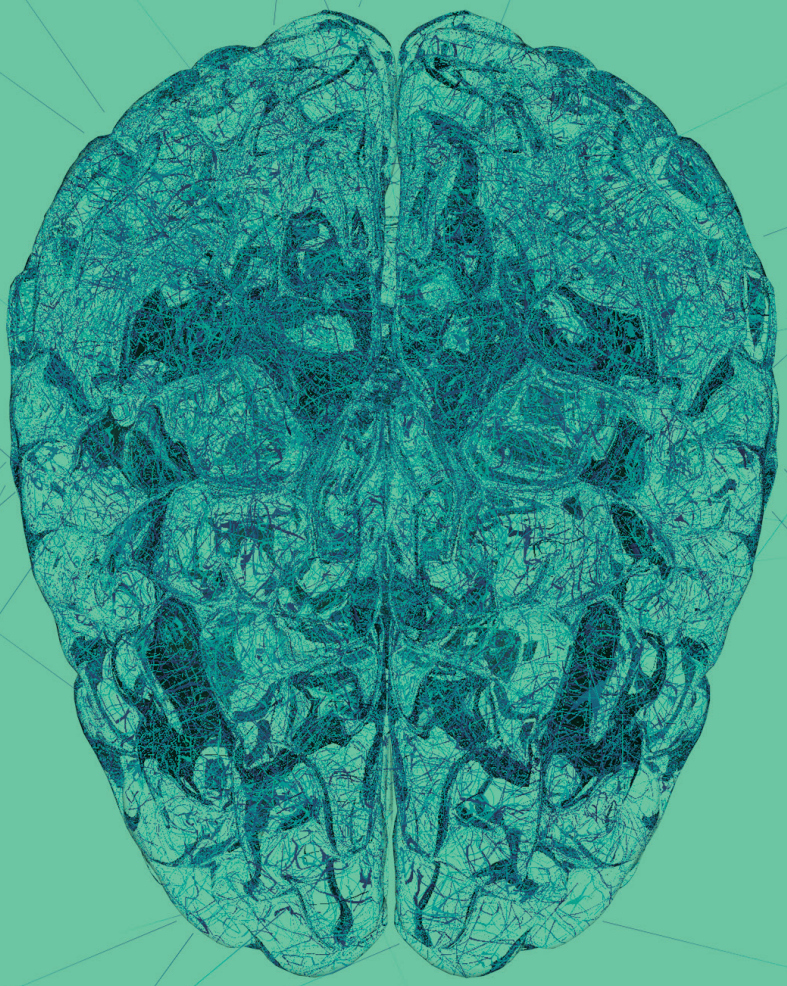
SiNAPSA

SLOVENSKO DRUŠTVO ZA NEVROZNANOST
SLOVENIAN NEUROSCIENCE ASSOCIATION

SNC'15

SINAPSA NEUROSCIENCE CONFERENCE '15



15–17 May, 2015
LJUBLJANA, SLOVENIA

Univerza *v Ljubljani*

REPUBLIKA SLOVENIJA
MINISTRSTVO ZA IZOBRAŽEVANJE, ZNANOST IN ŠPORT

Naložba v vašo prihodnost
OPERACIJO DELNO FINANCIRA EVROPSKA UNIJA
Evropski sklad za regionalni razvoj
Kohezijski sklad
Evropski socialni sklad

Sinapsa Neuroscience Conference ‘15

Cankarjev dom, Ljubljana, 15–17 May 2015

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

SNC’15 Programme Committee
Grega Repovš (Chair), Jure Bon, Maja Bresjanac, Dragana Filipović, David Neubauer, Peter Pregelj, Boris Rogelj, David B. Vodušek

SNC’15 Organising Committee
Blaž Koritnik (Chair), Rok Berlot, Jure Bon, Maja Bresjanac Simon Brezovar, Mateja Drolec Novak, Andraž Matkovič

Conference was supported by
Sanofi-Aventis, International Brain Research Organization, European Social Fund, European Union, Ministry of Education, Science and Sport, Republic of Slovenia, Eli Lilly, Apta Medica, Droga Kolinska, City of Ljubljana

Editors
Andraž Matkovič, Blaž Koritnik

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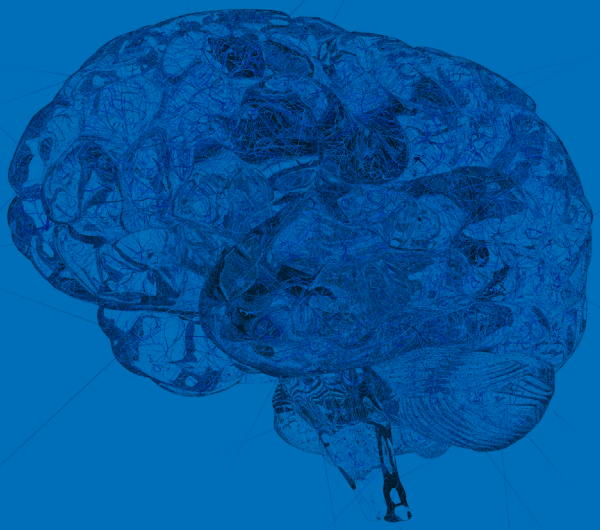

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Cankarjev dom, Ljubljana, Slovenia
15–17 May 2015

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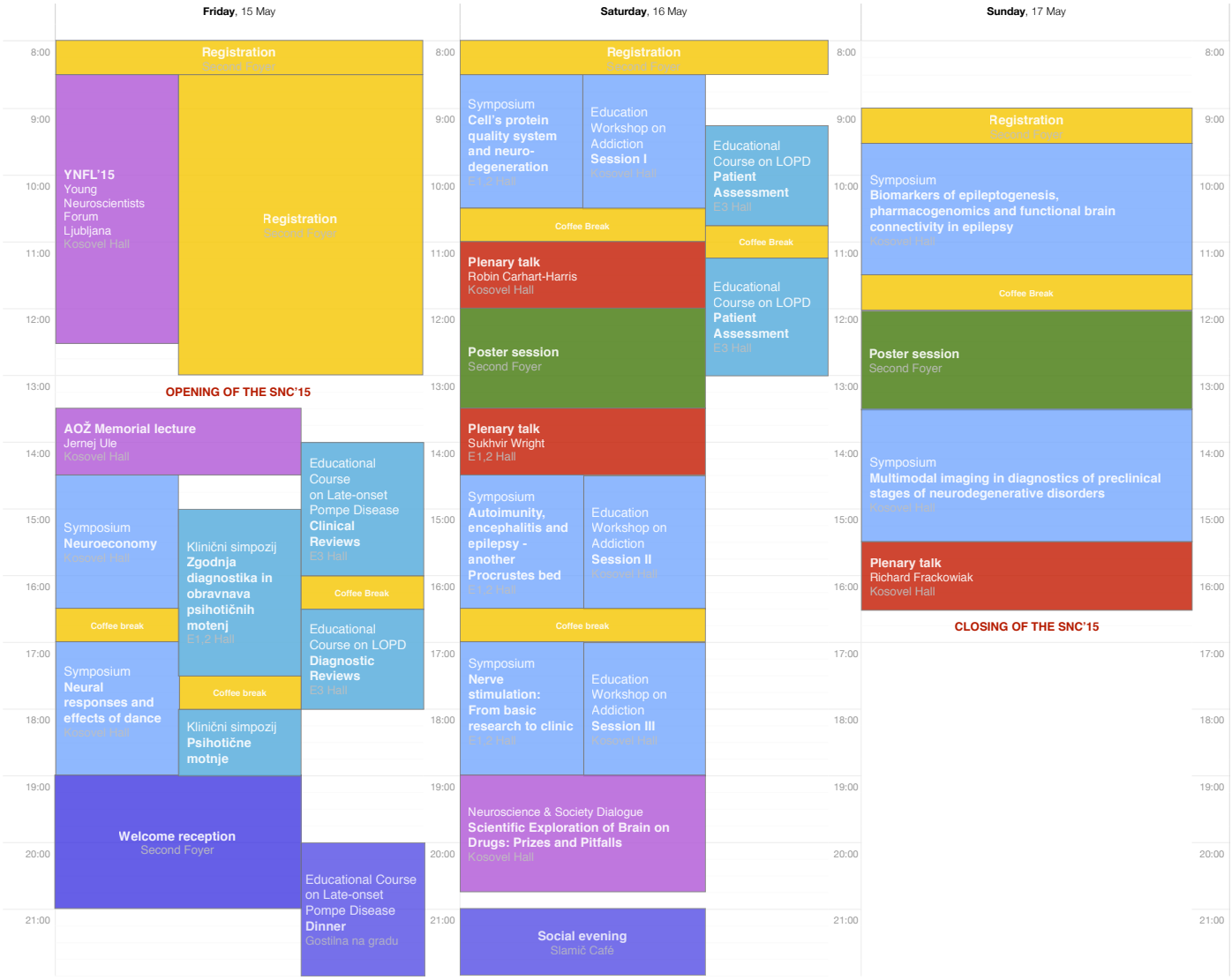

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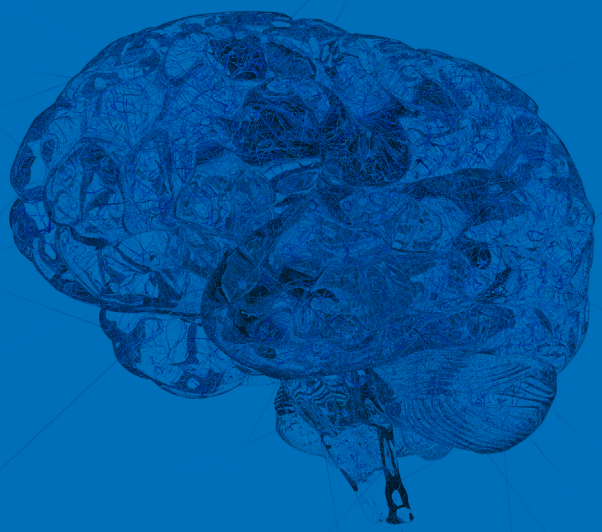

SiNAPSA Neuroscience Conference '15 Programme

www.sinapsa.org/SNC15
Cankarjev dom, Ljubljana, Slovenia
15–17 May 2015

SiNAPSA Neuroscience Conference ’15 Programme

Friday, 15 May

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

8:30—12:30 **Young Neuroscientists Forum Ljubljana ‘15** | Kosovel Hall 48

8:30 **Opening of the YNFL’15**

8:40 **The impact of upper motor neuron degeneration on respiration in wakefulness and sleep in amyotrophic lateral sclerosis**
Judita Jeran

9:00 **Stress affects survival of adrenal gland stem cells through leptin in Sprague Dawley rats**
Marta Balog

9:20 **Chronic social isolation reduces parvalbumin-positive interneurons in the medial prefrontal cortex of adult rats: protection by fluoxetine and clozapine**
Nevena Todorović

9:40 **Coffee break**

10:00 **The role of medial prefrontal cortex in uncertainty-based decision making in rats**
Nace Mikuš

10:20 **The vulnerability of the structural connectome to stroke in older adults**
Rok Berlot

10:40 **A simple and cost-effective q EEG evaluation shows marked differences between early Alzheimer’s disease patients and controls**
Bruna Pikš

11:00 **Coffee break**

11:20 **Coffee with neuroscientist Professor Jernej Ule**

12:20 **Closing of the YNFL’15**

13:00—13:30 **Opening of the SNC’15** | Kosovel Hall

13:30—14:30 Andrej O. Župančič Memorial lecture | Kosovel Hall. 29
The tricks neurons use to express their genes: jumping genes, zero-length exons and RNA loops
Jernej Ule

14:30—16:30 Symposium | Kosovel Hall. 32
Neuroeconomy
Chairs: Sergeja Slapničar, Grega Repovš

14:30 **Neuroeconomics and management control**
Sergeja Slapničar

15:00 **Decomposing cognitive control in economic decision making**
Grega Repovš

15:30 **Dopamine and decision making**
Robb Rutledge

16:00 **EEG investigations on the management control problem**
Philip Eskenazi

16:30—17:00 **Coffee break** | Second Foyer

17:00—19:00 Symposium | Kosovel Hall. 34
Neural responses and functional effects of dance on cognitive, emotional and motor performance
Chair: Maja Bresjanac

17:00 **The neural basis of dance and dance partnering**
Steven Brown

17:30 **Cognitive interactions in perceiving, performing and learning dance**
Bettina Bläsing

18:00 **Neural responses underlying dance imagery induced by music**
Maja Bresjanac

18:30 **Enhanced functional outcomes in older adults who dance regularly**
Rado Pišot

19:00—21:00 **Welcome reception** | Second Foyer

Saturday, 16 May

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

8:30—10:30 Symposium | E1,2 Hall 36
Cell's protein quality system and neurodegeneration
Chair: Eva Žerovnik

8:30 **Autophagy, p62/SQSTM1 and ALS-FTLD**
Alice Goode

9:00 **ALS- and FTLD-associated hexanucleotide repeat expansion mutation in C9orf72**
Boris Rogelj

9:30 **Modifications of FUS and implications in ALS and FTD**
Simona Darovic

10:00 **Mutual chaperoning by amyloid forming proteins/peptides**
Eva Žerovnik

10:30—11:00 **Coffee break** | Second Foyer

11:00—12:00 Plenary talk | Kosovel Hall 29
Psychedelic drugs in science and medicine
Robin Carhart-Harris

12:00—13:30 **Poster session A** | Second Foyer
Cellular neuroscience A
Clinical neuroscience A
Cognitive neuroscience A
Molecular neuroscience A
Systems neuroscience A

13:30—14:30 Plenary talk | E1,2 Hall 30
Autoimmune encephalitis and epilepsy – from synapse to symptoms
Sukhvir Wright

14:30—16:30 Symposium | E1,2 Hall 38
Autoimmunity, encephalitis and epilepsy - another Procrustes bed?
Chair: David Neubauer

14:30 **Autoimmune encephalitis and antibodies against neuronal cell antigens**
Sanja Stopinšek

15:00 **Severe form of autoimmune encephalitis in two children**
Mirjana Perkovič Benedik

15:30 **Autoimmunity and epilepsy in childhood**
Natalija Krajnc

16:00 **Can FIRES be a part of this story?**
Neli Bizjak

16:30—17:00 **Coffee break** | Second Foyer

17:00—19:00 Symposium | E1,2 Hall 40
Nerve stimulation: From basic research to clinic
Chairs: Janez Rozman, Polona Pečlin

17:00 **General overview of nerve stimulation: From past to future**
Winfried Mayr

17:20 **Implantable nerve interfaces developed in Slovenia and their use in research and clinical applications**
Janez Rozman

17:40 **Twenty-nine year stimulation of the common peroneal nerve: A case report**
Polona Pečlin

18:00 **Neuromodulation in the treatment of pelvic floor dysfunctions**
Adolf Lukanović

18:20 **Our experience with vagal stimulation for heart rate control**
Matej Podbregar

18:40 **Compound action potentials in an isolated rat sciatic nerve elicited with specific current stimulating pulses when exposed to anesthetic bupivacaine**
Monika C. Žužek

19:00—20:30 Neuroscience and society dialogue | Kosovel Hall
Scientific exploration of brain on drugs: Prizes and pitfalls

21:00—00:00 **Social evening** | Slamič Café 26

Sunday, 17 May

9:00—16:30 **Registration** | Second Foyer

9:30—11:30 Symposium | Kosovel Hall 43
Biomarkers of epileptogenesis, pharmacogenomics and functional brain connectivity in epilepsy
Chair: Bogdan Lorber

9:30 **Imaging epileptogenesis**
Matthias Koepp

10:10 **Graph-theoretical analysis of language networks in temporal lobe epilepsy**
David Gosar

10:50 **Pharmacogenomics of drug resistance in epilepsy**
Andreja Avberšek

11:30—12:00 **Coffee break** | Second Foyer

12:00—13:30 **Poster session B** | Second Foyer
Cellular neuroscience B
Clinical neuroscience B
Cognitive neuroscience B
Molecular neuroscience B
Systems neuroscience B

13:30—15:30 Symposium | Kosovel Hall 44
Multimodal imaging in diagnostics of preclinical stages of neurodegenerative disorders
Chairs: Zvezdan Pirtošek, Milica Gregorič Kramberger

13:30 **The overall design of the study, clinical and CSF data**
Milica Gregorič Kramberger

13:50 **Neuropsychological markers of mild cognitive impairment**
Simon Brezovar

14:10 **Can electrophysiological responses to AX-CPT task differentiate between early stages of neurodegenerative disorders?**
Jure Bon

14:30 **Altered white matter microstructure in mild cognitive impairment and Parkinson's disease**
Indre Pileckyte

14:50 **Resting state functional connectivity in patients with mild cognitive impairment and Parkinson's disease**
Anka Slana

15:10 **Metabolic biomarkers in patients with mild cognitive impairment and Parkinson's disease**
Petra Tomše

15:30—16:30 Plenary talk | Kosovel Hall 30
Human Brain Project: implications for neurology
Richard Frackowiak

16:30—16:45 **Closing of the SiNAPSA Neuroscience Conference '15** | Kosovel Hall

