical School, University of Maribor, Slovenia

Understanding dynamics of neurotransmitter release is one of the fundamental questions of contemporary neuroscience. Classical methods such as immunoassay, in situ hybridization and immunocytochemistry provide very limited information as they could not be used to study dynamics of neurotransmitter release. Novel methods such as cyclic voltammetry do allow real time measurement of neurotransmitter release, but are very limited in number of neurotransmitters that could be measured.

Therefore the aim of our study is to develop very sensitive and precise biosensor that could simultaneously detect more than one neurotransmitter in real time with precise spatial and temporal resolution. CMOS technology electronics coupled with aptamer based sensing is being used. The surface of the CMOS electrical sensor is covered either with SiO2 or SiN3 and functionalized with aptamers, short DNA molecules that could specifically bind certain small molecules including neurotransmitters. Each sensor is composed of two identical sensor fields, one functionalized with aptamers and one without. The neurotransmitter presence is detected by measuring the impedance difference of the sensors in a differential pair, caused by the binding of ligand (neurotransmitter) to the functionalized sensor.

Although in the initial stage we are developing sensors for detecting single substance (I.E: dopamine), we intend to further develop the technology, so that it will be possible to implement an array of differently functionalized sensors for simultaneous detection of different neurotransmitters, what would enable us to monitor activity of multiple brain cells in real time with good spatial and temporal resolution.

Keywords: electrochemical, biosensors, neurotransmitter, aptamer, dopamine

MET-B01 Saturday, September 28th, 12:00 [Poster section: Neuroscience methods B]

Neurophysiology model of the human lumbar cord separated from brain control by traumatic injury

Simon M. Danner[1,2], W. Barry McKay[3], Karen Minassian[2], Ursula S. Hofstoetter[2], Winfried Mayr[2], Frank Rattay[1], Milan R. Dimitrijević[4,5]

[1]Institute for Analysis and Scientific Computing, Vienna University of Technology, Austria
[2]Center for Medical Physics and Biomedical Engineering, Medical University of Vienna, Austria
[3]Hulse Spinal Cord Injury Lab, Crawford Research Institute, Shepherd Center, Atlanta, USA
[4]Department of Physical Medicine and Rehabilitation, Baylor College of Medicine, Houston, USA
[5]Foundation for Movement Recovery, Oslo, Norway

In animals, the research model for spinal cord injury is well defined by controlled, experimentally set lesions. With the most severe damage, spinal neural networks can be studied in the absence of supraspinal or peripheral inputs. In contrast, traumatic spinal injuries in human and the resulting pathological processes produce highly individualized models of supraspinal control over the spinal cord below the lesion. Previously, it has been shown that clinically motor-complete injuries in humans can retain residual brain influence over spinal cord function below the lesion evidenced through neurophysiological examination.

Fifteen clinically paralyzed subjects participated in this study of epidural spinal cord stimulation effects on spasticity control. Neurophysiological examination showed that three subjects retained the ability to volitionally induce task-appropriate electromyographic activity by the attempt of a single joint movement although no muscle contraction was clinically evident. Eight of the remaining subjects were able to diffusely activate muscles below the lesion in response to reinforcement maneuvers. This type of response was repeatable over 3 trials in 3 subjects. The remaining 4 subjects showed no clinical or subclinical signs of suprasegmental control.

These results suggest that this residual supraspinal influence modified the excitability of the neural networks caudal to the lesion, potentially contributing to the diversity of effects seen in interventions targeting the lumbar spinal cord after injury. Further, these findings highlight the importance of the use of neurophysiological assessment to characterize the lesions within the human research model of the lumbar spinal cord when studying the effects of interventional strategies.

Keywords: spinal cord injury, human, models

MET-B02 Saturday, September 28th, 12:00 [Poster section: Neuroscience methods B]

Electrophysiology of posterior roots-muscle reflex of the human lumbosacral cord

Matthias Krenn[1], Karen Minassian[1], Ursula S. Hofstoetter[1], Simon M. Danner[1,2], Milan R. Dimitrijević[3,4], Winfried Mayr[1]

[1]Center for Medical Physics and Biomedical Engineering, Medial University of Vienna, Austria
[2]Institute for Analysis and Scientific Computing, Vienna University of Technology, Austria
[3]Department of Physical Medicine and Rehabilitation, Baylor College of Medicine, Houston, USA
[4]Foundation for Movement Recovery, Oslo, Norway

Electrical stimulation of the human lumbosacral spinal cord via epidurally implanted electrodes can elicit muscle twitches in multiple lower limb muscles bilaterally [1]. These responses result from the depolarization of Ia afferent fibers within the posterior roots and the subsequent monosynaptic activation of motor fibers innervating the lower limb muscles. According to their initiation and recording sites, the responses were termed posterior root-muscle (PRM) reflexes [2]. Such PRM reflexes can be also elicited by transcutaneous spinal cord stimulation utilizing skin electrodes placed on the back at the level of the T11-T12 spinous processes and the lower abdomen [2]. Single stimulation pulses delivered from such site can consistently activate L2-S2 posterior root fibers bilaterally and thus evoke PRM reflexes in various lower limb muscles simultaneously. By varying the rostro-caudal position of the back electrodes (T11-T12 spinous processes +/– 4 cm), a more dominant stimulation of either the upper or the lumbar spinal cord segments can be achieved, as reflected by the thresholds of the PRM reflexes elicited in the L2-L4 innervated quadriceps vs. the L5-S2 innervated triceps surae. Electromyographically, the PRM reflexes are recorded as compound muscle action potentials (CMAPs). Under invariant stimulation conditions, the CMAPs of the thigh and lower leg muscles have short and constant onset latencies as well as characteristic morphologies. Transcutaneous spinal cord stimulation to elicit PRM reflexes is a comprehensive assessment method for human motor control studies.

1. Minassian K et al., Spinal Cord. 2004, 42(7):401-416
2. Minassian K et al., Muscle Nerve. 2007, 35(3):327-336

Keywords: PRM reflex, electrical stimulation, human motor control

MET-C01 Sunday, September 29th, 12:00 [Poster section: Neuroscience methods C]

Utility of over-determined ICA decomposition for ocular artifact removal from high-resolution EEG data

Jurij Dreo[1], Simon Brezovar[1], Blaž Koritnik[2]

[1]Laboratory for Cognitive Neuroscience, Department of Neurology, University Medical Centre Ljubljana, Slovenia
[2]Institute of Clinical Neurophysiology, Department of Neurology, University Medical Centre Ljubljana, Slovenia

Blinks are the largest amplitude physiological artifacts present in EEG data. Their efficient removal is thus paramount to EEG analysis. Independent Component Analysis (ICA) is a mathematical method of generating signals/components that are linear combinations of the original channels. While the resulting components do not necessarily have any a priori relation to physical sources, it is often noticed that they are similar to know signals (muscular, alpha, eye-movement…). Excluding components that likely contain blinks, before re-assembling the rest, effectively subtracts blinking artifacts from EEG data. While ICA normally produces as many components as there are EEG channels, it is possible to mathematically over-determine it by calculating fewer components.

We have systematically assessed the effect of such over-determination on the efficiency of blink removal and background EEG preservation. The former was measured by averaging 1 second EEG segments surrounding blink peaks after their removal by ICA. The average amplitude remaining after ICA on frontal EEG channels in the interval [-150,+150] ms relative to blink peaks was used as a measure of remaining blink activity. Since blinks are not randomly interspersed in EEG data but tend to roughly time-lock to external stimuli (Figure 1), we assessed the preservation of background EEG activity by comparing the remaining P3 amplitude in an Oddball task after ICA blink removal.