Poster sessions

Saturday, 16 May

Sunday, 17 May

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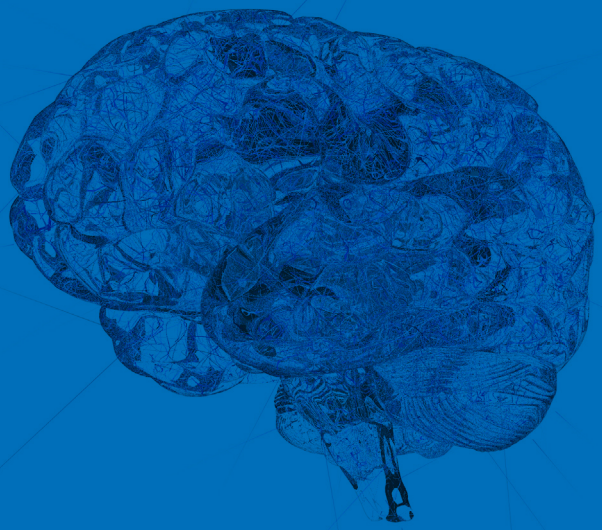

Educational Workshop on Addiction

Univerza *v Ljubljani*

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www.sinapsa.org/SNC15/workshop
Cankarjev dom, Ljubljana, Slovenia
16 May 2015

Saturday, 16 May

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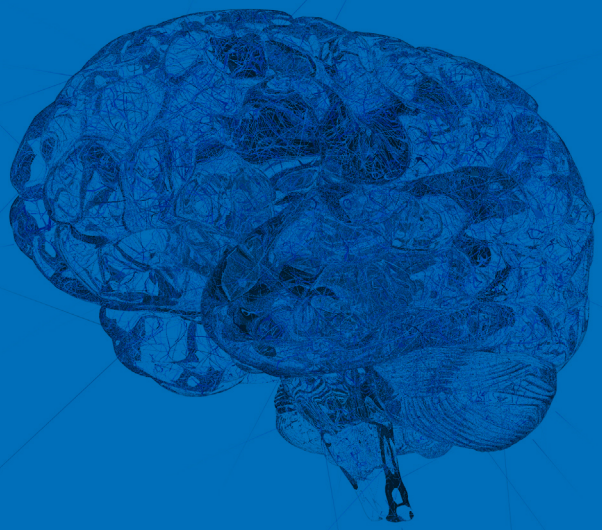

Educational Course on Late-onset Pompe Disease

www.sinapsa.org/SNC15/course
Cankarjev dom, Ljubljana, Slovenia
15–16 May 2015

Friday, 15 May

13:00—14:00 **Catering lunch, venue**

14:00—14:15 **Welcome speech, programme announcement** | E3 Hall
Organiser; Mr. Boris Šuštaršič (President of the Muscular Dystrophy Association of Slovenia)

14:15—16:25 **Clinical reviews** | E3 Hall 80

14:15 **Late Onset Pompe disease - overview**
Zoran Mitrović

14:35 **Diagnostic challenges in LOPD**
Agnes Herczegfalvi

14:55 **Case report – two sisters**
Katalin Vardi

15:10 **Pitfalls in adult Pompe disease diagnosis**
Georgios Konstantinos Papadimas

15:30 **LGMD and GAA "pseudodeficiency": a case from Croatia**
Rujana Šprljan Alfirev

15:45 **Patient perspective**
Marko Studen

16:05—16:25 **Coffee break**

16:25—18:00 **Diagnostic reviews** | E3 Hall 81

16:25 **LOPD in EMG laboratory: Where to start? What to expect?**
Ervina Bilić

16:40 **Case study: juvenile / adult patient**
Danijela Petković Ramadža

16:55 **Detecting GAA deficiency by DBS – how sensitive and how specific is it?**
Ksenija Fumić

17:10 **The impact of molecular diagnosis**
Karin Writzl

17:25 **Muscle biopsy in Pompe disease**
Marija Meznarič

17:40 **General Discussion**

17:55 **Wrap up and closing**

20:00—23:00 **Dinner** | Gostilna na gradu

Saturday, 16 May

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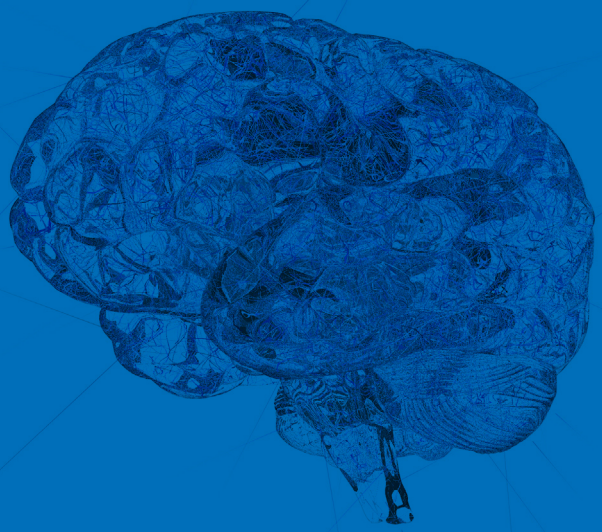

Klinični simpozij
Zgodnja diagostnika in obravnava psihotičnih motenj

www.sinapsa.org/SNC15/simpozij
Cankarjev dom, Ljubljana, Slovenia
15 May 2015

Petek, 15. maj

15:00—16:30 Klinični simpozij | Dvorana E1,2
Zgodnja diagostnika in obravnava psihotičnih motenj
Moderatorja: Borut Škodlar, Jurij Bon

15:00 **Uvod**
Jurij Bon

15:10 **Razvoj diagnostičnih kriterijev za prodromalna stanja in prve psihotične epizode**
Vesna Gaberšek

15:30 **Pomen bazičnih simptomov in motenj zavedanja sebe za zgodnjo diagnostiko**
Matej Potočan

15:50 **Psihotična stanja v otroštvu in mladostništvu - klinična slika, diagnostika in obravnava**
Barbara Šegula

16:10—16:30 **Odmor s kavo** | Drugo preddverje

16:30—17:30 **Satelitski simpozij (Eli Lilly)** | Dvorana E1,2
Moderator: Andrej Kastelic

16:30 **Uvod**
Andrej Kastelic

16:40 **Patofiziološko ozadje ADHD in možnost zdravljenja v odrasli dobi**
Jurij Bon

17:00 **Zdravljenje ADHD v odrasli dobi - praktični primer bolnika**
Hojka Gregorič Kumperščak

17:20 **Razprava in zaključki**
Andrej Kastelic

17:30—18:00 **Odmor s kavo** | Drugo preddverje

18:00—19:00 Klinični simpozij | Dvorana E1,2
Zgodnja diagostnika in obravnava psihotičnih motenj
Moderatorja: Borut Škodlar, Jurij Bon

18:00 **Pregled raziskav o medikamentoznem in psihoterapevtskem zdravljenju v prodromalnem obdobju**
Marko Saje

18:20 **Primerjava teoretičnih vidikov psihoterapevtskih pristopov v prodromalnih stanjih in pri prvi psihotični epizodi**
Borut Škodlar

18:40 **Kognitivne motnje in disfunkcije nevronskih omrežij v različnih fazah bolezni**
Grega Repovš

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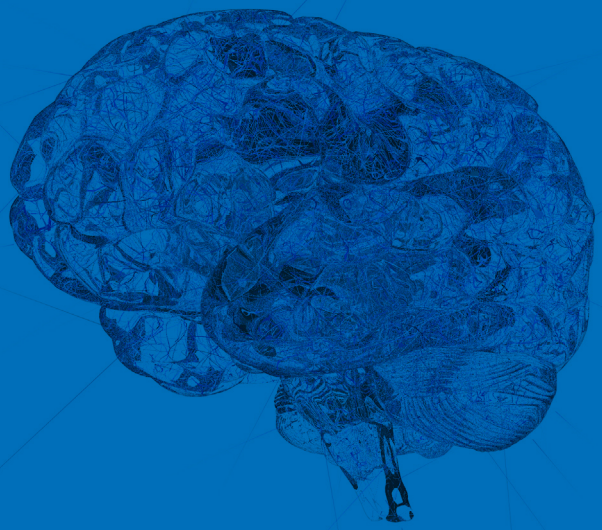

General information

www.sinapsa.org/SNC15
Cankarjev dom, Ljubljana, Slovenia
15–17 May 2015

General Information

Venue
Cankarjev dom, Cultural and Congress Centre
Prešernova 10, Ljubljana, Slovenia

Contact E-mail
For general queries, please write to: snc15@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 Second Foyer of Cankarjev dom and open as follows:
Friday, 15 May, 8:00–19:00
Saturday, 16 May, 8:00–19:00
Sunday, 17 May, 9:00–16:30

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'15.
The presenters are requested to be present and available for questions and discussion at the specified time-slot:
A - Saturday 12:00-13:30; B - 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 snc15@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
Wireless internet will be avaliable at the conference venue.

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 CME (Continuing Medical Education) credits.

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

Social Programme

Welcome Reception

Friday, 15 May, 19:00 - 21:00

Meet the conference participants at the Welcome Reception in the Second Foyer of Cankarjev dom.

SNC'15 & YNFL'15 Social

Saturday, 16 May, 21:00 - 00:00

Join us at the Slamič Café (Kersnikova ulica 1, http://www.slamic.si/) for a relaxing evening with drinks, music and dancing.
The social evening officialy starts at 9pm but you are welcome to join us from 8pm onwards.

LOPD Dinner

Friday, 15 May, 20:00 - 23:00

Participants of the Educational Course on Late-onset Pompe Disease are invited for dinner at the Gostilna na gradu restaurant on the Ljubljana Castle.

Meeting point at 19:30 in front of Hotel Slon for walking, at 19:40 on Erjavčeva Street (in front of Cankarjev dom) for bus transfer.

Committees and Organisation

SiNAPSA Neuroscience Conference '15 was organised by

SiNAPSA, Slovenian Neuroscience Association

Faculty of Medicine, University of Ljubljana

SNC'15 Programme Committee

Grega Repovš (Chair)

Jure Bon

Maja Bresjanac

Dragana Filipović

David Neubauer

Peter Pregelj

Boris Rogelj

David B. Vodušek

SNC'15 Organising Committee

Blaž Koritnik (Chair)

Rok Berlot

Jure Bon

Maja Bresjanac

Simon Brezovar

Mateja Drolec Novak

Andraž Matkovič

YNFL'15 Programme & Organising Committee

Simon Brezovar

Vida Ana Politakis

Anka Slana

Educational Workshop on Addiction Programme & Organising Committee

Maja Bresjanac

Mateja Drolec Novak

Educational Course on Late-onset Pompe Disease Programme & Organising Committee

Blaž Koritnik

Lea Leonardis

Zoran Mitrović

Klinični simpozij Zgodnja diagnostika in obravnava psihotičnih motenj - programski in organizacijski odbor

Jure Bon

Borut Škodlar

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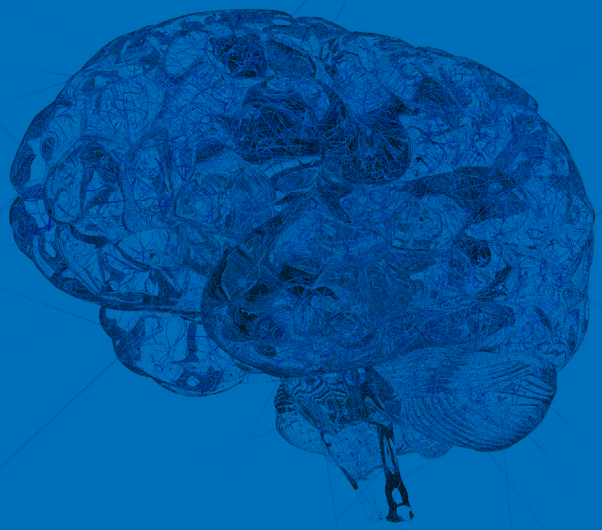

Abstracts

SNC'15 Plenary and Special Lectures

www.sinapsa.org/SNC15
Cankarjev dom, Ljubljana, Slovenia
15–17 May 2015

Friday, 15 May, 13:30
[AOŽ Memorial Lecture]

The tricks neurons use to express their genes: jumping genes, zero-length exons and RNA loops

Jernej Ule

Department of Molecular Neuroscience, Institute of Neurology, University College London, United Kingdom

As soon as DNA is transcribed into RNA, various RNA-binding proteins (RBPs) interact with the RNA, and thereby regulate the expression of proteins. This is particularly important in highly polarised cells, such as neurons and glia in the brain. RBPs control production of alternative mRNA isoforms and localisation of these mRNAs to specific cellular compartments, where mRNA translation can then be regulated in response to local stimuli. We have uncovered new regulatory features in transcripts that are produced in the brain, including transposable elements and zero-length exons. I will discuss how these features contribute to the regulation, diversity and evolution of gene expression. I will also present interactions of RBPs with the secondary structure of mRNAs. We recently developed a high-throughput method that can identify RNA duplexes that interact with RBPs in vivo. This revealed the existence of long-range RNA loops, which regulate mRNA stability and translation. Together, I will discuss how protein-RNA interactions enable the diverse and unique mechanisms for regulating gene expression in the brain.

Saturday, 16 May, 11:00
[Plenary Lecture]

Psychedelic drugs in science and medicine

Robin Carhart-Harris

Imperial College London, United Kingdom

Psychedelic drugs have been used for millennia by certain cultures and are now being used by scientists and doctors in contemporary science and medicine to understand the brain and treat certain mental disorders such as depression. Dr Robin Carhart-Harris will describe his research with these unusual compounds, which includes the first ever functional brain imaging studies with LSD and psilocybin (aka 'magic mushrooms') and an ongoing study investigating whether psilocybin can be used to treat depression.

Keywords: serotonin, hallucinogens, psychedelics, fMRI

Saturday, 16 May, 13:30
[Plenary Lecture]

Autoimmune encephalitis and epilepsy – from synapse to symptoms

Sukhvir Wright

University of Oxford and Department of Paediatric Neurology, Birmingham Children's Hospital, United Kingdom

Neuronal antibodies are now widely accepted as causative in autoimmune encephalitis, acting on the surface of essential synaptic proteins including the NMDAR, AMPAR, VGKC-complex and GABAR's. In this talk I will describe the pathophysiological effects of antibody binding that manifest in patients as clinical symptoms including psychosis, movement disorders and seizures. Most patients suffering from autoimmune encephalitis respond well to immunotherapy. In our recent prospective observational study of paediatric NMDAR-Ab encephalitis in the UK, 78 % of patients diagnosed and treated early made a full recovery. An update on the most recently described autoantibodies discovered in autoimmune encephalitis will also be given, and the controversial role of VGKC-complex antibodies, particularly in children. Finally, the relationship between neuronal antibodies and epilepsy will be discussed, including the short and long-term implications of positive neuronal antibodies in paediatric epilepsy, as well as our recent in vivo studies of antibody epileptogenicity.

Keywords: autoimmune encephalitis, NMDAR-Ab encephalitis, epilepsy, animal models

Sunday, 17 May, 15:30
[Plenary Lecture]

Human Brain Project: implications for neurology

Richard Frackowiak

Department of Clinical Neuroscience, CHUV University Hospital, Lausanne, Switzerland

We now know that a single human gene mutation may present with any of multiple phenotypes, and vice versa, that a range of genetic abnormalities may cause a single disease phenotype. These observations lead to the conclusion that a deeper understanding is needed of the way changes at one spatial or temporal level of brain organisation integrate and translate into others, eventually resulting in behaviour and cognition or their abnormalities. The traditional approach to determining disease nosology - eliciting symptoms and signs, creating clusters of like individuals and defining diseases primarily on those criteria has not generated fundamental breakthroughs in understanding sequences of pathophysiological mechanisms that produce the repertoire of psychiatric and neurological diseases.

It is time to radically overhaul our epistemological approach to such problems. We now know a great deal about brain structure and function. From genes, through functional protein expression the mechanisms are known in some detail. When it comes to cerebral microcircuits, to networks and to functionally specialised areas defined by physiological cell recording, microanatomy and human neuroimaging we have accumulated a mass of knowledge about the brain that so far defies easy integration and hence interpretation. Europe's Human Brain Project proposes a medical informatics platform that capitalises on modern advances in information technology, from supercomputers to distributed and interactive databases, allied to new mathematics and statistics, to federate and integrate existing and future clinical and neuroscientific data for a more biologically based, mechanistic approach to brain disorders. The implications for drug discovery range from more accurate, biologically supported diagnostics, new ways of identifying treatment targets, a priori profiling of primary and secondary effects of potential therapies in silico, a rethink about drug trial methodology and a route towards precision and personalised medicine.

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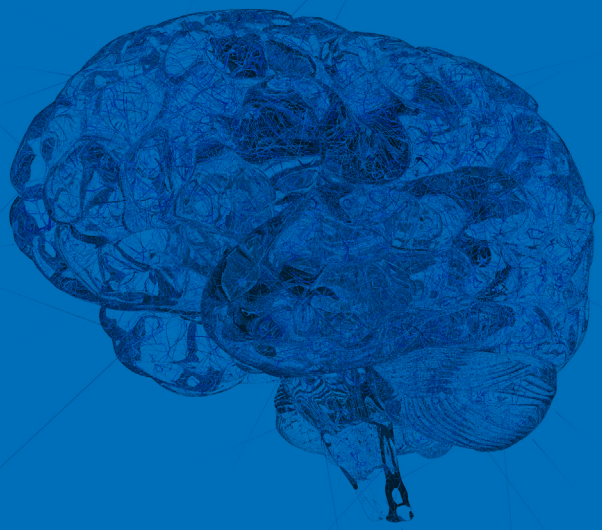

Abstracts

SNC'15 Thematic Symposia

www.sinapsa.org/SNC15
Cankarjev dom, Ljubljana, Slovenia
15–17 May 2015

Friday, 15 May, 14:30
[Symposium: Neuroeconomy]

Neuroeconomics and management control

Sergeja Slapničar

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At the wake of the global financial crisis which has been inarguably provoked by excessive risk taking in the financial sector, the debate has reopened in practice and academia about managerial incentive schemes that have been able to stimulate generally risk averse individuals for taking up excessive risks. Long-standing questions have resurrected about rationality of economic decision making, risk-inclination, the extent to which increasing magnitudes of rewards still motivate people, how people asses economic alternatives under risks and uncertainty and evaluate present vs. future outcomes. The aim of this presentation is to discuss how neuroeconomics can contribute to understanding of managerial decision making under risk and in time. Neuroeconomics as an inter-discipline of behavioural economics, psychology and neuroscience draws on techniques of imaging brain activity during execution of an economic task to explain the role that neural subsystems play in economic behaviour. Methodical advancements in this field allow researchers to open up what has been considered a 'black box' thus far. Joint research efforts of economist, psychologists and neuroscientists have resulted in discovery of brain systems that are underlying the cognitive processes related to coping with risk and uncertainty, intertemporal choices, reward and punishment. These same concepts are central also to the theory of management control systems, which typically seeks to understand how humans process information, make decisions, estimate the future, evaluate the past under a variety of financial incentives.

Friday, 15 May, 14:30
[Symposium: Neuroeconomy]

Decomposing cognitive control in economic decision making

Grega Repovš

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It is often—at least implicitly—assumed that better cognitive control should lead to more rational and therefore better decision making, an assumption which influences strategies for management control that often try to incentivize deliberate reasoning and explicit cognitive control. Increased cognitive effort is, however, costly, unreliable, and can lead to paradoxical strengthening of suboptimal decisions rather than enabling more optimal ones. In this talk, we will first explore how effective are incentives in improving cognitive control, both in terms of behavioral outcomes as well as brain activation. Next, we will review studies investigating the mechanisms of cognitive effort underlying different reward schemes, and comparing the efficiency and estimated cost of effortfull self-control vs. reframing to promote optimal choices. Finally, we will consider alternative strategies of employing cognitive control towards the path to better economic decision making.

Friday, 15 May, 14:30
[Symposium: Neuroeconomy]

Dopamine and decision making

Robb Rutledge

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The neuromodulator dopamine has a well-established role in learning, but its role in decision making is less well characterized. By boosting dopamine levels as subjects made economic decisions, we show that subjects are increasingly likely to take risks when options include potential gains but not losses. Aging, which is associated with a gradual decline in the dopamine system, has the opposite effect on behaviour. We introduce a parametric decision model that explains these effects as a change in Pavlovian approach behaviour. These results support a specific role for dopamine in decision making that may explain some changes in economic preferences over the lifespan.

Friday, 15 May, 14:30
[Symposium: Neuroeconomy]

EEG investigations on the management control problem

Philip Eskenazi

Rotterdam School of Management, Erasmus University, Rotterdam, The Netherlands

Developments in neuroscience can illuminate problems in management accounting and control. In a first project we build on research on the mirroring properties of the sensorimotor cortex to explain controller behaviour. Typically controllers are accountable to lower-level managers in their role of providing support for local decision making, but also have a fiduciary responsibility to ensure sound financial reporting to higher management. Lower-level managers have an incentive to pressure controllers to misreport. It is important to know what determines a controller's propensity to compromise on integrity under social pressure. We look at the suppression of EEG mu waves in the sensorimotor cortex while observing emotional facial expressions, and find it explains a substantial part of variation in controllers' responses to professional dilemmas. Our second project deals with insight in problem solving. The ability to find creative solutions is a key competence for modern organisations, but may be inhibited by the management control system. In particular, we suggest accountability inhibits insight in problem solving. One of the defining characteristics of insight is unawareness on the part of the solver of how the solution was found. This makes it a difficult approach to account for. For problems which also allow for alternative, more analytic solving strategies we expect a processing shift away from insight and towards analytic approaches. Three experimental studies, combining behavioural, EEG, and eye-tracking evidence, support this theory: imposing accountability can inhibit creative problem solving in the organisation.

Friday, 15 May, 17:00
[Symposium: Neural responses and functional effects of dance on cognitive, emotional and motor performance]

The neural basis of dance and dance partnering

Steven Brown

Department of Psychology, Neuroscience & Behaviour, McMaster University, Hamilton, Ontario, Canada

Dance is a form of patterned body movement, often done in synchrony with a timekeeper such as a musical beat. Recent neuroimaging studies have shed light on both the motoric and perceptual aspects of dance. Motor studies have looked at brain areas involved in navigation of the limbs through space, as well as the ability of people to synchronize these movements with musical beats. Most of the perceptual studies have looked at "expertise effects" related to trained dancers viewing movement patterns that they either can or cannot perform, as well as the development of sensorimotor linkages during the learning of dance movements. In addition to discussing such studies, I will present the results of a recent study from my lab involved in investigating brain areas that underlie leading vs. following when two people engage in joint movement with body contact.

Friday, 15 May, 17:00
[Symposium: Neural responses and functional effects of dance on cognitive, emotional and motor performance]

Cognitive interactions in perceiving, performing and learning dance

Bettina Bläsing

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Dance is intricately linked to the human motor system on different levels, from the most basic physical one, to higher order conceptual levels. Even though dancers are movement experts comparable to highly skilled athletes, their expertise comprises additional features that make dance an art form. In addition to complex coordinated movement, dance typically involves entrainment to music or rhythm, and multiple modes of interaction among dancers and between dancers and their audience. Neuropsychological studies have shown that the perception of others' bodies in motion is substantially influenced by reciprocal top-down and bottom-up processes between actors and observers. Neurocognitive processes involved in perceiving and performing dance have recently become topics of scientific interest, and an increasing number of dancers, choreographers and dance pedagogues show strong interest to be involved this research. With our studies on movement-related memory structures and the decomposition of dance movements, we have contributed substantially to the research on movement representation and learning. In this talk I will focus on my recent studies in this field, addressing (1) mental representations of movement in dancers' long-term memory, (2) observers' segmentation of dance movement, (3) entrainment between dancers, and (4) explicit and implicit modes of movement learning in dance. Findings from these studies will be discussed in the context of cognitive neuroscience, with implications for general motor learning and dance training.

Friday, 15 May, 17:00
[Symposium: Neural responses and functional effects of dance on cognitive, emotional and motor performance]

Neural responses underlying dance imagery induced by music

Maja Bresjanac

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Neural correlates of movement, movement perception and mental imagery of movement have been shown to extensively overlap. The aim of our pilot exploration was to employ music-induced dance imagery to study dance responses to music. Healthy, young adult volunteers (18 non-dancers (7 male and 11 female) and 17 dancers (9 male, 8 female)) were recruited for the fMRI-based study using a 3T scanner. Resting state BOLD signal was recorder first, followed by BOLD signal recordings during blocks of listening to music with instructions on how to respond to it with mental dance imagery. Clips of groovy (dance music) and non-groovy (foreign national anthems) instrumental music were used as stimuli. Immediate feed-back was obtained from the subjects on the extent of experienced mental imagery of dance as well as on their emotional engagement while listening to the music. The subjects' heart rate was simultaneously recorded to provide a physiological measure of arousal (Vovk et al., this volume). To obtain insight into neural activity underlying mental imagery of movement, movement observation and emotional engagement (without musical stimuli) in the same subjects, BOLD signal was also recorded while participants were instructed to imagine swimming, observing a swimmer, experiencing a passionate kiss, etc. (Politakis et al., this volume). The results revealed interesting behavioural as well as neural activation responses that point to expected commonalities, but also to some less expected differences between dancers and non-dancers in their responses to groovy and non-groovy music.

Friday, 15 May, 17:00
[Symposium: Neural responses and functional effects of dance on cognitive, emotional and motor performance]

Enhanced functional outcomes in older adults who dance regularly

Rado Pišot, Uroš Marušič, Saša Pišot, Boštjan Šimunič

University of Primorska, Koper, Slovenia

Dance is a promising intervention that combines physical and cognitive aspects such us balance, memory, motor coordination, acoustic stimulations and others. It could be performed in a variety of settings, according to the preferences and abilities of dancers and it is often a preferred choice of activity among older adults due to its social interactions. Dancing was proposed to be an intervention of choice for maintaining functional as well as cognitive abilities in old age.

A sample of 449 older adults was involved in the PANGeA mass measurement study (67.5 ± 5.4 years; 36.3 % men). Gait speed in normal and dual-task condition, blood pressure, heart rate, glucose, cholesterol, fitness index and the GPAQ questionnaire were obtained from each individual and analyzed between dancers (N = 39, who reported to dance on a regular basis) and the controls.

Results showed that the only significant difference between the two groups was in gait speed without dual-task ($p = 0.030$), where dancers showed greater velocity (1.41 ± 0.21 m/s) as compared to their counterparts (1.34 ± 0.22 m/s). Furthermore, when we divided groups by gender, we obtained a significant difference in females for the following parameters: cholesterol (Dancers: 5.31 ± 0.84, Controls: 5.78 ± 1.23, $p = 0.020$), fitness index (Dancers: 96.2 ± 10.4, Controls: 90.2 ± 21.6, $p = 0.050$) and gait speed without dual-task (Dancers: 1.44 ± 0.20, Controls: 1.35 ± 0.21, $p = 0.049$), while there were no significant changes in the group of males.

These findings suggest that dancing results in health benefits, and could be promoted as a form of leisure activity for older adults. Interestingly, no positive transfer was obtained on more demanding walking conditions, such as dual-task walking.

Research was supported by PANGeA project - Cross-border Cooperation Program Slovenia – Italy 2007-2013 and co-financed by the European Regional Development Fund as well as Slovenian and Italian national funds.

Saturday, 16 May, 08:30
[Symposium: Cell's protein quality system and neurodegeneration]

Autophagy, p62/SQSTM1 and ALS-FTLD

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Autophagy is a critical intracellular pathway for the degradation of damaged and aggregation-prone proteins and organelles and emerging evidence points to dysregulation of this process as a pathophysiological mechanism in ALS-FTLD. The p62/SQSTM1 protein is a cargo receptor for ubiquitin-mediated autophagy, wherein it simultaneously recognises lipid-anchored ATG8/LC3 proteins within the autophagosome membrane and ubiquitin-modified autophagic substrates. The former interaction is mediated through the LC3-interacting region (LIR, residues 337-347) of p62/SQSTM1 and recently mutations affecting the SQSTM1 gene, and more specifically the LIR, have been identified in patients with ALS-FTLD. Within the talk I will describe the functional and structural characterisation of a p62/SQSTM1-LIR mutant associated with ALS-FTLD, focussing on its impact on the interaction with LC3B. Biochemical analyses demonstrate that the disease-associated LIR mutation of p62/SQSTM1 results in defective recognition of LC3B. Complementary biophysical analyses confirm that the LIR mutant reduces p62/SQSTM1's affinity for LC3B, placing our observation on a firm structural and quantitative footing. Consistent with these observations, mammalian cell-based assays demonstrate reduced ability of the mutant p62/SQSTM1 to interact with the autophagic machinery. Our findings support the notion that disease aetiology in ALS-FTLD with SQSTM1 mutations involves dysregulation of autophagy, which we speculate may represent a wider mechanistic aberration that crosses over between other mutational and non-mutational cases.

Keywords: autophagy, p62, SQSTM1, ALS, FTLD

Saturday, 16 May, 08:30
[Symposium: Cell's protein quality system and neurodegeneration]

ALS- and FTLD-associated hexanucleotide repeat expansion mutation in C9orf72

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GGGGCC hexanucleotide repeat expansion mutation (HREM) in non-coding region of C9ORF72 gene has recently been identified as the most common genetic cause of devastating incurable neurodegenerative disorders amyotrophic lateral sclerosis (ALS) and frontotemporal lobar degeneration (FTLD). The disease relevant function of mutation is not clear. HREM may enable the formation of complex DNA and RNA structures, changes in RNA transcription and processing and formation of toxic RNA foci, which may sequester and inactivate RNA binding proteins. This complexity is further increased by the fact that expanded repeat is also transcribed in the antisense direction forming the CCCCGG (C4G2) repeat. According to some reports the antisense HREM transcript is even more abundant than the sense transcript. Additionally, the transcribed expanded repeats from both directions can undergo repeat-associated non-ATG-initiated (RAN) translation resulting in accumulation and aggregation of a series of dipeptide repeat proteins. Finally, HREM may also lead to haploinsufficiency of the C9orf72 protein. RNA pull-down study identifying some of the binding partners of GGGGCC repeat will be presented along with structural studies of the repeat DNA, which forms G-quadruplex structures.

Keywords: amyotrophic lateral sclerosis, frontotemporal dementia, C9orf72, RNA, aggregation

Saturday, 16 May, 08:30
[Symposium: Cell's protein quality system and neurodegeneration]

Modifications of FUS and implications in ALS and FTD

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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 familial ALS and 10 % of all FTLD cases (FTLD-FUS). FUS is a nuclear RNA/DNA binding protein with PY type nuclear localization signal present at its C-terminus which enables interaction with Transportin-1 and its transport into the 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-FUS do not have FUS mutations but FUS still accumulates in cytoplasmic inclusions, suggesting a different mechanism of inclusion formation in ALS and FTLD. Our aim is to find out whether nuclear localization signal of FUS is subjected to posttranslational modifications that have impact on its localization. We have identified a novel posttranslational modification in nuclear localisation signal of FUS. This modification destroys interaction with Transportin-1 and consequentially affects transport of FUS into the nucleus. Our study implicates new posttranslational modifications as one of the mechanisms by which nuclear transport of FUS is regulated and potentially perturbed in ALS and FTLD.

Keywords: FUS, posttranslational modifications

Saturday, 16 May, 08:30
[Symposium: Cell's protein quality system and neurodegeneration]

Mutual chaperoning by amyloid forming proteins/peptides

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We study the mechanisms of protein aggregation and cellular toxicity by the prefibrillar oligomers formed intracellularly by amyloidogenic proteins and some of their pathological mutants. It is an accepted view that the most toxic are soluble oligomers in range of 6 to 30 mers, that are membrane seeking and even make pores into membranes (1-2). I will discuss the proposal that changed pre-amyloidogenic conformations of amyloid forming proteins may act as mutual chaperones, leading to temporary inhibition of aggregation and toxicity. Examples will be described of crystallins, prion protein and stefin B; all binders of amyloid-beta (3). Small molecule inhibitors of protein aggregation will also be discussed. Our main model protein from the family of cystatins, stefin B will be described in more detail. It's possible function in the cell's response to protein mis-folding will be high-lighted (4).

1. Ceru, S., et al. Size and morphology of toxic oligomers of amyloidogenic proteins: a case study of human stefin B. Amyloid 15, 147-159 (2008).

2. Rabzelj, S., et al. Interaction with model membranes and pore formation by human stefin B: studying the native and prefibrillar states. Febs J 275, 2455-2466 (2008).

3. Skerget, K., et al. Interaction between oligomers of stefin B and amyloid-beta in vitro and in cells. J Biol Chem 285, 3201-3210 (2010).

4. Polajnar, M., et al. Human Stefin B Role in Cell's Response to Misfolded Proteins and Autophagy. Plos One 9, e102500 (2014).

Keywords: amateur chaperones, cell's response to protein misfolding, toxicity of prefibrillar oligomers, amyloid

Autoimmune encephalitis and antibodies against neuronal cell antigens

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Autoimmune encephalitis (AE) is an immune-mediated disease with diverse neurological symptoms. The discovery that several forms of encephalitis results from antibodies against neuronal cell antigens has led to a paradigm shift in diagnostic approach of encephalitis. AE has been associated with antibodies against intracellular neuronal antigens Hu, Ma2, Ri, CV2, amphyphisin and GAD. These antibodies occur in middle-aged or elderly patients sometimes with previous history of cancer. They do not appear to be directly pathogenic but can be very useful as a marker of disease. Because of irreversible cytotoxic neuronal damage, these patients do not respond well to immunotherapy. A rapidly expanding subset of AE occurs in association with antibodies to neuronal cell-surface or synaptic antigens like NMDAR, AMPAR, GABABR, LGI1, CASPR, DPPX and mGluR5. These antibodies occur in patients of all ages and are less commonly associated with cancer. They can be pathogenic by disrupting t he function of the target protein. The neurological symptoms may be reversible and respond well to immunotherapy. Laboratory tests for intracellular antigens frequently involve immunohistochemistry on tissue arrays and immunoblotting of proteins, while antibodies against neuronal cell-surface proteins are determined by cell-based assays with transfected cells expressing the antigen of interest. AE can resemble infectious encephalitis and comprises an expanding group of potentially treatable disorders that should be in the differential diagnosis of any type of encephalitis. A comprehensive analysis of clinical evaluation and determination of autoantibodies in patient's serum and/or cerebrospinal fluid is necessary to confirm the diagnosis of AE.

Keywords: autoimmune encephalitis, neuronal surface antibodies, paraneoplatic antibodies

Saturday, 16 May, 14:30
[Symposium: Autoimmunity, encephalitis and epilepsy - another Procrustes bed?]