ICA correction is found to be a trade-off between artifact removal and background EEG-preservation. Based on 128-channel data from 28 individuals the optimum balance seems to lie at around 60 ICA components (Figure 2).

Figures:
http://goo.gl/jnnOh

Keywords: Independent Component Analysis, ocular artifacts, event related potentials

MOL-A01 Friday, September 27th, 12:00 [Poster section: Molecular neuroscience A]

Novel modulation of P2X3 receptors by endogenous Calcium/calmodulin-dependent serine protein kinase (CASK)

T. Bele[2], A. Gnanasekaran[1], M. Sundukova[1], S. Hullugundi[1], A. Nistri[1], E. Fabbretti[1,2]

[1]Neuroscience Department, International School for Advanced Studies, Trieste, Italy
[2]Center for Biomedical Sciences and Engineering, University of Nova Gorica, Slovenia

Extracellular ATP is believed to be an important modulator of central synapses as well as a neurotransmitter of nociceptive signals. In peripheral neurons, among other subtypes, P2X3 receptors expressed principally by sensory neurons are sensitive to even nanomolar concentrations of extracellular ATP, and, therefore, play a major role in nociception, including chronic pain syndromes.
P2X3 receptor function is highly regulated by signal transduction mechanisms, protein-protein interactions, and discrete membrane compartmentalization. Our recent findings have demonstrated that P2X3 receptors interact in a state dependent fashion with the calcium/calmodulin-dependent serine protein kinase (CASK), a synaptic scaffold protein believed to modulate synaptic release and synaptic strength. We observed that, in mouse trigeminal ganglion neurons, CASK potently controls P2X3 receptor stability and efficiency. Blocking CASK impairs P2X3 receptor expression and function and is downregulated by P2X3 receptor desensitization. Activation of P2X3 receptors within the CASK/P2X3 membrane complex has, thus, important consequences for neuronal plasticity and possibly for the release of neuromodulators and neurotransmitters. Better understanding of the interactome machinery of P2X3 receptors and their integration with other receptors and channels on neuronal surface membranes, is proposed to be necessary to unveil the process of neuronal sensitisation and related, abnormal pain signalling. Supported by Cariplo Foundations, ARRS and Cross-border Cooperation Italy-Slovenia 2007-2013 (MINA).

Keywords: pain, synapse

MOL-A02 Friday, September 27th, 12:00 [Poster section: Molecular neuroscience A]

Unilateral striatal quinolinic acid injection as a model for the study of corticostriatal plasticity

Špela Glišović, Aleksandra Milutinović Živin, Marko Živin

Institute of Pathophysiology, Faculty of Medicine, University of Ljubljana, Slovenia

By stimulation of NMDA receptors, unilateral striatal injection of quinolinic acid (QA) provokes striatal overactivaty and excitotoxic injury. This triggers hemi-seizures that during recovery from anesthesia manifest as episodic barrel rotations and tonic-clonic forepaw movement and as secondary excitotoxic injuries of other brain regions.

We have used this model to study the expression of early response genes c-fos and synaptotagmin 4 (Syt4) and of brain derived neurotrophic factor (BDNF) by in situ hybridization of their mRNAs, 4h after unilateral QA intrastriatal injection. Corticostriatal neurons are the main source for striatal BDNF. Regulation of BDNF trafficking by Syt 4 may be important for the survival of striatal neurons. The upregulation of c-fos mRNA served as an indicator of the brain regions affected by seizure activity.

We found that QA induced overlapping pattern of up-regulation of c-fos and Syt 4 mRNAs in the cortex and other brain regions, while BDNF mRNA upregulation was restricted to the cortex and hippocampus of the lesioned hemisphere. These changes were dependent on NMDA receptor activation, since the antagonist of NMDA receptors, MK801, dose-dependently attenuated the seizures and the upregulation of mRNAs of all three genes.

We conclude that intrastriatal injection of QA may serve as a good model for the exploration of the role of Syt IV in the regulation of BDNF trafficking within cortical neurons. Further co-localization and time-course experiments will be conducted to determine if Syt 4 may be involved in the anterograde transport and transfer of BDNF from corticostriatal to striatal neurons.

Keywords: quinolinic acid, MK801, striatum, synaptotagmin IV, c-fos, BDNF

MOL-A03 Friday, September 27th, 12:00 [Poster section: Molecular neuroscience A]

The role of corticogenesis-regulating genes during brain repair and regeneration after ischemia

Dunja Gorup[1], Srečko Gajović[1], Marta Rosario[2]

[1]Croatian Institute for Brain Research, School of Medicine, University of Zagreb, Croatia
[2]Institute for Cell and Neurobiology, Charite Universitätsmedizin, Berlin, Germany

The neocortex is responsible for higher brain functions such as sensation, motor control and memory.

During development, generation of the 6 cortical layers is regulated by a handful of transcription factors. We hypothesized that these same molecules are involved not only in development, but also in the adult brain during repair and renovation following damage.
To test this, we have used the ischemic lesion model (MCAO, medial cerebral artery occlusion) in wild type mice and in mice lacking the Toll-like Receptor 2 (TLR2). TLR2 has been shown to be crucial for triggering the inflammatory response, enabling us to address the influence of inflammation on adult neurogenesis following lesion.

Induction of developmental genes was analyzed in control and stroke model wild type and TLR2 KO animals at different times following brain lesion.

We have observed changes in the levels of active serine/threonine kinase JNK2. In addition, we see alterations in the expression patterns of developmentally regulated transcription factors including CTIP2 and SATB2 in lesioned brains. There is de novo expression of the developmentally regulated transcription factor CTIP-2 and P-JNK 2 weeks after MCAO, while IHC has shown that endogenous neuronal stem cells that are activated after the lesion are positive for CTIP-2.

IHC with anti-SATB2 antibody has shown a change in expression after the lesion, compared to the expression in sham operated animals.

Our data suggests that there is an activation of corticogenesis regulating transcription factors following the ischemic lesion. In addition, inflammation appears to modulate this activation.

Keywords: corticogenesis, inflammation, MCAO

The role of Akt in neurotoxic effect of intracellular and extracellularal α-synuclein (ASYN) in vitro

Maja Jovanović[1], Marija Dulović[1], Vladimir Kostić[2], Andjelka Isaković[1], Marjan Popović[1], Sonja Misirlić Denčić[1], Vladimir Trajković[3], Ivanka Marković[1]

[1]Institute of Medical and Clinical Biochemistry, School of Medicine, University of Belgrade, Serbia
[2]Institute of Neurology, Clinical Center of Serbia, School of Medicine, Belgrade, Serbia
[3]Institute of Microbiology and Immunology, School of Medicine, University of Belgrade, Serbia

Alpha-synuclein (ASYN) is regarded as essential in Parkinson's disease (PD) pathogenesis. Number of signalling pathways seem to be altered as a result of ASYN neurotoxic effect.

The aim was to investigate the role of PI3K/Akt signalling pathway in neurotoxic effect of intra- and extracellularal ASYN.

All experiments were conducted in all-trans retinoic acid (RA) differentiated SH-SY5Y cells, conditionally expressing wtASYN, (ASYN- cells) and the control cells (beta-gal). The cell viability was assessed using crystal violet assay, whereas pan-caspase activity and DNA fragmentation were quantified by flow cytometry. Activation of Akt (pAkt) in cell lysates, and the presence of secreted ASYN in liophylized conditioned medium (CM), collected from ASYN-overexpressing cells, was confirmed by immunoblot.