Severe form of autoimmune encephalitis in two children

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Autoimmune N-methyl-D-aspartate receptor (NMDAR) encephalitis is increasingly recognized as a cause of encephalitis in children. The typical presentation is with subacute onset of neuropsychiatric symptoms, behavioural changes and seizures, usually with progression to movement disorder, reduced consciousness, hypoventilation and autonomic instability. Diagnosis is confirmed by detection of antibodies to the NR1 subunit of the NMDAR. The patients are treated with various immunotherapies. It is still unclear if earlier treatment results in better outcome. We present a case of severe form of NMDAR encephalitis in a young boy, who was referred late in the course of the disease to our centre. Treatment was started late with relatively good outcome. The second case, we present is a 6 years old girl who suffered severe form of tick-borne encephalitis (TBE) and two months afterwards developed also NMDAR encephalitis. To our knowledge this is the first case of NMDAR encephalitis triggered by TBE virus infection.

Keywords: autoimmune encephalitis, children, tick-borne encephalitis

Autoimmunity and epilepsy in childhood

Natalija Krajnc

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The causes of encephalitis are numerous, and extensive investigations for infectious agents and other etiologies are often negative. The discovery that many of these encephalitis are immune mediated has changed the approach to the diagnosis and treatment of these disorders. Moreover, the broad spectrum of symptoms including epileptic seizures, movement disorders and psychiatric symptoms usually requires a multidisciplinary treatment approach. Autoimmune etiology has been demonstrated (eg, anti-N-methyl-D-aspartate receptor encephalitis, anti-NMDA-R) or is strongly suspected (eg, Rasmussen encephalitis, encephalopathies with fever and status epilepticus) in several forms of encephalitis associated with epilepsy in children. Recognition of novel immune-mediated encephalitis-epilepsy spectrum of disorders is important because some of these are highly responsive to immunotherapy. Clinical presentation, diagnostic tools and possible treatment strategies of these disorders will be presented.

Keywords: epilepsy, autoimmunity, children

Saturday, 16 May, 14:30
[Symposium: Autoimmunity, encephalitis and epilepsy - another Procrustes bed?]

Can FIRES be a part of this story?

Neli Bizjak

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Febrile infection-related epilepsy syndrome (FIRES) is a severe postinfectious epileptic encephalopathy in previously healthy children. It is characterized by refractory status epilepticus immediately following an unspecific febrile illness and with subsequent pharmacoresistant epilepsy and intellectual disability. The etiology and the mechanisms underlying of FIRES are still unknown. Blaming an autoimmune mechansim is rather tempting, especially since most of the patients presented with seizures immediately following a febrile episode but without evidence for infectious encephalitis. Currently there is no efficient treatment available, with the possible exception of ketogenic diet. Given that treating patients with FIRES is very difficult and challenging, insight into underlying pathophysiology is clearly required.

Keywords: epileptic encephalopathy, children, febrile infection, resistant epilepsy, intellectual disability

Saturday, 16 May, 17:00
[Symposium: Nerve stimulation: From basic research to clinic]

General overview of nerve stimulation: From past to future

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Implants for Functional Electrical Stimulation (FES) are as old as application of mobile electronic equipment in general, starting in the 1950s after invention and availability of the bipolar transistor. Though quite many implants were tested in experimental and clinical studies, only few are established on the medical product market and treatment options for patients in need.

Cardiac pacers and cochlear implants gained rapid commercial success, and developed continuously from early simple basic functionality to highly sophisticated complex artificial organs.

There are a few more with clear benefit for treatment of neural or neuromuscular disorders, but with commercially limited impact, mainly due to cost restrictions in healthcare and high costs for regulatory obligations.

The widest market presence in those is achieved by "general purpose"; stimulators for deep brain (Parkinson, Epilepsy, or Depression treatment) and for epidural spinal cord stimulation (mainly for chronic pain relief, but also more recently for modification of spasticity and gait patterns). Underling common mechanisms are external modification of peripheral and central sensory-motor control mechanisms.

Others with smaller market volume, but important function improvements are Phrenic Pacers, bladder management implants and drop foot gait correction implants. Implants for restoration of hand grasp have been briefly on the market recently, but despite clear functional benefit failed on the market.

Even though general improvements in electronics miniaturisation, operation speed and dropping power consumption had constant impact in development of active medical implants, three big challenges of remained delicate for gaining development progress: electrode cables and interfaces, hermetic packaging and power supply. These are constantly under technical and experimental research and require ultimate attention before transfer of novel technical solutions to clinical application. Clinically a clearly visible trend will be optimization of technology for coupling with altered neurophysiology to activate idle neuronal functions in restoration of movement.

Keywords: implant, Functional Electrical Stimulation, FES, spinal cord, neuromuscular

Saturday, 16 May, 17:00
[Symposium: Nerve stimulation: From basic research to clinic]

Implantable nerve interfaces developed in Slovenia and their use in research and clinical applications

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Implantable medical devices provide therapy for treating numerous health conditions as well as monitoring and diagnosis. Considerable scientific and technological effort has been devoted to developing neuroprostheses and hybrid bionic systems that link the human nervous system with electronic prostheses with the main aim of restoring motor and sensory functions in disabled patients. The application of electrodes directly to peripheral nerve potentially provides a route for selective stimulation of the nervous system. Selective stimulation of peripheral nerves is necessary for most neural prosthetic applications and a powerful tool in studying the function of neural systems. The selection of a suitable nerve electrode for neuroprosthetic applications implies a trade-off between invasiveness and selectivity, wherein the ultimate goal is to achieve the highest selectivity for a high number of nerve fascicles by the least invasiveness and potential damage to the nerve. Cuff electrodes are currently the most suitable nerve-based electrode for selective electrical activation of the nervous system. They are the least invasive, are simple to install, and have an established clinical history. Herein, we intend to provide an overview of the peripheral interfaces available in different medical specialities and trace their use from research to potential clinical application. The current research intends to develop and test a pork model for modulation of vagus activity, targeting the SA and the AV node and ganglionated plexuses at or near the left atria-PVs junction of the heart that may have anti-fibrillatory effects via selective stimulation of superficial regions and fibre-type selective stimulation nerve fibres.

Keywords: neuroprostheses, selective nerve stimulation, nerve cuff electrodes, modulation of vagus activity

Saturday, 16 May, 17:00
[Symposium: Nerve stimulation: From basic research to clinic]

Twenty-nine year stimulation of the common peroneal nerve: A case report

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We present the results of long-term clinical follow-up in correction of drop-foot in one of hemiplegic patients with Implantable Gait Corrector (IGC) for stimulation of the common peroneal nerve (CPN). Selective stimulation of muscles tibialis anterior (TA) and the peroneus brevis (PB) that contribute to strong dorsal flexion and moderate eversion of the foot was achieved with a monopolar half-cuff (cuff) installed on the nerve behind the lateral head of the fibula. Results show that a selective and gradual recruitment of fibres within the CPN innervating aforementioned muscles was achieved. This could be attributed to the current, charge balanced, and biphasic stimuli with a rectangular cathodic, and exponential decaying anodic component delayed for 50μs which were employed for stimulation. Results of gait analysis demonstrate significant improvements of gait without excessive eversion. They also show that the velocity of natural gait, cadence and stride length were sign ificantly increased. However, the natural gait of the patient was still slower than in healthy individual. Results also show that the dorsal/plantar angular velocity of unstimulated foot could be estimated as slightly higher than the angular velocity of stimulated foot. Electrophysiological findings have not revealed any reliable sign which could be attributed to the damage of the CPN induced by the cuff or by the stimuli applied for seven years. Namely, motor conduction velocity of the CPN remained almost unchanged for whole period of the time.

Keywords: common peroneal nerve, nerve stimulation, cuff

Saturday, 16 May, 17:00
[Symposium: Nerve stimulation: From basic research to clinic]

Neuromodulation in the treatment of pelvic floor dysfunctions

Adolf Lukanović

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Pelvic floor dysfunction is a complex problem that can be refractory to current treatment modalities. Conservative terapy such as neuropathic pain modulators, local anaesthetics and corticosteroids, botox of trigger points, rarely result in a durable cure of patients. Various surgical procedures have significant side effects and less than optimal results. In the last decade nerve neuromodulation (posterior tibial nerve stimulation, sacral neuromodulation, pudendal neuromodulation) has been confirmed as a valuable treatment option to treat intractable overactive bladder, chronic pelvic pain and fecal incontinence, especially in patients with concurrent bladder symptoms such as urgency, frequency or retention. This therapy is available to a highly select group of patients with permanent pain who have failed multiple other therapies and who are willing to undergo a surgical procedure to have an electrical stimulation device implanted.

The first sacral nerve stimulators implanted by Tanagho and Schmidt (1981) were performed for the indications of urinary incontinence, urgency-frequency and nonobstructive urinary retention. Since that time, observations have been made for benefits beyond voiding disorders. These aditional benefits have included re-establishment of pelvic floor muscle awareness, resolution and pelvic floor muscle tension and pain, decrease in vestibulitis and vulvodynia, decrease in bladder pain (interstitial cystitis), and normalizatio of bowel function. However it is thought that sacral nerve stimulation induces reflex mediated inhibitory effects on the detrusor through afferent and or efferent stimulation of the sacral nerves.The implanted device stimulates the sacral nerves with mild electrical pulses which enables the patient to perceive the sensation of bladder fullness and the desire to void.

Long-term efficacy for pain relief is reported at less than 50 %, and complications include lead migration and infection at the surgical side.

Sacral nerve electrical stimulation via implantable devices is an effective and durable new approach to pelvic floor dysfunction with minimal complications and is emerging as a potential therapy for the future. Longer term and independent observational studies are needed to examine the longitivity of the neuromodulation and identification of the most appropriate patient who should undergo this treatment.

Saturday, 16 May, 17:00
[Symposium: Nerve stimulation: From basic research to clinic]

Our experience with vagal stimulation for heart rate control

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Activation of the parasympathetic pathway leads to negative chronotropic, dromotropic, and inotropic changes of heart function. The ability to selectively stimulate certain superficial compartments of peripheral nerves has been demonstrated previously. The aim of the present study was to find a clinically acceptable selective biphasic vagus nerve stimulation technique, which could allow gradual regulation of heart rate and systemic arterial pressure. In two patients, the left vagus nerve was stimulated with a combination of quasi-trapezoidal cathodic and rectangular anodic current pulses with different stimulation frequencies (10Hz, 20Hz, 30Hz) and increasing current. The heart rate and systemic arterial pressure decreased with increasing current at all different stimulation frequencies ($p<0.05$). The heart rate and arterial pressure response was more gradual with 10Hz compared to 20Hz/30Hz vagus nerve stimulation ($p<0.05$). In conclusion, selective vagus nerve stimulation, with a combination of quasi-trapezoidal cathodic and rectangular anodic current pulses at 10Hz, offers gradual heart rate and systolic arterial pressure control.

Keywords: vagus nerve stimulation

Saturday, 16 May, 17:00
[Symposium: Nerve stimulation: From basic research to clinic]

Compound action potentials in an isolated rat sciatic nerve elicited with specific current stimulating pulses when exposed to anesthetic bupivacaine

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We studied the functional performance of quasitrapezoidal current biphasic stimulating pulse to selectively activate specific nerve fibers in the isolated rat sciatic nerve exposed to anesthetic bupivacaine. The stimulus should predominantly stimulate myelinated Aβ-fibres, minimize the stimulation of the myelinated Aα-fibers and Aδ-fibres, and bypass the stimulation of the non-myelinated C-fibres. Compound action (CAPs) were measured with two pairs of recording hook electrodes at the two sites along the nerve segment located at the distances of 9.6 and 19.2 mm from the stimulating cathode. Isolated nerves were placed in the moist chamber and were stimulated at frequency of 1 Hz with supramaximal quasitrapezoidal biphasic current pulses ic = 2.5 to 3.35 mA in duration of 50 μs. Subsequently, nerves were exposed to bupivacaine dissolved in physiological solution at two different concentrations (3.8; n = 3 and 7.7 μM; n = 3) for 60 min at room temperature (22 °C). The evoked CAPs were digitalized at the sampling rate 100 kHz and stored on the computer. CAP parameters such as peak amplitude, peak to peak amplitude, time to peak were monitored/ analyzed for 60 min in 10 minutes intervals. Time response curves, as determined by % inhibitions of CAPs amplitude by bupivacaine were compared to control CAPs amplitude and time required to reduce CAPs for 25, 50 and 75 % then determined. The maximal blockade of CAPs amplitude was observed 60 min after exposure to 3.8 and 7.7 μM bupivacaine. Both concentrations of bupivacaine also prolonged 'time to peak' parameter in the CAP1 and CAP2.

Keywords: rat sciatic nerve, compound action potential, selective nerve stimulation, bupivacaine

Sunday, 17 May, 09:30
[Symposium: Biomarkers of epileptogenesis, pharmacogenomics and functional brain connectivity in epilepsy]

Imaging epileptogenesis

Matthias Koepp

Institute of Neurology, University College London, United Kingdom

Clinical neuroimaging is normal in over 50 % of new-onset focal epilepsies, and generally normal in idiopathic generalised epilepsies. How can advanced functional and structural imaging further our understanding of epileptogenesis and cognitive functions in focal and generalised epilepsies, and how might neuroimaging be used in the future to improve surgical outcome, as well as predicting response to medication? Group analyses of functional, structural and effective connectivity based on functional magnetic resonance imaging (fMRI) and diffusion tensor imaging provide evidence for unique anatomical structures that are involved in the modulation of seizure activity, and their role in specific syndromes. Whilst there is evidence that focal seizures arise and are sustained within a network of interconnected brain regions, the deep frontal piriform cortex plays an important role in modulating seizure activity. Altered connectivity with the supplementary motor area may represent the anatomical basis for cognitive triggering of motor seizures in juvenile myoclonic epilepsy. A major challenge for the future use of neuroimaging is the widening of applications beyond 'surgical imaging' to include individual predictions of disease progression and of response to medication.

Keywords: biomarker, epileptogenesis, imaging

Sunday, 17 May, 09:30
[Symposium: Biomarkers of epileptogenesis, pharmacogenomics and functional brain connectivity in epilepsy]

Graph-theoretical analysis of language networks in temporal lobe epilepsy

David Gosar[1], Angelika Mennecke[2], Julie Rösch[2], Kirsten Herfurth[3], Anja Čuš[4], Hajo Hamer[3], Arnd Dörfler[2], Elisabeth Pauli[3]

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Studying functional connectivity in the human brain has brought about significant insight into cognitive dysfunction and compensation in individuals with epilepsy. The utilization of graph-theory in these analyses offers a novel and powerful method to understand the impact of epilepsy on cognition.

Among the normal population and over 50 % of patients with drug drug-resistant temporal lobe (TLE) the left hemisphere is dominant for language. However, during evaluation for epilepsy surgery about 20-40 % of TLE patients are found who are able to speak while their left hemisphere is under temporary anesthesia. We chose to study epilepsy-related language dysfunction by using two fMRI language tasks (verbal fluency, verb generation) in six such patients. By comparing their fMRI activation and connectivity to that of six TLE patients with typical language representation and nine control participants we found that atypical language representation is associated with bilateral brain activation and higher connectivity in the right superior temporal gyrus and right insula. Network analysis also indicated that TLE patients had less efficient language networks than control participants. Poorer neuropsychological scores (Boston Naming Test and verbal IQ) were associated with this gre ater network inefficiency and inability to inhibit task-irrelevant brain regions. Earlier age of seizure onset was found to be associated with atypical language activation and connectivity.

Our results show that graph-theory-based analyses can help better understand how epilepsy impacts cognition. In TLE patients, they indicate that an inability to disengage task non-relevant brain regions may be a vital factor in cognitive dysfunction.

Keywords: functional connectivity, temporal lobe epilepsy, language networks, brain plasticity

Sunday, 17 May, 09:30
[Symposium: Biomarkers of epileptogenesis, pharmacogenomics and functional brain connectivity in epilepsy]

Pharmacogenomics of drug resistance in epilepsy

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Approximately 30 % of people with epilepsy continue to have seizures despite treatment with several antiepileptic drugs at maximum tolerated doses. Genomic variation is thought to contribute to drug resistance in all types of epilepsy. Several collaborative projects have been established with the aim to discover the genome-wide markers of drug resistance, using genome-wide association studies and next generation sequencing. But has any of them shed the light on the problem of drug resistance so far?

Sunday, 17 May, 13:30
[Symposium: Multimodal imaging in diagnostics of preclinical stages of neurodegenerative disorders]

The overall design of the study, clinical and CSF data

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This was a prospective study aiming to study different biomarkers (neuroimaging, CSF, neuropsychological, neurophysiological, olfactory impairment) in patients with MCI, PD and PDMCI. It is known that amnestic type of MCI would earlier and more likely progress to dementia. It is thought that cerebrospinal fluid (CSF) biomarkers can effectively predict conversion from MCI to AD dementia. Hence, in the new revised research criteria for AD (National Institute of Neurological and Communicative Disorders and Stroke– Alzheimer's Disease and Related Disorders Association), CSF biomarker levels are considered supportive feature. The predictive power of these diagnostic markers in a preMCI stage, before any measurable cognitive impairment, has not yet been fully investigated. Consequently, identification of biomarkers of the earliest cognitive changes in patients with MCI and PDMCI that best predict conversion of MCI to AD, or PDMCI to PDD, would improve patient care, allow early interventions, as well as reveal new insights into disease natural history in different population of patients.

From the Centre for cognitive and Centre for extrapyramidal disorders we subsequently recruited 76 participants (22 controls, 21 MCI, 17 Parkinson's disease (PB), and 16 PB with MCI) to obtain the information about their cognitive functions and CSF biomarker status. Cognitive and mood screening tools were used. Basic demographic and screening results are presented in the table.

Diagnosis	N	Age	Gender M: F	MMSE	BDI	MOCA
HC	22	68 (7.8)	6:15	29 (1.2)	7 (5.6)	26 (2.1)
MCI	21	70 (7.4)	6:16	28 (1.4)	9 (6.0)	24 (3.3)
PDMCI	16	69 (7.4)	7:9	29 (0.9)	13 (6.7)	25 (2.5)
PD	17	66 (5.7)	13:4	29 (1.0)	7 (3.2)	27 (1.8)

Nrs represent mean (SD), age presented in years, N – Nr, HC – healthy controls, MCI – mild cognitive impairment, PDMCI – Parkinson's disease with mild cognitive impairment, PD – Parkinson's disease, MMSE – Mini Mental State Examination, MOCA – Montreal Cognitive Assessment, BDI – Beck Depression Inventory.

The analysis is still ongoing. Interpretation of results and the CSF data will be reported at the symposium.

Keywords: mild cognitive impairment, clinical data, CSF biomarkers

Sunday, 17 May, 13:30
[Symposium: Multimodal imaging in diagnostics of preclinical stages of neurodegenerative disorders]

Neuropsychological markers of mild cognitive impairment

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Mild cognitive impairment (MCI) represents clinically significant cognitive decline with preserved everyday functioning. Vast amount of studies have shown that patients with MCI have increased risk for development symptoms of dementia. The probability of slowing down symptoms of dementia is closely related with an early diagnosis and intervention. Therefore, correct and reliable diagnosis of MCI plays very important role for clinicians, patients and their care-givers in making important decisions in subsequent treatment.

Neuropsychological assessment aims to address question regarding level and type of cognitive decline. In the MCI literature we can find large amount of studies where neuropsychological data have been combined with other examinations (e.g. CSF, MRI, EEG). These studies have usually addressed question which combination of biomarkers are optimal in predicting individual progress to dementia.

The aim of neuropsychological part of our study was (i) to find the neuropsychological measurements which are the best in predicting conversion from MCI to dementia, (ii) to separate different MCI subgroups by means of calculating robust memory and non-memory components, (iii) to combine the most predictive neuropsychological variables with other examinations and (iv) to address the question how are neuropsychological scores in MCI patients related to different modes of cognitive control. We recruited 80 participants (20 controls, 20 MCI, 20 Parkinson's disease (PB), and 20 PB with MCI) to obtain the information about their cognitive functions.

Results of the analysis which is still in progress will be presented at neuropsychological part of symposia.

Keywords: mild cognitive impairment, neuropsychological assessment, component analysis, cognitive control

Sunday, 17 May, 13:30
[Symposium: Multimodal imaging in diagnostics of preclinical stages of neurodegenerative disorders]

Can electrophysiological responses to AX-CPT task differentiate between early stages of neurodegenerative disorders?

Jure Bon[1], Milica Kramberger[1], Maja Trošt[1], Anka Slana[1 2], Simon Brezovar[1], Sebastijan Veselič[1], Timotej Volavšek[1], Jaka Bon[1], Grega Repovš[2], Zvezdan Pirtošek[1]

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Evoked related potentials (ERP) derived from continuous electroencephalography recording while subjects perform a cognitive task have a long tradition in cognitive neuroscience research. They are specifically well placed to answer questions on timing and momentary changes in cognitive strategies while they are also subjected to a lot of data preprocessing in order to improve signal to noise ratio, which can introduce artifactual patterns in results. AX-CPT is a complex version of a continuous performance task, which puts emphasis on maintenance of contextual cues and forces subjects to use proactive or reactive cognitive strategies to different degrees to successfully maintain their attention to stimuli. It is thought that proactive and reactive cognitive styles coexist in individuals and change according to current circumstances of cognitive processing, while their overall balance shifts due to different reasons, ageing being one of the most researched.

In present study we sought to differentiate healthy young subject sample from healthy old subjects and patients with mild cognitive impairment, Parkinson's disease and mild cognitive impairment related to Parkinson's disease based on their responses to different parts of the AX-CPT trial: processing and maintaining the cue over short and long delay, inhibiting or activating response to target. Results will be presented and the possibility for the inclusion of this specific ERP in multimodal integrative markers of disease related cognitive decline will be discussed.

Keywords: event related potentials, EEG, AX-CPT, neurodegeneration, biomarkers

Sunday, 17 May, 13:30
[Symposium: Multimodal imaging in diagnostics of preclinical stages of neurodegenerative disorders]

Altered white matter microstructure in mild cognitive impairment and Parkinson's disease

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Cortical disconnection due to white matter damage seems to play an important role in cognitive decline related to neurodegeneration. White matter microstructural alterations can be studied non-invasively with diffusion MRI. In the present study, we used diffusion MRI and tract-based spatial statistics to investigate microstructural alterations associated with mild cognitive impairment, the prodromal stage of Alzheimer's disease, and Parkinson's disease. Further, we compared white matter microstructure in patients with Parkinson's disease with and without mild cognitive impairment. We will present the observed group differences and relate them to other clinical data.

Keywords: diffusion MRI, white matter, neurodegeneration, cognitive impairment

Sunday, 17 May, 13:30
[Symposium: Multimodal imaging in diagnostics of preclinical stages of neurodegenerative disorders]

Resting state functional connectivity in patients with mild cognitive impairment and Parkinson's disease

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Functional connectivity is a relatively novel technique of fMRI data analysis, which focuses on identifying connectivity between brain regions by analysing correlations of spontaneous fluctuations of brain activity across time. It was shown that brain regions that form functional networks show coherent BOLD fluctuations under resting conditions, and that this functional architecture is disturbed in various brain disorders. The aim of this study was to explore possible differences in brain connectivity in patients with mild cognitive impairment and Parkinson's disease with and without PD related mild cognitive impairment, which could serve as diagnosis biomarkers in early stages of the disease.

72 participants—21 healthy individuals, 22 participants with mild cognitive impairment, 14 participants with Parkinson's disease, 15 participants with Parkinson's disease related mild cognitive impairment—underwent resting-state functional magnetic resonance imaging. Results of investigation of group differences in network connectivity and global brain integration will be reported and discussed.

Keywords: functional networks, fMRI, neurodegeneration, biomarkers

Sunday, 17 May, 13:30
Symposium: Multimodal imaging in diagnostics of preclinical stages of neurodegenerative disorders]

Metabolic biomarkers in patients with mild cognitive impairment and Parkinson's disease

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Voxel-by-voxel comparison of FDG/PET brain images of patient groups with MCI, PD and PD-MCI and normal controls will be presented which reveal hyper- and hypometabolic regional differences between groups. Expression of specific AD-related metabolic pattern (ADRP) and Parkinson disease cognitive pattern (PDCP) recently identified using spatial covariance analysis with FDG/PET data, will be shown for individual subjects and its ability to differentiate between groups, and correlation with CSF biomarkers for AD will be discussed.

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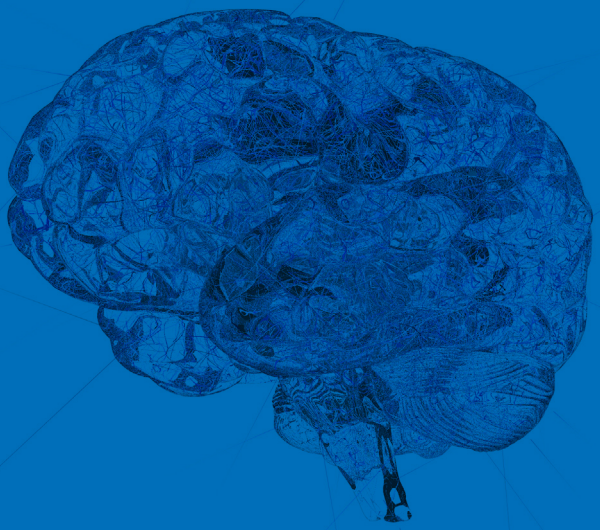

Abstracts

Young Neuroscientists Forum Ljubljana '15

www.sinapsa.org/SNC15/YNFL15
Cankarjev dom, Ljubljana, Slovenia
15 May 2015

Friday, 15 May, 08:40

The impact of upper motor neuron degeneration on respiration in wakefulness and sleep in amyotrophic lateral sclerosis

Judita Jeran, Lea Leonardis, Leja Dolenc Grošelj, Polona Klinar, Blaž Koritnik, Janez Zidar

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Amyotrophic lateral sclerosis (ALS) is characterized by degeneration of upper (UMN) and lower motor neurons (LMN), which eventually leads to respiratory insufficiency. The individual differences between patients in the presentation of respiratory insufficiency signs in wakefulness and sleep are marked and poorly understood. We hypothesized that they are related to the extent of UMN and respiratory LMN degeneration and aimed to describe this relationship.

We assessed the severity of UMN and respiratory LMN degeneration in 15 ALS patients who presented with at least one sign or symptom of respiratory insufficiency. Further, we correlated the degeneration pattern with several respiratory variables. For comparison we tested 14 healthy age, and sex matched participants.

We found that the patients with concomitant severe UMN and respiratory LMN degeneration were more likely to have normal pCO2 and HCO3 upon awakening, and a normal proportion of REM sleep as opposed to patients with severe LMN degeneration. In addition, these patients were also breathing faster than healthy participants ($p = 0.017$), and activated their accessory respiratory muscles in NREM sleep the most.

We conclude that the concomitant degeneration of UMN and respiratory LMN, but not an isolated degeneration of respiratory LMN, allows the development of a respiratory adaptation, similar to acclimatization to high altitudes. This adaptation leads to increased respiratory drive in sleep, and protects the patients from morning hypercapnia and loss of REM sleep. This compensation is initially protective, but can mask the respiratory vulnerability of these patients.

Keywords: amyotrophic lateral sclerosis, respiration, sleep, upper motor neurons, respiratory muscles

Friday, 15 May, 09:00

Stress affects survival of adrenal gland stem cells through leptin in Sprague Dawley rats

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Stress is an everyday challenge in the modern world. It is strongly engaging the hypothalamic-pituitary-adrenal axis. Acute stress promotes ″fight-or-flight″ response while chronic stress leads to a variety of diseases. Leptin is an important hormone affecting adrenal gland, the chief organ of the stress response. In this study we hypothesize that leptin plays an important role in adrenal gland stem cells survival through its receptor. 22 male, 24 female (NON-OVX) and 24 ovariectomized female (OVX) of 4-months-old Sprague Dawley rats were used in the study. Animals were further divided in control, acute and chronic stress groups. Adrenal glands of 7-months-old rats were immunostained with leptin receptor (Ob-R) primary antibody and secondary FITC-conjugated fluorescent antibody. Images were photographed by Leica TCSSP8 confocal microscope and analyzed by ImageJ software.

We noticed immunostaining in the stem cells layer of adrenal gland. NON-OVX control group had statistically higher immunostaining intensity than OVX control group ($F = 6.2$; $p < 0.05$). Males had statistically higher fluorescence intensity than NON-OVX upon acute stress ($F = 6.56$; $p < 0.05$). Chronic stress did not produce statistical significances among groups, but immunostaining intensity was stronger in all groups than upon acute stress. Important statistical significance in immunostaining intensity occured inside animal groups – males ($\chi^2(2) = 12.31$; $p = 0.002$), NON-OVX ($\chi^2(2) = 12.11$; $p = 0.002$) and OVX ($\chi^2(2) = 15.15$; $p = 0.0005$).

Leptin might be involved in homeostasis in females and in general stress regulation. Since leptin regulates glucose uptake and inhibits stress-induced apoptosis this finding might indicate its important role in stem cells survival and long-term affect on stress response by adrenal gland.

Keywords: stress, adrenal gland, stem cells, leptin

Friday, 15 May, 09:20

Chronic social isolation reduces parvalbumin-positive interneurons in the medial prefrontal cortex of adult rats: protection by fluoxetine and clozapine

Nevena Todorović, Dragana Filipović

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Depression is one of the leading causes of disability worldwide. Recent studies have indicated that there is a link between depressive symptoms and disregulation of GABAergic system. Decrement of parvalbumin (PV)-positive GABAergic interneurons in the medial prefrontal cortex (mPFC), brain area highly implicated in depressive symptomatology, has been observed in psychiatric patients. We aimed to determine whether chronic social isolation of adult male Wistar rats for a period of 21day, which represents an animal model of depression, affects the number of PV-positive interneurons in medial precentral (PrCm) area, cingulate cortex, area 1 (Cg1), prelimbic (PrL), infralimbic (IL) area and dorsal peduncular cortex (DP) of mPFC. Since GABAergic signaling has been proposed as a potential therapeutic target for antidepressants or antipsychotics, we examined if the treatment with antidepressant fluoxetine, a selective serotonin reuptake inhibitor (15 mg/kg/day) or atypical antipsychotic clozapine (20 mg/kg/day) administered during the 21day may offer the protection from eventual isolation-induced alternation in PV-positive GABAergic interneurons. Results of immunofluorescence analysis revealed that social isolation reduced number of PV-positive interneurons in all examined areas of mPFC. Fluoxetine prevented reduction of number of these GABAergic interneurons in PrCm, PrL and DP, while clozapine only protected PrCm and PrL area. Finally, fluoxetine administration to control rats caused decrement in number of PV-positive interneurons in Cg1, while clozapine-treated control animals exhibited reduced number of these interneurons in DP. In summary, chronic administration of fluoxetine and clozapine showed area specific protection of PV-positive interneurons in the mPFC from deleterious effect of chronic social isolation.

Keywords: parvalbumin, medial prefrontal cortex, chronic social isolation, fluoxetine, clozapine

Friday, 15 May, 10:00

The role of medial prefrontal cortex in uncertainty-based decision making in rats

Nace Mikuš, Johannes Passecker, Thomas Klausberger

Center for Brain Research, Department for Cognitive Neurobiology, Medical University Vienna, Austria

The prefrontal cortex plays a crucial role in decision making in humans with a certain degree of functional specialisation of the prefrontal subregions. The current state of the art implies that the lateral, ventral and medial areas of the prefrontal cortex might encode different aspects of the decision process, namely: representing various states of the environment, predicting the different outcomes of alternative choices and updating the desirability of alternative actions, respectively. Additionally, the dorsolateral cortex is believed to be involved in risk-based decision making.

The medial prefrontal cortex in rats and the anterior cingulate cortex and dorsolateral prefrontal cortex in humans seem to share some functional and anatomical features. To shed further light on how specific parts of the prefrontal cortex contribute to reward-based decision making and processing of risk we have recorded the activity of cells in the medial prefrontal cortex in rats while performing a risk-based decision task. For this the rat chooses between a safe arm with a fixed reward and a risky arm where it gets a bigger reward with different probabilities across different blocks.

Using a reinforcement learning model to model the behaviour of the rat, we observed cells that are linked to choice and outcome value, othercells that might be involved in the animals' internal representation of the reward or the probability of positive outcome related to each choice. Furthermore we investigated how the uncertainty of the rewards reflects in the activity of cells. Overall, our data indicate that different aspects of the behavioural task are supported by divers activity patterns of prefrontal neurons.

Keywords: medial prefrontal cortex, decision making, risk

Friday, 15 May, 10:20

The vulnerability of the structural connectome to stroke in older adults

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Strategic infarction describes how lesions in particular locations have disproportionate effects on brain function. Strategic locations can reflect "bottlenecks" in functional networks for movement or cognition. Another hypothesis is that strategic effects are an emergent property of the brain's network architecture. We aimed to examine the effect of simulated lesions on the global properties of the structural connectome. Simulated lesions were made in two sets of locations: i) subcortical nuclei recognised as sites of strategic infarction; ii) highly connected hubs that are part of the brain's "rich club", a group of highly interconnected hubs that mediate long-distance connectivity in the brain.

39 healthy volunteers aged 53-93 years underwent diffusion-weighted MRI. Whole-brain tractograms were represented as network graphs. Lesions were simulated by removing a node and its connections from the graph. The proportional change in network global efficiency due to each lesion was calculated.

Lesions of rich-club nodes led to larger reductions in global efficiency than lesions outside the rich club. Lesions of the precunei produced the largest effect. Among subcortical nodes, vulnerability was highest for thalamic lesions. Age was positively correlated with vulnerability to lesions in the thalami.

The structural connectome of healthy individuals aged over 50 is vulnerable to strategic lesions of rich-club nodes, though some of the key hubs are in sites rarely affected by stroke. The vulnerability of the structural connectome to thalamic stroke increases with age. This is likely to be a factor in the influence of age on stroke outcome.

Keywords: stroke, strategic infarction, ageing, brain network, lesion simulation

Friday, 15 May, 10:40

A simple and cost-effective q EEG evaluation shows marked differences between early Alzheimer's disease patients and controls

Bruna Pikš, Andreja Emeršič, Jurij Dreo, Zvezdan Pirtošek

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Due to population ageing prevalence of Alzheimer's disease is expected to rise, therefore early diagnosis is paramount. Currently, AD diagnosis relies largely on clinical presentation and exclusion of other causes of dementia. To increase the diagnostic accuracy the use of imaging and CSF biomarkers is encouraged, however their sensitivity and specificity is limited and procedures for their assessment are either invasive or expensive. EEG is a non-invasive, cheap method that might offer time-sensitive biomarkers with comparable performance.