Differentiation with RA had pronounced cytotoxic effect on ASYN overexpressing cells (ASYN), accompanied by the decrease in pAkt, and consequent apoptosis induction, whereas increase in Akt activity was observed in the control beta-gal cells. Insulin-dependent Akt activation, caused significant increase in viability of ASYN- cell ($p<0.05$). Application of CM containing secreted ASYN caused significant decrease in viability of recipient RA-differentiated SH-SY5Y cells, whereas insulin partially rescued the neuroblastoma cells from neurotoxicity of extracellular ASYN.

These results confirm the role of Akt in neurotoxic action of both intracellular and extracellular wtASYN, and indicate that modulation of this pathway may be an intriguing possibility for neuroprotection in PD.

Keywords: Parkinson's disease, α-synuclein (ASYN), neurotoxicity, Akt

Association of variable number of tandem repeats polymorphism in the third exon of DRD4 gene and catechol-O-methyltransferase Val108/158Met polymorphism with alcoholism and alcohol-related phenotypes

Gordana Nedić Erjavec[1], Korona Nenadić Šviglin[2], Matea Nikolac Perković[1], Dorotea Muck-Šeler[1], Nela Pivac[1]

[1]Division of Molecular Medicine, Ruđer Bošković Institute, Zagreb, Croatia
[2]Center for Alcoholism and Other Addictions, Psychiatric Hospital Vrapce, Zagreb, Croatia

Alcoholism is common and very complex psychiatric disorder whose neurobiological basis largely encompasses dopaminergic system malfunction with an emphasis on the role of dopamine receptors and metabolic enzymes.

In this study we investigated the association of genetic polymorphisms of dopamine receptor D4 (DRD4) and dopamine degrading enzyme, catechol-O-methyltransferase (COMT) with alcoholism and alcohol-related phenotypes. Selected polymorphisms were variable number of tandem repeats (VNTR) polymorphism in the third exon of DRD4 gene and COMT Val108/158Met single nucleotide polymorphism.
The study included 690 alcoholic patients and 580 healthy control subjects. Alcoholic patients were subdivided according to the presence of different alcohol-related phenotypes: withdrawal, aggressive behavior, severity of alcohol dependence, delirium tremens, comorbid depression, suicidal behavior, suicide attempt and onset (early/late) of alcohol dependence.

Results showed a significant difference in the frequency of DRD4 VNTR genotypes between controls and alcoholic patients, while COMT Val108/158Met polymorphism had no significant effect on the development of alcoholism. COMT Val108/158Met polymorphism was associated with suicidal behavior, suicide attempt and the onset of alcohol dependence.

The results of the study strongly imply that DRD4 VNTR could be used as a peripheral biomarker of alcohol addiction, while COMT Val108/158Met could be a biomarker of tendency toward suicidal behavior.

Keywords: COMT Val108/158Met, DRD4 VNTR, alcoholism, alcohol related phenotypes

MOL-A06 Friday, September 27th, 12:00 [Poster section: Molecular neuroscience A]

Does stress induced reduction of translational fidelity play a role in ALS/FTLD?

Sabina Vatovec, Maja Štalekar, Jure Pohleven, Boris Rogelj

Department of Biotechnology, Jožef Stefan Institute, Ljubljana, Slovenia

Amyotrophic lateral sclerosis (ALS) and frontotemporal lobar degeneration (FTLD) are two devastating, progressive and ultimately fatal neurodegenerative diseases, caused by the selective loss of motor neurons in the central nervous system, and loss of brain cells in frontal and temporal lobes of the brain, respectively. Both diseases are clinically heterogeneous with a high variability in the rate of symptom progression. Nuclear DNA/RNA-binding protein transactive response DNA-binding protein (TDP-43) is a major component of the characteristic cytoplasmic inclusions in 95% of ALS and 50% of FTLD cases. Upstream signalling pathways leading to TDP-43 aggregation and the mechanisms leading to the resulting neurodegeneration are currently still unclear. Changes in de novo synthesis levels, localisation and turnover of TDP-43 may all play a role in the ALS/FTLD.

The main aim of this project is elucidating the role of post-transcriptional and post-translational processes in TDP-43 induced proteinopathies, using cellular models of oxidative stress. It has been shown that cellular stress can affect TDP-43 localisation and aggregation. Stress has also been shown to have an effect on aminoacyl tRNA synthetases, leading to a decrease in translational fidelity through incorporation of wrongly-coded amino acids into the nascent protein sequence. If stress-induced changes occur in the C-terminal part of the TDP-43 there is a possibility that such protein may act in the similar manner as the mutant TDP-43 protein, arising from non-synonymous gene mutations.

We will present our data on investigating stress related changes in the TDP-43 transcription and translation, leading to the amino acid sequence changes.

Keywords: ALS, TDP-43, misacylation

MOL-B01 Saturday, September 28th, 12:00 [Poster section: Molecular neuroscience B]

Zoledronic acid induces apoptosis via stimulating ERN1, TLR2 and IRF5 genes' expressions in glioma cells

Cansu Caliskan, Burcu Erbaykent, Sunde Yilmaz Susluer, Bakiye Göker, Tugce Balci, Cagla Kayabasi, Besra Özmen Yelken, Cumhur Gunduz, Çığır Biray Avcı

Department of Medical Biology, Ege University Medical School, Bornova-Izmir, Turkey

Glioblastoma multiforme (GBM) is the most prevalent and most lethal brain tumor in elderly people. It is non-responsive to chemotherapy in many cases and carries the lowest chances of survival. Despite various treatment, the patiens with glioblastoma exhibits a poor prognosis and live less than one year. Zoledronic acid (ZA) is a nitrogen-containing bisphosphonate that demonstrated anticancer activity in various cancers.

The aim of the study was to evaluate the effect of zoledronic acid on the expression of 44 genes including several signal transduction pathways such as; cytokines and costimulator molecules, interferons, NF-KB and Toll-like receptors in U87-MG cells.

In our experiments, U87-MG cell line (Human glioblastoma-astrocytoma, epithelial-like cell line) is used as a vitro model of human glioblastoma cells to investigate the cytotoxic and apoptotic effect of zoledronic acid towards glioma cells. U87-MG cells were treated with 25 μM (IC50) ZA during 72 hours. Apoptosis assays were performed by using ApoDIRECT In Situ DNA Fragmentation Assay. The RT-qPCR (LightCycler480 System) is used for gene expressions analysis.

Results showed that IC50 dose of ZA induced apoptosis 1.27 fold when compared to untreated control cells. Also RT-qPCR results showed that; ERN1 (the endoplasmic reticulum-nuclei-1), TLR2 (toll like receptor 2) and IRF5 (Human IFN regulatory factor 5) tumor suppressor genes' expressions increased 2.05, 2.08 and 2.3 fold, respectively according to control cells.

These novel findings showed that ZA is very important in glioma progression and could be used as a pioneering target agent in glioma treatment.

Keywords: Glioma, zoledronic acid, apoptosis, gene expression

MOL-B02 Saturday, September 28th, 12:00 [Poster section: Molecular neuroscience B]

Epigenetic regulation of some typical genes in rat fast and slow skeletal muscles

Špela Glišović, Jasmina Tušar, Peter Pregelj, Janez Sketelj

Institute of Pathophysiology, Faculty of Medicine, University of Ljubljana, Slovenia

Muscle fibers differ in the expression profiles of many proteins. Fibers can be classified as slow and several kinds of fast fiber types. Adaptive changes of muscle fibers occur in response to several stimuli. We tested the hypothesis that epigenetic mechanisms are involved in the regulation of some proteins typical for either fast or slow muscle fibers. Therefore, rats were injected with (a) trichostatin A, which is a histone deacetylase inhibitor and could alter gene expression by preserving high acetylation state of histones which favors the access of transcriptional factors to gene promoters, and (b) decitabine, which inhibits DNA methyltransferase activity resulting in gene activation due to decreased methylation of cytosines in gene promoters. It is known that fast muscle fibers can change their phenotype when exposed to chronic low frequency electrical stimulation (CLFS) which mimics the tonic low-frequency activation pattern of the slow soleus muscle. We found that epigenetic regulation by histone acetylation status is probably responsible for: (a) AChR expression increase in denervated slow muscles; (b) MyHC I (but not ColQ) decrease in denervated slow muscles; (c) high parvalbumin (but not AChE) levels in fast muscles. It is probably not involved in: (a) low MyHC I and ColQ expression in control and denervated fast muscles; (b) AChE decrease in denervated fast muscles. Epigenetic regulation by promoter methylation is probably not responsible for the resistance of regenerating fast muscles to increase MyHC I or ColQ expression after CLFS.

Keywords: epigenetics, skeletal muscles, chronic low frequency stimulation, denervation

MOL-B03 Saturday, September 28th, 12:00 [Poster section: Molecular neuroscience B]

Association of XRCC1 single nucleotide polymorphisms with Alzheimer's disease – preliminary studies

Sylwia M. Gresner[1,3], Monika Sieruta[1], Ewa Golanska[1], Maria Styczynska[2], Beata Pepłonska[2], Maria Barcikowska[2], Pawel P. Liberski[1]

[1]Department of Molecular Pathology and Neuropathology, Medical University of Lodz, Poland
[2]Department of Neurodegenerative Disorders, Medical Research Centre, Polish Academy of Sciences, Warsaw, Poland
[3]Department of Immunopathology, Medical University of Lodz, Poland

Alzheimer's disease (AD) is a progressive neurodegenerative disorder that has been showed to be highly associated with cellular oxidative stress and oxidative DNA damage. It is well known that oxidative DNA damage is one of the earliest event of progression from normal brain to dementia.

The aim of our study was to test if the XRCC1 polymorphisms may influence the susceptibility to AD. For that purpose we performed a case-control study involving 212 Polish late-onset patients with AD and 152 non-demented elderly controls to evaluate the role of rs3213245 and rs25487 SNPs as the risk factor for AD. The observed genotype frequencies in control and AD groups were compared assuming both dominant and recessive genetic models.

A significant risk-increasing effect of rs25487 SNP (p=0.05; OR=1.9, CI:1.0–3.7) was observed only under dominant model, suggesting that the risk of AD among carriers of rare-allele-containing genotypes is almost 2-fold higher than among those who have only wild-type allele in their genotypes. No effect was found for rs3213245 under dominant as well as recessive model (p=0.3; OR=0.8, CI:0.5–1.2; p=0.6; OR=0.9, CI:0.5–1.5, respectively). Moreover, under the recessive model a significant relationship was discovered between rs25487 SNP and the age of onset. Mean onset age among patients carrying CC/CT was 74 years while among those with TT it was 70 years (log rank test p=0.03). The association between rs25487 SNP and susceptibility to AD deserves further investigation.

Keywords: Alzheimer's disease, DNA damage, XRCC1

MOL-B04 Saturday, September 28th, 12:00 [Poster section: Molecular neuroscience B]

Ser310Ala functional polymorphism in the GluR7 glutamate receptor subunit gene and alcohol dependence

Boris Kuzman[1], Marina Morić[1], Gordana Nedić Erjavec[1], Matea Nikolac Perković[1], Korona Nenadić Šviglin[2], Dorotea Muck-Šeler[1], Nela Pivac[1], Dubravka Švob Štrac[1]

[1]Division of Molecular Medicine, Ruđer Bošković Institute, Zagreb, Croatia
[2]Center for Alcoholism and other Addictions, Psychiatric Hospital Vrapče, Zagreb, Croatia

Glutamate receptors, the major excitatory neurotransmitter receptors in the brain, have been implicated in acute and chronic effects of alcohol, including alcohol dependence and withdrawal. Kainate ionotropic glutamate receptors have emerged in recent years as important targets of alcohol's action in the central nervous system. The GRIK3 gene, encoding GluR7 subunit of kainate receptors, is localized on chromosome 1, close to a region associated with alcoholism and alcoholism-related phenotypes. However, diverse results obtained regarding the association of GRIK3 gene with alcoholism might be due to the heterogeneity in alcoholism etiology and phenotype characteristics.

Hence, the aim of this study was to investigate the role of the GRIK3 functional polymorphism in patients with alcoholism subdivided according to early/late onset of alcohol abuse, the presence/absence of aggressive behavior and suicide attempts.

Genotyping of Ser310Ala polymorphism (rs6691840) in the GRIK3 gene was performed in 275 alcohol-dependent patients of both genders and different smoking status, by using TaqMan Real-Time allelic discrimination after DNA extraction from the blood.

The distribution of genotypes and alleles did not differ significantly in alcohol-dependent patients stratified by gender, smoking status, aggressive behavior or suicide attempts. However, the results demonstrated that alcohol-dependent patients with late onset had a higher frequency of a homozygous CC genotype than patients with the early onset of alcohol abuse often reflecting greater alcoholism severity, higher risk for recurrence, as well as comorbid antisocial personality disorder and conduct disorder. Additional studies are needed to further investigate the role of GRIK3 gene in the development of alcoholism.

Keywords: alcoholism, alcoholism-related phenotypes, GRIK3 gene, polymorphism, glutamate

MOL-B05 Saturday, September 28th, 12:00 [Poster section: Molecular neuroscience B]

The effect of enriched environment on the modulation of perineuronal nets and synaptic remodeling in the cerebellum of tenascin C - deficient mice

V. Stamenković[1], S. Stamenković[1], T. Jaworski[2], M. Gawlak[2], M. Jovanović[1], M. Schachner[3], G. Wilczynski[2], L. Kaczmarek[2], L. Radenović[1], P. R. Andjus[1]

[1]Center for Laser Microscopy, Department of Physiology and Biochemistry, Faculty of Biology, University of Belgrade, Serbia
[2]Nencki Institute of Experimental Biology, Laboratory of Neuromorphology, Polish Academy of Science, Warsaw, Poland
[3]Center for molecular neurobiology, University of Hamburg, Hamburg, Germany

Tenascin-C (TnC) is an extracellular matrix glycoprotein with an important morphoregulatory role during development, while in adult CNS its expression is limited to areas of neuronal plasticity.

Since enriched environment (EE) stimulates neuronal plasticity, we examined the role of TnC by observing the distribution of perineuronal nets (PNNs) in TnC deficient (TnC-/-) and wild-type (TnC+/+) mice in deep cerebellar nuclei (DCN) after rearing for 8 weeks in EE (vs. standard conditions) starting from postnatal day 21. Furthermore, possible involvement of matrix metalloproteinases, MMP-2 and MMP-9, in PNN reorganization was examined by following their activity at two distinct time points, 4 and 8 weeks, using gel (GZ) and in situ zymography (ISZ), respectively.

A significant reduction of PNNs was shown in DCN of TnC+/+ animals after 8 weeks in EE, while in TnC-/- animals this effect was absent. In addition, GZ revealed a significant increase of MMP-9 activity after 4 weeks of EE in both genotypes, while MMP-2 activity remained unchanged. Furthermore, ISZ showed a significant decrease in MMPs activity after 8 weeks in TnC+/+ and a generally weak ISZ signal in TnC-/- animals. Finally, the investigation of synaptic density in DCN revealed increased density of inhibitory synapses in TnC-/- compared to TnC+/+ mice regardless of rearing conditions, while the density of excitatory synapses was increased in TnC+/+ mice after EE with no changes in TnC-/- mice.