A 20 min long 64-channel resting EEG with eyes open (EO) and closed (EC) was recorded on 14 AD patients and 37 controls. Recordings were segmented, FFT transformed and averaged for EO and EC separately. Peak alpha frequency (PAF), the frequency at which the alpha band (7-13 Hz) exhibits largest power, was determined for each channel and compared between groups. The average reference was used for all analyses.

Differences were most evident in EO ($p < 0.001$) with patients having lower PAF than controls; specifically at fronto-central and temporal regions. Differences in EC were somewhat less pronounced but still significant ($p < 0.01$) with patients having lower PAF at frontal and centro-parietal regions. Patients consistently exhibited lower PAF across all scalp regions.

The main objective of this study was to assess the difference in PAF between AD patients and controls. Our results indicate that quantitative EEG is a promising method that could aid in AD evaluation. Its low cost and noninvasiveness make it particularly appealing for wide scale application in clinical practice.

Keywords: Alzheimer's disease, EEG, frequency analysis, alpha band

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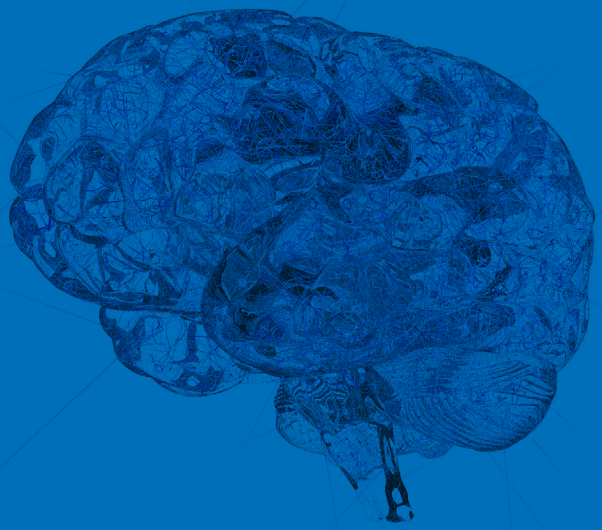

Abstracts

SNC'15 Posters

www.sinapsa.org/SNC15/YNFL15
Cankarjev dom, Ljubljana, Slovenia
15–17 May 2015

CEL.01 Saturday, 16 May, 12:00
[Poster section: Cellular neuroscience A]

Adrenergic receptor stimulation leads to distinct intracellular cAMP and Ca^{2+} dynamics in single rat astrocytes

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Astrocytes previously regarded as only supportive cells are now considered important players in the central nervous system function. They express a variety of receptors on the cell surface, including G-protein coupled α- and β-adrenergic receptors (ARs) that can respond to release of noradrenalin from locus coeruleus neurons either with increase in secondary messengers Ca^{2+} or cAMP, respectively. Activation of AR signaling pathway in astrocytes modulates various cellular processes including cellular metabolism. Astrocytes are the only cells in the CNS that store glycogen. Upon AR stimulation glycogen can be metabolized to glucose, from which lactate or even gliotransmitters glutamate and ATP can be synthesized. Both glucose and lactate can be transferred to neurons and used as energy fuel. Important regulators of AR-induced glucose and lactate formation in astrocytes are cAMP and Ca^{2+}, however detailed measurements of these second messengers in living astrocytes are lacking. To study the real-time dynamics of cAMP and Ca^{2+} signaling in single rat astrocyte upon β- and α-AR stimulation, we used confocal microscopy in combination with fluorescent FRET-based cAMP/PKA nanosensor AKAR2 and fluorescent Ca^{2+} indicator Fluo4-AM dye. Activation of β-ARs led to persistent increase in cAMP-dependent PKA activity ~100 s upon stimulation (tonic response), however activation of α1-ARs caused Ca^{2+} oscillations with peak amplitudes already 4 s upon stimulation (phasic response). We suggest that tonic cAMP signaling may have a role in slow integrating cellular processes. Moreover, activation of cAMP-signaling pathway facilitated α1-AR induced Ca^{2+} oscillations and vice versa, indicating that in astrocytes these two pathways interact.

Keywords: astrocytes, adrenergic receptors, cAMP, Ca^{2+}

CEL.03 Saturday, 16 May, 12:00 [
Poster section: Cellular neuroscience A]

Time-dependent regulation of membrane fusion, vesicular release and Ca^{2+} signalling by cholesterol in electrically excitable and non-excitable cells

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Cholesterol, an essential component of cellular membranes, is crucial for regulated membrane fusion and calcium signaling. Using two physiologically distinct cell types, electrically excitable lactotrophs and non-excitable astrocytes, we performed high-resolution patch-clamp measurements to determine the effects of cholesterol depletion and replenishment on dynamics of membrane fusion. Fluorescence measurements revealed that acute cholesterol depletion from lactotrophs increases $[Ca^{2+}]_i$, promotes membrane fusion and augments the release of prolactin (PRL). In astrocytes, acute cholesterol depletion decreased $[Ca^{2+}]_i$, yet the release of fluorescently-tagged atrial natriuretic peptide (ANP.emd) was enhanced, suggesting that acute cholesterol depletion stimulates exocytosis directly, through changes in membrane biophysical properties. Long-term exposure to methyl-β-cyclodextrin (MβCD), cholesterol depleting agent, decreased $[Ca^{2+}]_i$ and inhibited membrane fusion in both cell types. Cholesterol replenishment to above-control concentration rescued the frequency of membrane fusion only partially, an effect likely related to physiological role of cholesterol in the membrane fusion.

Keywords: cholesterol, membrane fusion, vesicular release, regulated exocytosis, calcium

CEL.05 Saturday, 16 May, 12:00
[Poster section: Cellular neuroscience A]

Hypothermia does not reverse cellular responses in infection-sensitised hypoxic-ischemic neonatal brain injury

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Bacterial lipopolysaccharide (LPS) injection prior to hypoxia-ischemia (HI) significantly increases HI brain injury in 7 day-old (P7) rats. In addition, therapeutic hypothermia (HT) is not neuroprotective in this setting. This study was designed to investigate the underlying cellular mechanisms in this double hit model of infection-sensitised HI brain injury.

P7 rat pups were injected with either vehicle or LPS, and after a 4 h delay were exposed to left carotid ligation followed by global hypoxia inducing a unilateral stroke-like HI injury. Pups were randomised to the following treatments: (1) vehicle treated pups receiving normothermia treatment (NT) (Veh-NT; n = 40); 2) LPS treated pups receiving NT treatment (LPS-NT; n = 40); 3) vehicle treated pups receiving hypothermia (HT) treatment (Veh-HT; n = 38); or 4) LPS treated pups receiving HT treatment (LPS-HT; n = 35). On postnatal day 8 or 14, western blot analysis or immunohistochemistry was performed to examine neuronal death, apoptosis, astrogliosis and microglial activation.

LPS sensitisation prior to HI significantly exacerbated apoptotic neuronal loss. NeuN was significantly reduced in the LPS-NT and LPS–HT groups ($p = 0.008$). Caspase-3 activation was significantly increased in the LPS sensitised groups ($p < 0.001$). A significant increase in astrogliosis (GFAP expression, $p < 0.001$) was seen, as well as a trend towards increased microglial activation (Iba 1 expression, $p = 0.051$) in LPS sensitised animals. Treatment with HT did not counteract these changes.

LPS-sensitised HI brain injury in newborn rats is mediated through neuronal death, apoptosis, astrogliosis and microglial activation. In this model, treatment with HT does not ameliorate these changes.

Keywords: hypoxia-Ischemia, hypothermia, infection, lipopolysaccharide, neuroprotection

CEL.02 Sunday, 17 May, 12:00
[Poster section: Cellular neuroscience B]

Extracellular S100B internalization and positive trafficking vesicles by astrocytes culture

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The astroglial S100B is primarily intracellular protein that can be secreted in response to inflammatory stimuli or released by damaged cells. In nanomolar extracellular concentration, it exerts neuroprotective action; in higher concentrations, however, it may induce neuronal apoptosis and activation of glia. Despite most action of extracellular S100B is triggered by protein binding to receptor for advanced glycation end products (RAGE), little is known about how this protein is cleared from the extracellular space by the brain cells. We here examined the astroglial uptake process of exogenous S100B-Alexa488 and studied trafficking of fluorescently labeled protein following its internalization by the time-lapse confocal microscopy. Cultured astrocytes internalized fluorescent S100B to mobile vesicles in a time dependent manner. In cells co-incubated with S100B-Alexa488 and Dextran546, a fluid phase uptake marker, a time-dependent increase in fluorescence colocalization was found (ranging from 26.5 ± 4.4 % at 15 min to 82 ± 1.8 % at 24 h), indicating that two molecules initially internalized to distinct vesicles, but were subsequently routed to the common compartment. In support, S100B-Alexa488-positive vesicles colocalized with immunocytochemically labeled endosomes/lysosomes and with lysotracker dye (38.5 ± 1.8 %) over time. The fraction of directionally moving S100B-Alexa488-positive vesicles also increased over time (from 2.2 % at 15 min to 13 % at 24 h), while cell stimulation with ATP reduced mobility of vesicles, indicating calcium-dependent regulation of mobility. Our findings indicate a new physiological role for astrocytes in vivo, as being cellular elements involved in removal of excess extracellular S100B to mitigate its toxic effects that may compromise brain functions.

Keywords: S100B, astrocytes, vesicle trafficking

CEL.04 Sunday, 17 May, 12:00
[Poster section: Cellular neuroscience B]

Mechanisms of TDP-43 propagation between cells in ALS patients

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Amyotrophic lateral sclerosis (ALS) is an adult onset disorder, which is phenotypically characterized by progressive muscle weakness and neuropathologically by degeneration of upper and lower motor neurons and frontal cortex. TDP-43 protein was identified as a major component of the ubiquitinated cytoplasmic inclusions in 97 % of all ALS cases, whether sporadic or familial.

Structurally, TDP-43 belongs to the heterogeneous nuclear ribonucleoprotein (hnRNP) family and consists of two RNA recognition motif domains (RRM-1 and RRM-2), nuclear localization signal (NLS), nuclear export signal (NES) and a Gly-rich C-terminal region, which mediates protein-protein interactions. In healthy individuals, TDP-43 is localized predominantly in the nucleus but constantly shuttles between the nucleus and the cytoplasm. In the affected cells, it is cleared from the nucleus and ubiquitinated, hyperphosphorylated and cleaved into aggregation-prone C-terminal fragments forms pathologic inclusions in the cytoplasm. Most of the mutations identified in ALS cases are located in the highly conserved region of the C-terminus of the TDP-43, which was shown to have prion-like properties. In recent years a new prion paradigm has emerged, which suggests that the misfolded proteins associated with neuronal deterioration can spread the pathology in a "prion-like" manner and thus facilitate the disease progression. Our aim is to determine the mechanisms, which allow TDP-43 spread between mammalian cells in the culture.

Keywords: ALS, TDP-43, prion-like propagation

CLI.01 Saturday, 16 May, 12:00
[Poster section: Clinical neuroscience A]

A pilot research of dance movement and social aspects of application of Argentine tango in the population of deaf people

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The deaf people are a group of people that is usally not involved in the dance, mainly because of the stereotiped beleive that the perception of music as a sound is mandatory to the dance.

Argentine Tango is a dance, danced in a couple, where the most important element is communication between the partners. The music is used in a creative way and the rhytm is not followed in a strict manner.

Individual interpretation of the music gives a solid base for working with deaf people. The movement is a consequence of the vibrations of music, which the dancer feels or a consequence of the inner rhytm, if the music is not present.

The aim of the research is application of Argentine Tango into population of deaf people and critical assesment of dance movement and social aspects of it.

The research gives an insight into new possibilities of the recreation and the socialization of deaf people, which have not been considered yet.

The research proves that in different fields of dance such as learnig new movements, research of communication in the couple and comprehension of the space, deaf people do not differ from people, who can hear. It also confirms that individual interpretation of the music in Argentine Tango enable deaf people to follow the music through the feeling of vibrations.

Keywords: dance, Argentine tango, deafness, deaf person

CLI.03 Saturday, 16 May, 12:00
[Poster section: Clinical neuroscience A]

Correlation between postural balance and clinical scores in patients with Parkinson's disease

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Postural instability is one of the four cardinal symptoms of Parkinson's disease (PD). Impaired balance can cause frequent falls and therefore contributes to patients' disability and quality of life. The pull test is the most commonly used measure in clinical assessment of the postural instability. Our study examines a possible way to more objectively assess postural instability in PD.

We tested 21 patients, the median age was 64 and 15 were male. Each participant underwent postural balance assessment which included two quiet stance tasks (eyes open and eyes closed) and an unstable sitting task (actively preserving balance while sitting on a wobble board). A force plate was used to measure centre-of-pressure (CoP) sway which was calculated from force plate signals. The following CoP derived parameters were calculated: area of best-fit ellipse, velocity, frequency and amplitude of CoP movement. Correlations between the CoP postural parameters and the clinical scores (Unified Parkinsons's disease Rating Scale Motor Examination, Hoehn and Yahr scale) were observed ($p < 0.05$).

In the quiet stance task with eyes open we found statistically significant correlations between the scores of clinical assessments and the CoP parameters. In the quiet stance task with eyes closed we found statistically significant correlations only with the velocity component of the CoP measurements. However, in the unstable sitting task, no statistically significant correlations were found between clinical assessment and CoP measurements.

The technique used for postural balance assessment represents a quantitative approach to assess the postural instability in PD patients that offers a more concise and reproducible way of measuring disease progression.

Keywords: Parkinson's disease, posture, postural mechanisms

CLI.05 Saturday, 16 May, 12:00
[Poster section: Clinical neuroscience A]

Subchronic treatment with LEK-8829 for the determination of its antipsychotic properties

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LEK-8829 has D1 agonistic and D2 antagonistic properties on dopaminergic transmission. Prolonged treatment with antypsichotic drugs, such as D2 antagonist haloperidol often produces unwanted inhibitory psychomotor effects. It has been proposed that the unusual antagonistic/agonistic dopaminergic profile of LEK-8829 may confer a lower propensity of LEK-8829 for the induction of above mentioned unwanted psychomotor effects. The aim of our study was for the first time to evaluate the effects of prolonged pretreatment with LEK-8829 on the expression acutely evoked psychomotor behavioral parameters.

In two experiments, animals were treated daily for 21 days with LEK-8829 and haloperidol in doses 2 mg/kg and 0.2 mg/kg, respectively. We measured the catalepsy on the 1st day, on the 21st day and on the 28th day. In third experiment animals were treated daily for 21 days with LEK-8829 and haloperidol in doses 2 mg/kg and 0.2 mg/kg, respectively. Before and after the treatment we do the test inhibition of amhetamine-induced locomotion activity with test compounds (LEK-8829 and haloperidol).

Results show that haloperidol 2 mg/kg and 0.2 mg/kg produced significant catalepsy in rats. LEK-8829 2 mg/kg shows similar catalepsy effect as haloperidol 0.2 mg/kg (on the 1st day). LEK-8829 and haloperidol 2 mg/kg shows similar catalepsy effect on the 21st day, but on the 28th day LEK-8829 does not show increase catalepsy effect. In third experiment LEK-8829 retained its efficacy for the inhibition of amphetamine-induced psychomotor stimulation the efficacy of haloperidol was significantly diminished.

LEK-8829 is better antipsychotic than haloperidol because it causes less EPS (proven with catalepsy test) and does not show supersensitivity.

Keywords: LEK-8829, dopamine D1 agonist, dopamine D2 antagonist, haloperidol, subchronic treatment

CLI.02 Sunday, 17 May, 12:00
[Poster section: Clinical neuroscience B]

EEG mu rhythm power oscillations and decrease in thalamus size in patients with amyotrophic lateral sclerosis

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EEG mu rhythm is generated over the sensorimotor cortical regions while its pacemaker is thalamus. There are few reports of the decrease of mu power and of thalamic neuron degeneration in patients with amyotrophic lateral sclerosis (ALS). Our aim was to evaluate whether they can be used as a disease marker. 17 ALS patients were compared to healthy controls. EEG was recorded in supine position with eyes closed. Three consecutive recordings were done on 11 of the patients in three months interval. Power analysis was performed and log transformed data were statistically analysed. MRI head scans were performed on 12 of the patients to compare with healthy controls. Diffusion tensor imaging was used to run Tract-Based Spatial Statistics (TBSS). Thalami mean diffusivity and volumetric measurements were also assessed. Mu rhythm power was significantly increased in patients compared to controls. ANOVA repeated measures with post hoc testing showed significant differences between 1st and 3rd, and 2nd and 3rd EEG recording in patients with decrease of mu power over time. We found no significant changes with TBSS and in thalami mean diffusivity but we observed significantly reduced thalami volumes in patients. We expected power decrease of EEG mu rhythm in ALS patients but we observed an increase compared to controls and gradual decrease in patients over time. The volumetric decrease in patients' thalamus shows nerve cell degeneration. All findings could be due to interplay of compensatory mechanisms early in disease and cell loss in the sensorimotor cortex and thalamus with disease progression.