These results emphasize a significant role of TnC in neuronal plasticity and synaptic remodeling, and imply a possible involvement of MMP-9 in this effect.

Keywords: Tenascin C, neuronal plasticity, perineuronal nets, matrix metalloproteinases-2 and -9

MOL-B06 Saturday, September 28th, 12:00 [Poster section: Molecular neuroscience B]

Integrated analysis of global transcriptome and methylome alterations in peripheral blood of patients with Huntington's disease

Maja Zadel[1], Aleš Maver[1], Luca Lovrečić[1], Jan Kobal[2], Borut Peterlin[1]

[1]Clinical Institute of Medical Genetics, University Medical Centre Ljubljana, Slovenia
[2]Department of Neurology, University Medical Centre Ljubljana, Slovenia

Huntington's disease (HD) is an autosomal dominant neurodegenerative disorder, characterized by progressive motor dysfunction, dementia, emotional disturbances and weight loss. The disorder is caused by expansion of unstable CAG triplet repeat in exon 1 of the HD gene, which results in production and accumulation of mutant huntingtin protein.
Transcriptional changes of several genes have already been identified in HD. Additionally, studies performed to date have shown that mutant huntingtin interferes with the function of a variety of transcription factors widely expressed in various tissues, including peripheral blood. Because of discrepancies in expressions alterations reported by various studies, we aimed to look for consistent transcriptional biomarker of high predictive value. In addition, we also considered the possibility that transcriptional changes result from altered methylation patterns.

Our study included HD patients (symptomatic and pre-symptomatic) and healthy controls. Alterations in pattern of global gene expression and global methylation were analyzed using oligonucleotide microarrays.
Genome-wide expression profiling in our study confirmed alterations in peripheral blood gene expression in HD, with several genes significantly up-regulated symptomatic form of HD.

Global methylation profiling indicated differences between late-symptomatic HD patients when compared to healthy controls but after correction for multiple testing measured differences failed to achieve statistical significance.
We substantiated the presence of alterations in peripheral gene expression in HD.

Our results indicate that expression differences in peripheral blood may not be attributed in large part to altered methylation, but further studies on other tissue types are required to clarify the role of methylation alterations in HD.

Keywords: Huntington's disease, global gene expression, global methylation

MOL-C01 Sunday, September 29th, 12:00 [Poster section: Molecular neuroscience C]

Posttranslational modifications of FUS

Simona Darovic, Boris Rogelj

Department of Biotechnology, Jožef Stefan Institute, Ljubljana, Slovenia

Frontotemporal lobar degeneration (FTLD) and amyotrophic lateral sclerosis (ALS) are neurodegenerative disorders with clinical, genetic, and neuropathological overlap. Aberrant cytoplasmic aggregation of FUS (fused in sarcoma) is associated with 3 % of ALS and 10 % of FTLD cases. FUS is a nuclear RNA/DNA binding protein, which contains PY type nuclear localization signal present at its C-terminal, which enables interaction with Transportin-1 and thus its transport to nucleus. ALS patients with FUS positive cytoplasmic inclusions contain mutations in gene encoding FUS. The majority of these mutations fall within the nuclear localization signal, which disables its transport to nucleus. On the other hand patients with FTLD do not have FUS mutations, but FUS still accumulates in cytoplasmic inclusions.

Our aim is to find out whether nuclear localization signal of FUS is subjected to posttranslational modifications (PTM) that have impact on its localization. Neurodegenerative diseases are associated with oxidative and nitrosative stress, which may lead to modifications of the nuclear localization signal of FUS and impair nuclear transport. In order to determine the effects of PTM of FUS on its nuclear localisation, we have expressed His tagged FUS in selected cell lines and subjected the isolated FUS to differential 2D-western blot and proteomic analysis. Determination of any postranslational modifications would further elucidate the mechanism of FUS misaccumulation and may have a role in FTLD.

Keywords: FTLD, FUS, posttranslational modifications

MOL-C02 Sunday, September 29th, 12:00 [Poster section: Molecular neuroscience C]

Screening for THAP1 (DYT6) mutations in Polish patients with dystonia. A preliminary report

Ewa Golanska[1], Agata Gajos[2], Monika Sieruta[1], Malgorzata Szybka[1], Sylwester Piaskowski[1,3], Pawel P. Liberski[1], Andrzej Bogucki[2]

[1]Department of Molecular Pathology and Neuropathology, Medical University of Lodz, Poland
[2]Neurology and Movement Disorders Department, Medical University of Lodz, Poland
[3]Department of Biology of Cancer, Medical University of Lodz, Poland

The dystonias are a group of movement disorders characterized by contractions of agonist and antagonist muscles leading to involuntary movements and abnormal postures of various parts of the body. Several genetically determined types of dystonia are known, including DYT1 and DYT6 autosomal dominant traits associated with mutations within TOR1A and THAP1 genes, respectively. The THAP1 gene is mapped on chromosome 8p11.21 and encodes for a DNA-binding transcription factor named thanatos-associated protein domain containing apoptosis-associated protein 1. Over 50 missense, nonsense and frameshift mutations within THAP1 gene have been described in dystonia patients in various populations.

Here we analyzed the THAP1 coding sequence in 90 Polish patients with dystonia, recruited at the Neurology and Movement Disorders Department, Medical University of Lodz. In all patients DYT1 mutations were excluded. As controls we analyzed 150 neurologically healthy individuals. DNA was isolated from blood leucocytes; screening for mutations was performed using PCR and DNA sequencing methods.

Two missense heterozygous point mutations were identified, both located in THAP1 exon 2. The codon 80 Ile/Val substitution was found in two patients, and codon 56 Glu/Gly mutation, in one patient. Neither of the nucleotide changes were found in healthy subjects.

The codon 56 substitution is a novel one which has never been reported. Further studies are needed in order to establish its possible influence on the protein function.

The study was supported by the Polish National Science Centre grant No NN401571838.

Keywords: dystonia, DYT6, THAP1, mutations

MOL-C03 Sunday, September 29th, 12:00 [Poster section: Molecular neuroscience C]

Unlocking of the prion protein globular domain is a crucial step in prion protein conversion

Iva Hafner-Bratkovič[1], San Hadži[2,3], Roman Jerala[1,2,4]

[1]Department of Biotechnology, National Institute of Chemistry, Ljubljana, Slovenia
[2]Faculty for Chemistry and Chemical Technology, University of Ljubljana, Slovenia
[3]Structural Biology Brussels, Vrije Universiteit Brussel, Belgium
[4]EN-FIST Centre of Excellence, Ljubljana, Slovenia

Prion diseases are fatal transmissible neurodegenerative diseases affecting many mammalian species. The normal prion protein (PrP) converts into a pathological aggregated β-sheet-enriched form. While the high resolution structure of the normal PrP was determined, the structure of the converted form of PrP remains inaccessible to high resolution techniques.

In order to map the PrP conversion process we introduced disulfide bridges into different positions within the globular domain of PrP, tethering selected secondary structure elements. Further, to define effects of specific amino acid residues, we prepared many single or multiple substitutions. Conversion prophensity of mutated PrPs was followed by fibrillization in vitro and by scrapie cell assay.

The majority of tethered PrP mutants exhibited increased thermodynamic stability, nevertheless they converted efficiently. Only the disulfides that tether subdomain B1-H1-B2 to subdomain H2-H3 prevented PrP conversion in vitro and in prion infected cell cultures. Reduction of disulfides recovered the ability of these mutants to convert, demonstrating that the separation of subdomains is an essential step in conversion. We further showed that several natural pathological mutations facilitate this step.