Keywords: ALS, EEG, mu rhythm, MRI, thalamus

CLI.04 Sunday, 17 May, 12:00
[Poster section: Clinical neuroscience B]

Cognitive functioning and temperament in infants with and without neurological problems

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In pilot research we investigated relationship between early characteristics of temperament and cognitive functioning in infants with two instruments. A caregiver report of temperament for infants - Infant Behaviour Questionnaire–Revised (IBQ–R) measures 3 dimensions: Surgency, Negative Affect and Effortful Control. Fagan Test of Infant Intelligence (FTII) which measures preference for novelty (visual) stimulus was administered as a measure of infant intelligence.

We tested 33 infants at 27, 29, 39 and 52 weeks of gestational age. Experimental group consisted of 12 infants with various neurological problems. Control group consisted of 21 infants without neurological problems. After infants were tested with FTII, parents completed the IBQ-R. Results showed no significant difference in effectiveness of information processing between the two groups ($U = 51.00$, $p = .476$) nor difference in Effortful Control on IBQ-R ($U = 52.00$, $p = .400$). Contrary to expectations younger infants were more successful in the novelty preference ($r = -.478$, $p < .05$). Older infants were reported to be more motor active and emotionally responsive ($r = .831$, $p < .001$) than younger infants. The study shows that the Fagan Test of Infant Intelligence measures only one aspect of cognitive functioning and that the IBQ-R seems to be useful tool in assessment of early behavioral characteristics in infants.

Keywords: infants, early cognitive functioning, early temperament traits

COG.01 Saturday, 16 May, 12:00
[Poster section: Cognitive neuroscience A]

Monetary incentive vs. social pressure: a neuroscientific investigation

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Accountability is typically introduced in organizations to enhance performance of agents. This positive performance effect is thought to occur because of increased cognitive effort and greater 'rationality' of decision making that accountability induces in human agents. The effects of imposing accountability are, however, not always positive, neither predictable, due to the fact that human decisions are not always analytical and are often subject to cognitive flaws. To enhance our understanding of what makes accountability effective requires an examination of how accountability affects fundamental drivers of cognition.

In this paper we examine the effect of accountability on cognitive control, which underlies the human ability to control impulses and think analytically. We aim to asses and compare the effectiveness of two accountability mechanisms, monetary incentive and peer pressure, and related cognitive mechanisms, as reflected in brain activity.

30 Slovenian financial managers took part in an fMRI recording while performing Eriksen Flanker Task (Eriksen & Eriksen, 1974). Results show that accountability provides a strong impetus for behavioural performance improvement, evident also in the pattern of brain systems activation, affecting both general speed of processing as well as efficiency of cognitive inhibition. While not evident in behavioural results, analysis of trial related brain responses reveals differences in the effect of monetary incentive and peer pressure.

Keywords: accountability, monetary incentive, peer pressure, cognitive control, Eriksen Flanker Task

COG.03 Saturday, 16 May, 12:00
[Poster section: Cognitive neuroscience A]

Stimulus modality and task difficulty in a 3-stimulus Oddball: an fMRI study

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The ability to detect and respond to rare stimuli is commonly studied using the Oddball paradigm, which involves sequential presentation of a standard stimulus sometimes interrupted by an occurrence of an "oddball" stimulus. In event-related potential research, the presentation of a rare stimulus that requires a response (target) reliably evokes a late positive component over the midline electrodes, dubbed P3b, whereas a rare stimulus that does not require a response (distractor) elicits a more central and slightly earlier P3a component.

These components are thought to reflect early attentional and memory processes and their significance has been demonstrated in studies involving both normal and clinical populations.

Due to its limited spatial resolution, EEG can not provide information about specific brain regions involved in the generation of the observed ERP components. The goal of the present study was thus to use fMRI to identify brain areas that show a marked response to oddball (target or distractor) compared to standard stimuli. In addition, we investigated which of these differences are stimulus modality specific, and which might reflect general attentional processes. Finally, as it has been shown to influence both P3a and P3b components, we also explored fMRI correlates of target-standard discrimination difficulty. To address these questions, 19 healthy participants performed a 3-stimulus oddball task in a 2 (visual/audio modality) x 2 (easy/hard discrimination) within-subjects counterbalanced factorial design while their brain activity was recorded using 3T fMRI. The results reveal specific patterns of activation related to task modality, stimulus type and task difficulty.

Keywords: attention, P3a, P3b, stimulus modality, task difficulty

COG.05 Saturday, 16 May, 12:00
[Poster section: Cognitive neuroscience A]

Visual deficits in dyslexia

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In recent years, dyslexia studies have more rigorously focused on possible cognitive sources of developmental dyslexia (Ramus, 2014; Ramus & Szenkovits, 2008; Vidyasagar & Pammer, 2009). Although phonological deficits seem to be prevalent in dyslexia, various studies are persistent in showing various visual deficits, at least in some dyslexic participants. It possible that developmental dyslexia originates from two separate cognitive sources, which may result in at least two independent subgroups of dyslexia (Lallier et al., 2009; Lobier & Valdois, 2015). It nonetheless remains an open question whether the existence of such subgroups is a regular phenomenon in all group studies with dyslexic participants, or not. As a part of a Genedys study (Cognitive, cerebral, and genetic origins of developmental language disorders; France, 2007-2010), 164 dyslexic children and 118 control children matched for age and non-verbal cognitive capacities were tested on their phonological awareness capacities, visual attention, and visual stress.

The results show that a vast majority shows the phonological deficits, whereas visual deficits are found in lower proportion of dyslexic children. Although the prevalence of visual deficits is stronger in dyslexic than in control participants, only few individuals have exclusively visual and no phonological deficits. These results confirm the presence of visual problems in a subgroup of dyslexics with phonological deficits, but cannot confirm the hypothesis about possible separate/unrelated sources of developmental dyslexia.

Keywords: dyslexia, abstract phonological representations, visual attention, visual stress

COG.07 Saturday, 16 May, 12:00
[Poster section: Cognitive neuroscience A]

Sources of difficulty in dance style acquisition

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The paper at hand examines the hypothesis that in addition to the motor component there are cognitive and psychological aspects influencing the perceived difficulty of learning dance style moves. This study is based on a behavioral motion capture experiment, including modified NASA Task Load Index questionnaires and semi-structured qualitative interviews focused on the sources of difficulty for the participants. A group of professional ballet dancers and a control group of non-dancers were presented with a short hip hop movement at a time and were subsequently instructed to perform it. Preliminary research findings confirm the hypothesis and reveal that the most reliable predictor of difficulty is complexity of the movement. However, according to the data other factors such as awkwardness, familiarity with or attitudes towards the movement have an impact on its difficulty rating. The qualitative results also reveal different strategies of assessing the difficulty of a given move. It remains to be seen how the performance outcomes, as captured by the AnimaZoo MoCap suit, relate to the participants' differences in expertise and difficulty assessments.

Keywords: task difficulty, dance style, motor learning, NASA TLX, AnimaZoo, motion capture

COG.09 Saturday, 16 May, 12:00
[Poster section: Cognitive neuroscience A]

Neural correlates of emotional and task-similar distraction of spatial working memory

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A crucial component of working memory (WM) is the ability to shield information from distraction. Distraction can stem either from similarity of distractors to the remembered material or from general attention-grabbing factors (sensory strength or emotional charge). The aim of the study was to examine the effects of different types of distractors on maintenance of position in spatial WM.

25 participants (8 male, age M(SD) = 23.2(3.0)) remembered the positions of round scrambled images (2 s) and used a joystick to move a circle to the remembered position after a delay (8 s), which was either empty (no distraction) or contained a presentation of a distractor (2 s)—a round image that was either scrambled (task-similar), neutral or negative. During the task, brain activity was recorded with a 3.0T fMRI.

We performed statistical tests for differences in activation (BOLD) between different distractors (scrambled, neutral and negative). Resulting activation maps were divided into 113 ROIs with an automated peak-searching algorithm. Based on the pattern of activation, identified regions were classified into those primarily responsive to either emotional or task-similar distraction.

Emotion responsive regions comprised ventral and medial prefrontal cortex, temporo-parietal junction, amygdala and posterior cingulate. The task-related group included typical task positive network nodes—dorso-lateral prefrontal cortex and posterior parietal cortex—and activation along middle frontal gyrus. The results confirm the basic dorsal-ventral distinction found in previous studies of visual WM and imply that engagement of separable but overlapping systems is necessary when confronted with emotional and task-similar distraction.

Keywords: spatial working memory, task similarity, emotional distraction

COG.11 Saturday, 16 May, 12:00
[Poster section: Cognitive neuroscience A]

The balance between proactive and reactive cognitive control in relation to personality traits in healthy young subjects

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Cognitive control is the ability to regulate, coordinate and sequence thoughts and actions to achieve internal behavioral goals. The dual mechanisms of control (DMC) framework proposed by Braver (2012) introduces a distinction between two qualitatively different modes of cognitive control: proactive and reactive. Proactive control is characterized by active maintenance of goal-related information in the working memory, while reactive control only utilizes attention when it is needed. However, it is still not clear how the two mentioned modes of cognitive control are influenced by different aspects of personality.

Healthy, young adults (N = 30, 15f; M_{age} = 22.57 years, SD_{age} = 1.74) were asked to participate in the 'AX'-type Continuous Performance Task (CPT) (Rosvold et al., 1956). Subjects' mode of cognitive control was determined by ERP responses recorded on a 32-channel EEG and their behavioral results on the AX-CPT. Furthermore, to test our initial hypothesis, four different personality questionnaires were included in the study: The Big Five Inventory (BFI) (John and Srivastava, 1999), Zuckerman's Sensation Seeking Scale (SSS-V) (Zuckerman, 1994), the BIS/BAS scale (Carver, 1994), and Barratt's Impulsiveness Scale (BIS) (Patton et al., 1995). Subjects were also required to complete the Iowa Gambling Task (Bechara et al., 1994) as an additional behavioral measure.

Behavioral results will be analysed in parallel with differences in latencies and amplitudes of ERP responses between different conditions, to establish patterns of proactive and reactive control and correlate them with personality traits.

Keywords: AX-CPT, cognitive control, personality traits, Iowa Gambling Task (IGT)

COG.13 Saturday, 16 May, 12:00
[Poster section: Cognitive neuroscience A]

Heart rate variability during experiencing audio and video stimulation

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Heart rate variability (HRV) is the physiological phenomenon of variation in the time interval between heartbeats. It is measured by the variation in the beat-to-beat interval. Cardiac activity is regulated through reflex loops (baroreflex, respiration, chemoreflex). This includes brainstem centers that regulate the relative activities of the sympathetic and parasympathetic efferent arms (Guyenet, 2013). Recent behavioral and neuroimaging studies have also identified several pathways by which cardiac vagal tone is linked to neural networks implicated in emotional and cognitive self-regulation such as midcingulate cortex, insula and amygdala (Thayer et al., 2009).

In our study we were interested in HRV while listening to music, during presentation of emotional facial expressions, and while immersed in imagery. To be able to later relate HRV to brain activity, we presented AV stimuli to our subjects and measured their HR during functional imaging inside the MR tomograph. HR was measured with PPG (photoplethysmogram) combined with a pulse oxymeter, which illuminates the skin and measures changes in light absorption due to variations of Hb/HbO_2 ratio. Measured AC component is directly attributable to variation in blood volume in the skin caused by the pressure pulse of the cardiac cycle. The experimental design enabled the analysis of the differences in HRV between different mental activities, content with a positive or negative co-notation, audio and video stimuli. Data were first carefully inspected for errors and then analyzed with the HRV library in the R statistical environment. Time domain and frequency domain methods were used for HRV analyses.

Keywords: heart rate variability, brain activity

COG.02 Sunday, 17 May, 12:00
[Poster section: Cognitive neuroscience B]

Neural substrates of imagery of different activities

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Mental imagery is a complex cognitive process that engages a multitude of different brain processes. It resembles the experience of perceiving an object without a physical stimulus. Despite existing research, it remains unclear, which areas of the brain subserve specific imagery processes. Researchers agree that many neural processes that underlie perception are also engaged in imagery. Depending on the modality of the imagined activity, mental imagery involves correspondent neural sensory mechanisms and is characterized by vivid re-experience of previously viewed, heard or otherwise experienced content. The aim of our study was to explore the neural substrates of imagery of different types of activities (locomotor, observation) and emotional content (positive, negative), and identify possible differences. 38 healthy, young adult participants were asked to imagine swimming, catching a baloon, kissing, observing a traffic accident, and observing somebody else swimming, while their brain activity was recorded using a 3T fMRI. The results revealed that imagery engages multiple brain systems: motor, emotional, perceptual, spatial, memory, sensory and cognitive control, with specific pattern of activity dependent on the type and content of imagery, indicating that there is no single "imagery system". Direct comparison between imagery conditons suggested that imagining emotional content compared to locomotor imagery, demands stronger involvement of limbic stuctures, whereas imagery of locomotor activities evokes stronger activation in motor regions of the brain. The comparison between imagery of locomotion vs. observing one revealed that both activate motor regions, however, imagery of observation also implicates regions related to memory retrieval, visuospatial and self-reflecting processes.

Keywords: fMRI, imagery, brain systems

COG.04 Sunday, 17 May, 12:00
[Poster section: Cognitive neuroscience B]

At the junction of the oldest and newest media

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The aim is to investigate the common denominators of human body as the oldest known media and the new media, as well as the perception of the viewer as an end user of performance work.

The defined common denominators between human body and new media objects are: the original data is not visible to the observer and it is only represented/communicated through an interface, which is limited by its own capability, data are modular so different elements can exist independently, data are variable and can be represented in multiple versions, data can be automated and transcoded.

In the field of performing arts the human body(ies) and new media object(s) can co-create theatrical moment, which is a result of parallel process of representation by a human on one side and the computer on the other, based on defined common denominators. Furthermore, human body(ies) and new media objects can co-depend on each other to produce complete information to the observer. Complex digital systems can also communicate with performer (sensors + programed response) but only in the paradigm of partnering (positive reaction of the system if parameters are met) and not in the paradigm of complex human response.

The effective strategy of implementation of human body(ies) and new media object(s) in performance space is finally defined by the multimodal perception capabilities of the observer.

Keywords: dance, new media, stage design, performance art, theatre

COG.06 Sunday, 17 May, 12:00
[Poster section: Cognitive neuroscience B]

fMRI correlates of visuospatial working memory capacity

Anka Slana, Martina Starc, Grega Repovš

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The capacity of working memory (WMC) to maintain visuospatial representations is highly limited (1 to 5 objects) and varies significantly across individuals. In a series of EEG studies Vogel et al. (2004) identified an ERP correlate of visual WMC. The goal of our study was to identify and investigate an fMRI analogue.

26 participants took part in an fMRI recording while performing a WM task in which they were asked to remember color, position or both properties of 2 or 4 presented objects. This enabled separate estimates of WMC for visual, spatial, and integrated information, as well as investigation of related brain activity.

Repeated measures ANOVA revealed significant effect of modality on WMC, reflecting highest WMC for visual, smaller for spatial, and smallest for integrated information. In agreement with independent subsystems hypothesis, correlation between visual and spatial WMC did not reach significance. WMC for integrated information however significantly correlated with individual's lowest performing (visual or spatial) system, showing that integration does not involve a separate representational system.

The analysis of brain activity revealed significant effect of memory load in frontal and parietal brain regions. Furthermore, the related increase in brain activity correlated significantly with visual WMC in right inferior frontal gyrus, with spatial WMC in left precuneus, and WMC for integrated information in left middle frontal gyrus. These results identify modality specific fMRI correlates of WMC, confirming that maintenance of visual, spatial, and integrated information depends on separable brain systems.

1. Vogel et al. (2004). Nature, 428(6984), 748-751.

Keywords: working memory, capacity, visuospatial integration

COG.08 Sunday, 17 May, 12:00
[Poster section: Cognitive neuroscience B]

Neurofeedback and anxiety level reduction in young athletes

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Neurofeedback is a learning procedure. It works by allowing people to watch their brain activity, and find a way to improve it. Neurofeedback monitors brain activity, then brainwaves are fed back to the individual in some form displayed on screen, and the participant learns to control it.

The main purpose of our research was to evaluate the results of neurofeedback training on sportsmen's anxiousness and wellness.

Five neurofeedback trainings were carried out with 20 college students (athletes 16-19 years old). EEG was recorded from 2 cortical leads (O1, O2) during 15 min of relaxation. Alpha-rhythm power was transformed into the line on the screen. Anxiety level (Spielberger and Teylor scales) and self-reports was collected before and after last neurofeedback training. Alpha, beta and theta power was calculated at the beginning and at the end of each session. Statistical analysis was done using SPSS software package.

Students showed a trend toward decreased beta power and increased alpha power from the beginning to the end of the relaxation period. According to correlation analysis there were a lot of significant correlation between brain activity and anxiety level in male athletes, but no significant correlations in females. We also found a decrease of the reactive anxiety only in males. According to the self-reports, most of students became more concentrated, less anxious, had better sleep and some of them forgot about headaches.

These results suggests that EEG-neurofeedback can positively influence the psychological state (reduce reactive anxiety) and sports performance of the students.

Keywords: neurofeedback, EEG, anxiety, athletes

COG.10 Sunday, 17 May, 12:00
[Poster section: Cognitive neuroscience B]

Effects of visual stimuli characteristics to the information processing in children with autism – outline of a study

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According to DSM-5 (APA, 2013), autism spectrum disorder (ASD) is defined as a neurodevelopmental disorder featuring qualitative impairment in social interactions, verbal and non-verbal communication with restricted and repetitive patterns of behaviour and interests. In studies, stimuli triggered by computer screen are used in order to capture and reveal eye gaze fixation patterns. Eye-tracking studies investigate whether individuals with ASD tend to focus less on communicator's eyes while gathering all the necessary information from the mouth region as the character speaks, or from the objects in a background, which attracts their attention. Inconsistent findings suggest that this could highly depend on the nature of stimuli that are used. Few studies found that abnormal eye gaze fixation patterns in participants with ASD were present only to ecological stimuli (movies and pictures with human actors), but appeared to be normal to less realistic depictions, such as cartoons. It remains unknown if a person with ASD, who shows a normal response to stimuli, can make any use of the information available.