In contrast to previously proposed models suggesting conversion of large secondary structure segments, we provide evidence for the conservation of secondary structure elements of the globular domain upon PrP conversion. We show that separation and swapping of subdomains of the globular domain is necessary for conversion. Therefore, we propose that domain-swapped dimer of PrP precedes amyloid formation and represents a potential target for therapeutic intervention.

Keywords: prion, amyloid, conversion

MOL-C04 Sunday, September 29th, 12:00 [Poster section: Molecular neuroscience C]

Monitoring cytosolic glucose concentration in single astrocytes

M. Muhič[1], R. Zorec[1,2], M. Kreft[1,2,3]

[1]Laboratory of Neuroendocrinology-Molecular Cell Physiology, Institute of Pathophysiology, Faculty of Medicine, University of Ljubljana, Slovenia
[2]Celica Biomedical Center, Technology Park, Ljubljana, Slovenia
[3]Biotechnical Faculty, University of Ljubljana, Slovenia

It is becoming increasingly clear that astrocytes are no longer playing a subservient role to neurons in the central nervous system (CNS), and that these cells are being considered as active communication integrators. They respond to neurotransmitters by the regulated release of gliotransmitters. The delay between neurotransmitter activation and the release of gliotransmitters from astrocytes is in the time-domain of subseconds, much slower than the submillisecond synaptic delay. Astrocytes also control microcirculation and provide metabolic support for neurons. However, the dynamics of their energy metabolic response to neurotransmitter application is not known.

We are using a FRET glucose nanosensor to measure the cytosolic glucose concentration in single astrocytes to study the metabolic dynamics of single astrocytes and in networks. We are currently interested in regulators of glycogen sythesis and degradation, such as noradrenaline, insulin and IGF-1.

Keywords: astrocyte, glycogen, glucose, FRET, nanosensor

MOL-C05 Sunday, September 29th, 12:00 [Poster section: Molecular neuroscience C]

RNA with ALS/FTLD-associated hexanucleotide repeats attracts several proteins

Maja Štalekar[1], Jure Pohleven[1], Marko Fonovič[2], Boris Turk[2], Marko Živin[3], Boris Rogelj[1]

[1]Department of Biotechnology, Jožef Stefan Institute, Ljubljana, Slovenia
[2]Department of Biochemistry and Molecular and Structural Biology, Jožef Stefan Institute, Ljubljana, Slovenia
[3]Institute of Pathophysiology, Faculty of Medicine, University of Ljubljana, Slovenia

Amyotrophic lateral sclerosis (ALS) and frontotemporal lobar degeneration (FTLD) are two phenotypically very different incurable neurodegenerative disorders, the first characterised as a fatal progressive paralysis due to degeneration of motor neurons and the latter as a form of dementia, but share some common molecular characteristics. Recently, GGGGCC hexanucleotide repeat expansion in non-coding region of C9ORF72 gene has been identified as the most common genetic cause of ALS and FTLD, but the function of mutation is still not clear. At least three hypotheses emerged. First, expanded repeats can deregulate expression of C9ORF72, a protein with unknown function. Second, aggregating polypeptides generated by an unconventional repeat associated non-ATG translation may be toxic to cells. And third, accumulated RNA with repeat expansion can sequester proteins, preventing them from carrying out their normal function.

We focused on the last hypothesis and performed an RNA pull-down study with in vitro transcribed (GGGGCC)48 RNA from rat brain cortex and cerebellum nuclear and cytoplasmic extracts to identify proteins that bind to (GGGGCC)n RNA. Bound proteins were eluted with RNase treatment, separated with SDS-PAGE and analysed by mass spectrometry.

We identified several (GGGGCC)n-binding proteins. The function of these proteins and the processes in which they are involved may be compromised in affected cells in ALS and FTLD.

Keywords: C9ORF72, repeat expansion, pull-down, RNA, ALS, FTLD

SYS-A01 Friday, September 27th, 12:00 [Poster section: Systems neuroscience A]

Spectral analysis of EEG PCA components in young healthy adults

Aleš Belič[1], Špela Lesar[2], Tina Bregant[3]

[1]Laboratory of Modelling, Simulation and Control, Faculty of Electrical Engineering, University of Ljubljana, Slovenia
[2]Middle European interdisciplinary master programme in Cognitive Science, University of Ljubljana, Slovenia
[3]Department of Paediatric Neurology, University Children's Hospital, University Medical Centre Ljubljana, Slovenia

Spectral analysis of EEG has been a standard procedure in EEG analysis since the beginning of EEG, when alpha rhythms have been discovered. Since then several other rhythms and their meaning have been discovered. In spite of such long research history, brain rhythms and their function are still controversial. One of the problems are effects of liquor and several types of tissues on conduction of electrical signals from the brain to the scalp. Non-linear conduction characteristics of the liquor and tissues can significantly affect frequency composition of the signals and govern electric current distribution to the scalp. Therefore, recorded EEG signals have considerably different characteristics than the signals at their origin. The principal component analysis (PCA) is one of the linear statistical methods that is commonly used for the analysis of the signals originating from several independent sources, recorded with several recorders and representing a total activity of a system.

In this study we were interested in differences in spectral analysis results of EEG and its principal components. We studied EEG from ten healthy students: 5 females (50.0%), mean age 23.2±1.1 years. Participants were examined and interviewed, follow-up with the EEG after sleep deprivation. EEG was recorded with 19 electrodes at 256Hz sampling rate. Significant differences in alpha rhythm powers in EEG and its principal components were observed. Spectral analysis of principal components should provide more realistic information than of EEG channels, since it party abolishes the distribution effect of the tissues and since it also eliminates some artefacts.

Keywords: PCA, spectral analysis, alpha rhythm

SYS-A02 Friday, September 27th, 12:00 [Poster section: Systems neuroscience A]

Characterization of cognitive deficits in rats with selective cholinergic, noradrenergic and dopaminergic lesions

Elena Di Martino, Margherita Riggi, Andrea Valeri, Roberta Pintus, Giampiero Leanza

B.R.A.I.N. Lab for Neurogenesis and Repair, Department of Life Sciences, University of Trieste, Italy

Besides classic motor symptoms associated to the loss of nigrostriatal neurons, cognitive deficits and dementia are now emerging as important non-motor features of Parkinson's disease (PD). Noradrenergic (NA), cholinergic (ACh) and dopaminergic (DA) neurons in the Locus Coeruleus (LC), Basal Forebrain (BF) and Ventral Tegmental Area (VTA), respectively, degenerate early in PD and appear to be involved in its non-motor manifestations, however their role has so far been much less studied.

Here, we sought to address this issue in the rat, by producing selective immuno- and neurotoxic lesions, either single or combined, in order to investigate the occurrence of possible interactions between transmitter systems in the production of cognitive deficits. Starting from 12 weeks post-surgery, the animals were tested in the Morris Water Maze (MWM) and the Radial Arm Water Maze (RAWM) tasks, specifically designed to evaluate reference and working memory abilities.

All animals with single lesions did not show significant impairments in the reference memory task compared to control. By contrast, significant working memory deficits were exhibited by the single-lesioned animals, being seen more pronounced in the double- and particularly severe in triple-lesioned animals.

The results suggest that monoaminergic neuron systems may functionally interact for sustaining normal cognitive abilities, their dysfunction being possibly responsible for several of the non-motor symptoms of PD.

Keywords: PD, monoamines, cognition

SYS-A03 Friday, September 27th, 12:00 [Poster section: Systems neuroscience A]

Multiple effects of selective cholinergic lesions combined with local infusion of pre-aggregated amyloid peptide

Margherita Riggi[1], Andrea Valeri[1], Roberta Pintus[1], Maurizio Romano[2], Giampiero Leanza[1]

[1]Lab for Neurogenesis and Repair, Department of Life Sciences, B.R.A.I.N., University of Trieste, Italy
[2]International Centre for Genetic Engineering and Biotechnology, Trieste, Italy

Cholinergic loss, amyloid peptide deposition and tau hyperphosphorylation are important hallmarks of Alzheimer's Disease (AD). Besides, overexpression and aggregation of transactive response DNA- binding protein 43 (TDP-43) have been associated to the disease. However, it is not known whether these features interact in AD.

Here, the possible relationships between the various hallmarks in producing cognitive deficits have been addressed by combining selective lesioning of basal forebrain cholinergic neurons with hippocampal injection of pre-aggregated beta (25-35) amyloid peptide, the latter giving rise to local accumulation of amyloid oligomers and protofibrils. Four to five weeks post-surgery, the animals were subjected to sequential behavioural tasks aimed at evaluating reference and working memory abilities, followed by post-mortem histo- and immunohistochemistry, as well as western blot and RT-PCR assessments.

The results show robust deficits in both reference and working memory, associated to widespread cholinergic depletions, the occurrence of amyloid aggregates in the neocortex and hippocampus, marked regional increases of APP and tau levels, as well as abnormal TDP-43 mRNA expression levels, which were seen more pronounced in the animals subjected to double, but not to either single treatment.

Thus, amyloid, tau and TDP-43 pathologies may require association with disturbances in monoaminergic (e.g. cholinergic) neurotransmission for inducing cognitive impairments.

Keywords: AD, cholinergic loss, amyloid-beta, TDP-43

SYS-B01 Saturday, September 28th, 12:00 [Poster section: Systems neuroscience B]

Early exposure to enriched environment reverses learning deficits and improves hippocampal neuron survival in rats with selective cholinergic lesion

Pela Bisatti, Marino Coradazzi, Lucia Verga Falzacappa, Giampiero Leanza

B.R.A.I.N. Laboratory for Neurogenesis and Repair, Department of Life Sciences, University of Trieste, Italy

Cholinergic loss induces severe cognitive deficits and affects neuron proliferation in the hippocampal dentate gyrus (DG). Conversely, exposure to an enriched environment (EE), is known to enhance neurogenesis, in addition to improving learning abilities, suggesting a relationship between these features. However, this issue has never been addressed in developing animals. Here, the effects of early exposure to EE upon spatial learning and on survival of newborn cells in DG were investigated in rats with a selective cholinergic lesion.

Two litters of rats were used. In each litter, half of the animals underwent immunotoxic or sham-lesions at post-natal day 4. Groups of randomly selected lesioned and control animals were caged in a specially designed EE whereas the remaining rats were maintained under standard (i.e. non-enriched) conditions. At 3 months of age, all animals were tested in a Water Maze task to evaluate possible differences in their spatial learning abilities. One month before sacrifice, all rats were treated with BrdU to assess the survival of newborn neurons in DG.

Lesioned animals caged in standard conditions exhibited mild, but significant working memory deficits, whereas lesioned animals exposed to the EE performed as efficiently as controls. EE exposure enhanced survival of newly generated neurons both in control and in lesioned rats, but did not lead to any behavioural improvements in the former group.

Thus, compensatory mechanisms associated with prolonged EE exposure may enhance survival of newly generated cells in DG, and prevent the mild cognitive deficits induced by an early cholinergic depletion.

Keywords: hippocampal lesion, neurogenesis, working memory, water maze

Lack of sex steroid hormones, but not social isolation, during puberty affects maternal behavior in adult female mice

J. Kerčmar[1], S. A. Tobet[2], G. Majdič[1,3]

[1]Center for Animal Genomics, Veterinary Faculty, University of Ljubljana, Slovenia
[2]Department of Biomedical Sciences, Colorado State University, Fort Collins, USA
[3]Institute of Physiology, Medical School, University of Maribor, Slovenia

Maternal behavior is crucial to offspring survival in most mammals. As maternal behavior is elicited through a combination of hormonal factors and external stimuli from the pups, nulliparous rats and mice can also show this behavior when presented with pups. Female mice of many strains show faster spontaneous maternal responses to pups in comparison to rats, suggesting that the expression of maternal behavior in mice is less dependent on hormonal mediation than in rats. Housing conditions also represents an important environmental variable, especially as mice are naturally social animals. Social stress profoundly and persistently affects brain development, which results in altered behavioral responses in adulthood.

The influences of sex steroid hormones and social stress during adolescent period on maternal behavior in adult female mice were assessed in the present study. C57BL/6J mice were divided into four groups: socially isolated or group housed, ovariectomized before (on day 25) or after puberty (on day 60). After day 75 mice were tested for maternal behavior.

Mice ovariectomized after puberty showed better maternal behavior (shorter latency to retrieve the pups into the nest, higher number of retrieved pups, longer crouching over pups) than those ovariectomized before puberty. However, social isolation during puberty did not affect maternal behavior regardless of the time of gonadectomy.

The results suggest that exposure to gonadal hormones during puberty is important for the expression of maternal behavior in inexperienced adult female mice.

Keywords: female mice, puberty, ovariectomy, social isolation, maternal behavior

Maternal behavior in heterozygous SF-1 knockout mice

T. Španič[1], S. A. Tobet[2], G. Majdič[1,3]

[1]Center for Animal Genomics, Veterinary Faculty, University of Ljubljana, Slovenia
[2]Department of Biomedical Sciences, College of Veterinary Medicine and Biomedical Sciences, Colorado State University, Fort Collins, USA
[3]Institute of Physiology, Medical School, University of Maribor, Slovenia

Maternal care for the offspring has an important role in the offspring's survival. Previous studies have shown that maternal behavior in mice of both sexes starts spontaneously within a few minutes after exposure to pups.

In the present study, mice with one disrupted allele of sf-1 (SF-1+/-) and wild type (WT) mice were tested for maternal behavior. Testing revealed difference in maternal behavior, especially in the retrieval of pups to the nest with SF1+/- females needed more time for retrieving pups and spending less time nursing the pups. As reduced maternal behavior could be caused by an increase in anxiety- or depressive-like behaviors, mice were tested in elevated plus maze (EPM) and forced swim (FST) tests. There were no differences, suggesting a specific effect of haploinsuficiency for the sf-1 gene on maternal behavior. This reduced maternal behavior could be a consequence of a poor maternal care by SF-1+/- mothers of tested mice, pups from SF1+/- and WT mothers were therefore cross-fostered on PN3. In adulthood, females from these cross-fostered litters were tested for maternal behavior, and in EPM and FST. Results revealed that both WT and SF-1 +/- cross-fostered females had severely reduced maternal behavior in comparison to non-cross-fostered females while they performed similarly in EPM and FST.

These results suggest that cross-fostering has major effects on maternal behavior in mice independent of any effects on anxiety and depressive-like behaviors.

Keywords: Steroidogenic factor 1, maternal behavior, SF-1 heterozygous mice

SYS-B04 Saturday, September 28th, 12:00 [Poster section: Systems neuroscience B]

Allopregnanolone influences on seizures induced by homocysteine

A. Rašić-Marković[1], D. Hrnčić[1], O. Stanojlović[1], Đ. Macut[2]

[1]Laboratory for Neurophysiology, Institute of Medical Physiology "Richard Burian", Faculty of Medicine, University of Belgrade, Serbia
[2]Clinic for Endocrinology, Diabetes and Metabolic Diseases, Faculty of Medicine, University of Belgrade, Serbia

Neurosteroids have protective activity in diverse experimental seizure models. Therefore, the aim of our study was to investigate the effects of 3β-hydroxy 5α-pregnan-20-one, (3β,5α allopregnanolone) on behavioral and EEG characteristics of homocysteine induced seizures in female rats.

Adult female Wistar rats were divided into groups: 1. Saline-treated (C); 2. DL homocysteine-thiolactone 8 mM/kg, i.p.(H) 3. 3β,5α allopregnanolone in doses 5, 20 and 50 mg/kg, i.p. (A5, A20, A50); and 4. A 30 minutes prior to H (A5H, A20H, A50H). Seizure behavior was assessed by incidence, latency, number and intensity of seizure episodes. Seizure severity was determined by a descriptive scale with grades from 0 to 4. Lethality was recorded after 90 min and 24h. For EEG recordings, three gold-plated electrodes were implanted into the skull. The observational period (120 min) was divided into eight 15 min intervals and mean total power spectral density (PSD) was calculated (fast Fourier transform method).

There were no behavioral signs of seizure activity in C and A groups. Acute treatment with A did not affect incidence and latency of seizures in experimental groups. Severity of seizure episodes was lower in A50H compared to the H group ([1 (1-1)] vs. [2(2-2)] $p<0.01$). Dissociation between EEG pattern and motor phenomena was common to all experimental recordings. Higher doses of allopregnanolone (20 and 50 mg/kg) when applied alone or co-administered with H significantly changed PSD.

Our findings suggest that acute administration of A lowers the intensity of convulsions induced by DL homocysteine-thiolactone, and changes PSD in female rats.

Keywords: 3β,5α allopregnanolone, DL-homocysteine thiolactone, epilepsy, power spectral density, rats

SYS-C01 Sunday, September 29th, 12:00 [Poster section: Systems neuroscience C]

Disruption of prion protein affects intermale aggression in mice

Tomaž Büdefeld[1], Aljaž Majer[1], Gregor Majdič[1,2]

[1]Centre for animal genomics, Veterinary faculty, University of Ljubljana, Slovenia
[2]Institute of Physiology, Medical school, University of Maribor, Slovenia

Function of the cellular prion protein (PrPc) has been extensively studied using various biological models. Its role in neurodegenerative diseases is well documented, however biological functions of the PrPc remain elusive. So far in the nervous system PrPc has been linked to copper homeostasis, cell signaling, neurogenesis, apoptosis, axon growth and synaptogenesis. Mice lacking Prnp gene (Prnp-/-) show impaired memory and altered circadian rhythms, sleep patterns, stress response and olfaction.

To further clarify PrPc function in behaviour, we examined intermale aggression in Prnp-/- mice derived from Prnp-/- Zürich I line and backcrossed to C57BL/6J background for four generations. Male aggressive behaviour was observed for a period of five consecutive days in a standard resident - intruder test using bulbectomized wild type (WT) male conspecifics. All behavioural tests were recorded and later analysed for aggressive behaviour using StopWatch+ software by an observer blind of the mouse genotype.

Statistical analysis showed the effect of genotype on latencies to first attack and bite over a period of five days with Prnp-/- males having shorter latencies to first attack ($p<0.05$) and first bite ($p<0.05$) than WT males. Percentage of Prnp-/- males showing aggression (attacking and biting stimulus males) in the first testing day was also higher ($p<0.05$) than in WT males. Latencies to first tail rattling, chase and aggressive grooming were similar between genotypes.

Our results showed increased offensive aggression in Prnp-/- mice, therefore cellular prion protein might be considered a new molecule regulating aggressive behaviour in mice.

Keywords: prion protein, Prnp knockout mice, aggressive behaviour

SYS-C02 Sunday, September 29th, 12:00 [Poster section: Systems neuroscience C]

Brain doping at the university: Pharmaceutical cognitive enhancement among Slovenian students

Toni Pustovrh

Center for Social Studies of Science, Faculty of Social Sciences, University of Ljubljana, Slovenia
Institute for Developmental and Strategic Analysis, Ljubljana, Slovenia

Rapid advances in neuroscience are increasing our understanding of the neurological foundations and workings of many aspects of the human mind, including cognitive functions such as attention, concentration and memory. Pharmaceutical drugs, which were originally developed to treat neurological disorders such as ADHD and narcolepsy, also offer the promise of modifying "normally" functioning cognitive processes in healthy people, at least according to some experts. Over the past decade, a considerable amount of attention in academia, and increasingly in the media as well, has been devoted to pharmaceutical cognitive enhancement (PCE), that is, the use of stimulant drugs such as methylphenidate (Ritalin) and modafinil by healthy individuals of various populations with the aim of improving cognitive performance. Both academic authors and the media have generally emphasized a widespread and increasing trend of PCE use, especially among university students. While the academic literature took this trend as lending urgency and salience to efforts aimed at debating and formulating appropriate public policies for the enactment of suitable regulation and actions addressing PCE use, this contribution focuses on an empirical examination of PCE use among Slovenian students. Specifically, it presents the results of an in-depth survey among 700 students from several Faculties of the University of Ljubljana, exploring their experiences with as well as their attitudes towards PCE, elaborating the results in the context of the wider discourse on cognitive enhancement.

Keywords: pharmaceutical cognitive enhancement, students, Ritalin

SYS-C03 Sunday, September 29th, 12:00 [Poster section: Systems neuroscience C]

Dopaminergic modulation of striatal expression of Synaptotagmin IV

Larisa Tratnjek, Gordana Glavan, Marko Živin

Brain Research Laboratory, Institute of Pathophysiology, Faculty of Medicine, University of Ljubljana, Slovenia

Synaptotagmin IV (Syt IV) is a product of an immediate early gene implicated in synaptic plasticity. Our experiments demonstrate D1 dopamine receptor-mediated upregulation of Syt IV mRNA in dopaminergically hypersensitive striatum of 6-hydroxydopamine hemiparkinsonian rats. These results implicate Syt IV in the mechanism of development of dopaminergic denervational hypersensitivity. The increased D1 dopamine receptor-mediated signalling in dopamine-depleted striatum may be the cause for dyskinesia that develops in response to standard long-term antiparkinsonian treatment with levodopa. On the other hand, antipsychotic drugs that inhibit D2 receptors-mediated signalling are used for the treatment of positive symptoms of schizophrenia. In the present study, we have explored the colocalization of Syt IV with marker neuropeptides for the striatal neuronal populations of the direct and indirect pathways, respectively. Then we explored the effects of dopamine depletion and the effects of acute selective pharmacological stimulation of dopamine D1 receptors and the inhibition of dopamine D2 receptors on the expression Syt IV within both striatal neuronal populations. Furthermore, a time course study after pharmacological stimulation of D1 receptors indicated axonal transport of de-novo synthetized Syt IV protein to the target areas of the direct pathway neurons. We will discuss the possible role of Syt IV for synaptic plasticity in the treatment of Parkinson's disease and for the treatment of the positive symptoms of schizophrenia.

Keywords: Synaptotagmin IV, hemiparkinsonian rats, D1 stimulation, D2 inhibition

Lundbeck je globalno farmacevtsko podjetje, s sedežem na Danskem, ki raziskuje, razvija, izdeluje, trži, prodaja in dostavlja inovativne rešitve na področju zdravljenja obolenj možganov.

LuSi xx0312011

Obiščite www.lundbeck.si, www.lundbeck.com

Lundbeck