In our study we present participants a series of human-actor and cartoon situations seen in a film. We compare eye gaze fixation patterns and test the information gain by film-related questions. We compare two groups: children with ASD and healthy controls, matched by age and sex. Entrance criteria for our participants is healthy children above 5 years from a local community, screened by Bayley III and the Autism Screening Questionnaire and children with ASD which are already receiving the programme of rehabilitation at URI Soča, Ljubljana. Children with severe hearing and/or visual impairment are excluded from the study. Data are collected by using an eye-tracker and two groups are compared by applying two-way ANOVA.

Keywords: autism spectrum disorder, eye-tracker, ecological stimuli, cartoon, information processing

COG.12 Sunday, 17 May, 12:00
[Poster section: Cognitive neuroscience B]

The effect of personal prayer on resting heart rate variability

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Increased resting heart rate variability (HRV) parameters, indicating parasympathetic (PSYM) modulation, are well acknowledged independent protective factors against cardiovascular diseases and mortality. It is known that meditation increases PSYM modulation of the heart rate. However, it is not known if prayer, which in our cultural environment best resembles meditational state of mind, affects resting HRV parameters.

The aim of this study was to examine whether PSYM modulatory activity is affected by a personal catholic prayer. For this purpose we compared a high frequency (HF) band of HRV, indicating PSYM modulation, before and during a personal prayer in subjects who regularly pray.

This cross-sectional study included 15 healthy subjects (age 37 ± 12, 5 males), who regularly pray. The subjects sat in a quite room equipped with two wrist ECG electrodes for the heart rate measurement and a plethysmographic belt around their thorax for breathing rate control. After 15 minutes rest they performed a personal prayer for 15 minutes. By using five minutes long ECG recordings values of HF band of HRV were compared between the resting state and personal prayer.

We found statistically significant lower average value of HF band of HRV during personal prayer in comparison to the resting state ($p = 0.035$).

Preliminary results of our study showing decreased values of HF band of HRV during the personal prayer might indicate that personal prayer, in contrast to the meditation, decreases PSYM modulatory control of the heart rate.

Keywords: heart rate variability, prayer, autonomic nervous system

MOL.01 Saturday, 16 May, 12:00
[Poster section: Molecular neuroscience A]

GAP43 and CASP3 increase after onset of stroke in mouse

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Onset of stroke is followed by panoply of events balancing the inflammation to subsequent recovery or final deterioration. GAP43 is a protein involved in neurite outgrowth during development and thereby it was considered as a marker of regeneration, while CASP3 represented the other side of Janus-faced cascades. However, recently it has been discovered that GAP43 is a ligand of CASP3 mediated receptor endocytosis. In this study, using a GAP43-GFP-luc transgenic mouse strain carrying a bioluminescent reporter for GAP43 and in vivo bioluminescence essay for detecting CASP3 activity, we demonstrated that the initial acute increase in CASP3 and GAP43 expression is synchronous and moreover colocalized. The in vivo approach of CASP3 and GAP43 colocalization imaging using VivoGlo™ CASP 3/7 substrate (Z-DEVD-Aminoluciferin) was further validated and quantified by immunofluorescence. Confocal imaging enabled precise counting of positively stained cells and 3D reconstruction of fluorescent signal achieved by immunohistochemistry. Colocalization with CASP3 was present in 82 % GAP43 positive cells. This suggests that at acute stages increase in CASP3 is not exclusively related to neuronal death and apoptosis, but that GAP43 and CASP3 might be a part of common molecular pathway, both representing constituents in early positive response after an ischemic event.

Keywords: GAP43, CASP3, MCAO

MOL.03 Saturday, 16 May, 12:00
[Poster section: Molecular neuroscience A]

The association of rs13212041 polymorphism in 5-HT1B receptor gene and akathisia in haloperidol-treated patients with schizophrenia

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Schizophrenia is a serious chronic psychiatric disorder with neurobiological basis still unclear. Some patients do not respond satisfactorily to antipsychotics, while others develop extrapyramidal side-effects (EPS). In addition to the dopaminergic system, serotonergic mechanisms might be also involved in EPS, either by the effects on dopamine release or via serotonergic receptors. The aim of the study was to examine the association of 5-HT1B receptor gene with acute EPS in 200 male schizophrenic patients following 2 weeks haloperidol therapy. Simpson Angus Rating Scale for Extrapyramidal Side Effects (SAS), Barnes Akathisia Rating Scale (BARS) and Extrapyramidal Symptom Rating Scale (ESRS) were used to evaluate the EPS severity in schizophrenia-diagnosed patients (DSM-IV criteria). Genotyping of rs13212041 polymorphism in 5-HT1B receptor gene was performed using Real-Time PCR following extraction of blood DNA. The results were evaluated using chi2 test and Kruskal-Wallis test followed by Dunn's Multiple Comparison test. EPS appeared in 52.5 %, akathisia in 22.5 %, acute dystonia in 18.5 % and dyskinesia in 32.0 % patients with schizophrenia. The results demonstrated no differences in the genotype frequencies of 5-HT1B receptor gene polymorphism between patients subdivided according to EPS, acute dystonia and dyskinesia. However, the distribution of rs13212041 genotypes was significantly different between schizophrenia patients subdivided according to akathisia, suggesting higher frequency of TT genotype carriers in patients with akathisia. In line with this finding, patients carrying TT genotype had significantly higher BARS scores when compared to carriers of CC genotype. These results suggest potential involvement of serotonergic system in the development of akathisia following haloperidol treatment.

Keywords: schizophrenia, haloperidol, extrapyramidal side-effects, 5-HT1B receptor gene, rs13212041 polymorphism

MOL.05 Saturday, 16 May, 12:00
[Poster section: Molecular neuroscience A]

Structural species of c9orf72 expanded repeat DNA

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Amyotrophic lateral sclerosis (ALS) and frontotemporal lobar degeneration (FTLD) are devastating neurodegenerative diseases that form two ends of a complex disease spectrum and share aberrant RNA processing. The G4C2 hexanucleotide repeat expansion, located in the first intron of the C9ORF72 gene, represents a major genetic hallmark of both ALS and FTLD in populations of European origin. Several novel mechanisms have been proposed on how the expanded repeats contribute to disease, as the repeats enable: the formation of complex DNA and RNA structures; affect the level of RNA transcription and expression of C9ORF72 protein; influence processing and formation of toxic RNA foci, which may sequester and inactivate RNA binding proteins; and finally even undergo repeat-associated non-ATG-translation (RAN translation) resulting in accumulation of a series of dipeptide repeat proteins. All of the proposed mechanisms start with the transcription of the expansion, where undoubtedly the structure of the repeat DNA plays an important role. Due to its high guanine and cytosine content, both the expanded repeat DNA as well as the transcribed RNA can form several exotic nucleic acid structural species, such as G-quadruplexes, R-loops and hairpins. Using circular dichroism spectroscopy and nuclear magnetic resonance, we show that rather than being structurally uniform, based on sequence length, DNA G-quadruplexes can form either inter- or intra-molecularly in either parallel or anti-parallel orientation. This structural heterogeneity likely exists in vivo and should be taken into account when studying the role of expanded repeats in disease pathogenesis.

Keywords: ALS, FTLD, expanded repeats, G4C2, G-quadruplex

MOL.07 Saturday, 16 May, 12:00
[Poster section: Molecular neuroscience A]

Chronic oral D-galactose treatment affects cognitive performance in rats

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Chronic injection of D-galactose in rodents simulates the symptoms of natural senescence leading to cognitive fading and motor skill enervation and thus represents a reliable brain aging model. However, effects of oral D-gal treatment concerning cognitive abilities still remain poorly investigated. In order to study possible changes in synaptic integrity that may underlie cognitive dysfunction, three-month old male Wistar rats were treated for 6 weeks with D-gal (200 mg/kg or 500 mg/kg, dissolved in drinking water), and subjected to object recognition test (ORT) and object location test (OLT) to asses cognitive performance. Also, the expression of syntaxin-1 and synaptophysin, key components of the synaptic vesicle docking/fusion machinery and post-synaptic scaffolding protein PSD-95 were determined by Western blot technique in crude synaptosomal fraction of prefrontal cortex (PFC) and hippocampus (HIP). Two applied behavioral tests indicated impairment of both spatial and non-spatial memory of D-gal treated rats, compared to control group. Protein expression analysis showed that both D-gal treatments decreased syntaxin-1 protein level in PFC and HIP, while synaptophysin remained unchanged. Interestingly, cortical PSD-95 was increased in both treated groups, while in HIP only higher dose of D-gal augmented its level. These findings suggest that chronic oral D-gal exposure might modulate the expression of synaptic proteins essential for neurotransmission and synaptic plasticity affecting memory and learning skills. Therefore,applied treatment may be considered as an additional model of accelerated brain aging in rats, although oral D-gal induced alterations need to be further investigated.

Keywords: D-galactose,cognitive impairment, synaptic proteins

MOL.09 Saturday, 16 May, 12:00
[Poster section: Molecular neuroscience A]

10 years of ibogaine research in Slovenia

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The root bark of iboga plant - Tabernanthe iboga has been used traditionally in Central Africa as a psychoactive substance in religious rituals, while in smaller doses it is appreciated due to its stimulant properties. The iboga root bark, iboga extract or pure ibogaine are being recognized in the West as an anti-addiction remedy and their use is increasing. The project aims to disclose the common mechanism of action at these seemingly diverse indications for iboga use, to predict eventual adverse effects and to build the grounds for its safe and beneficial utilization.

Our results showed that ibogaine triggers adaptation of house keeping metabolism. Under the initial energy load this results in a stabile shift in epigenetic landscape that improves cellular energetic state and can be considered as nootropic. While healthy organism profits from improved fitness and mental performance and can withstand higher stress without risking a disease, due to the same principles ibogaine provides beneficial support at the recovery after diseases including addiction syndrome.

Keywords: ibogaine, addiction, detoxification, energy metabolism, psychedelic

MOL.02 Sunday, 17 May, 12:00
[Poster section: Molecular neuroscience B]

Stress affects survival of adrenal gland stem cells through leptin in Sprague Dawley rats

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Stress is an everyday challenge in the modern world. It is strongly engaging the hypothalamic-pituitary-adrenal axis. Acute stress promotes ″fight-or-flight″ response while chronic stress leads to a variety of diseases. Leptin is an important hormone affecting adrenal gland, the chief organ of the stress response. In this study we hypothesize that leptin plays an important role in adrenal gland stem cells survival through its receptor.

22 male, 24 female (NON-OVX) and 24 ovariectomized female (OVX) of 4-months-old Sprague Dawley rats were used in the study. Animals were further divided in control, acute and chronic stress groups. Adrenal glands of 7-months-old rats were immunostained with leptin receptor (Ob-R) primary antibody and secondary FITC-conjugated fluorescent antibody. Images were photographed by Leica TCSSP8 confocal microscope and analyzed by ImageJ software.

We noticed immunostaining in the stem cells layer of adrenal gland. NON-OVX control group had statistically higher immunostaining intensity than OVX control group ($F = 6.2$; $p < 0.05$). Males had statistically higher fluorescence intensity than NON-OVX upon acute stress ($F = 6.56$; $p < 0.05$). Chronic stress did not produce statistical significances among groups, but immunostaining intensity was stronger in all groups than upon acute stress. Important statistical significance in immunostaining intensity occured inside animal groups – males ($\chi^2(2) = 12.31$; $p = 0.002$), NON-OVX ($\chi^2(2) = 12.11$; $p = 0.002$) and OVX ($\chi^2(2) = 15.15$; $p = 0.0005$).

Leptin might be involved in homeostasis in females and in general stress regulation. Since leptin regulates glucose uptake and inhibits stress-induced apoptosis this finding might indicate its important role in stem cells survival and long-term affect on stress response by adrenal gland.

Keywords: stress, adrenal gland, stem cells, leptin

MOL.04 Sunday, 17 May, 12:00
[Poster section: Molecular neuroscience B]

Variant repeats as genetic modifiers of DM1- a case report

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Myotonic dystrophy type 1 (DM1) is the most common muscular dystrophy in adults that is caused by the expansion of CTG repeats in the DMPK gene. It is characterized by huge phenotypic heterogeneity which is only partially explained by the size of expansion. Several studies reported variant repeats (GGC, CCG, CTC) within the (CTG)n tract that could act as potential disease modifiers.

In the group of 190 DM1 patients variant repeats were identified at the 3' end of expansion in 3.7 % of the patients. Here we report one family (DF1) with identified CCG repeats in all affected members. The family included a mother (DF1-1) with the expansion size of 400-1200 repeats and two sons (DF1-2 and DF1-3) whose expanded alleles had 300-700 and 400-1100 repeats, respectively. All three family members were shown to have an expanded allele with the interruption pattern (CTG)n(CCGCTG)3(CTG)4CCGCTGCCG(CTG)2CCG(CTG)17. These patients had a later onset of the disease than it would have been expected from the expansion size. They exhibited little or no signs of percussion myotonia, a symptom that is frequently seen in DM1 patients. In addition, DF1-2 and DF1-3 had calf hypertrophy, a common symptom of myotonic dystrophy type 2 (DM2) but absent in DM1.

In accordance with previous studies, presented family supports the observation that variant repeats may be the cause of milder clinical presentation of DM1 than expected solely from the number of CTG repeats.

Keywords: myotonic dystrophy, variant repeats, genetic modifiers

MOL.06 Sunday, 17 May, 12:00
[Poster section: Molecular neuroscience B]

Superoxide dismutase and catalase activity in rat brain cortex after stress exposure

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Stress exposure alters oxidant/antioxidant balance leading to various pathological states. Brain is the target for many stressors because its sensitivity to stress-induced degenerative conditions. We examined the effects of two types of acute stress and combined effects of chronic and acute stress on antioxidant enzymes: MnSOD, CuZnSOD and CAT activity in rat brain cortex. Female Wistar rats, 2.5 months old, were exposed to 3 weeks of chronic stress by swimming (15 min) followed by immobilization or cold exposure (4 °C) for 2 hours and animals exposed to acute stress only (immobilization or cold)/no stress served as controls.

Compared to intact controls, acute stress by immobilization induced significant increase of MnSOD (4.36 ± 0.33 vs. 14.75 ± 1.55, $p < 0.001$) and CuZnSOD activity (17.26 ± 0.73 vs. 28.27 ± 3.81, $p < 0.05$), while cold exposure did not affect enzyme activities in brain cortex ($p > 0.05$). Animals exposed to chronic stress by swimming for 21 days had elevated activity of all examined antioxidant parameters (MnSOD, CuZnSOD, CAT: 4.36 ± 0.33 vs. 17.86 ± 2.06, $p < 0.001$; 17.26 ± 0.73 vs. 41.17 ± 3.40, $p < 0.001$; 2.31 ± 0.35 vs. 5.71 ± 0.30, p <; 0.001, respectively). In animals pre-exposed to chronic stress by swimming, immobilization resulted in significant decrease of CAT activity (5.71±0.30 vs. 1.68 ± 0.11).

The results indicate that exposure to acute stress by immobilization/ chronic stress by exercise training induces oxidative stress in brain cortex. Also, adaptation to chronic stress involves mechanisms that alter the stress-specific antioxidant response to acute stress exposure. Compared with our previous results on hippocampus, the regional specificity in the way that brain responds to different types of stress may be observed.

Keywords: antioxidant enzymes, brain cortex, stress

MOL.08 Sunday, 17 May, 12:00
[Poster section: Molecular neuroscience B]

Repeated low-dose progesterone treatment modulates expression of apoptotic elements within Akt and Erk signalling pathways in subcellular specific manner in rat hippocampus following chronic cerebral hypoperfusion

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The present study attempted to verify whether chronic cerebral hypoperfusion (CCH) and repeated low dose progesterone (PR) treatment affects the neurodegenerative processes as well as the expression of key apoptotic elements (NF-κB, caspase 3 and PARP) within Akt and Erk signal transduction pathways. The results revealed absence of usually coupled Akt and Erk activation in CCH in cytosolic, mitochondrial and synaptosomal fractions, indicating lower threshold of Akt activation in brain ischemia, while PR elevated their levels above control. Although CCH induced increase in caspase 3 and PARP gene and protein expression, PR returned examined molecules expression in all examined fractions, except synaptic levels of caspase 3 which highlighted its possible non-apoptotic or even protective function. Our study showed absence of NF-κB response to this type of ischemic condition and its strong activation under the influence of PR in all examined subcellular fractions. Finally, the initial increase in the number of apoptotic cells and amount of DNA fragmentation induced by CCH was significantly reduced by PR. Our findings support the concept that repeated low-dose post-ischemic PR treatment reduces CCH-induced neurodegeneration in hippocampus through the activation of investigated kinases and regulation of their downstream molecules in subcellular manner, indicating that low-dose PR treatment in repeated regiment of administration, exerts neuroprotective potential, and thus, may be promising therapy for various ischemic brain conditions and other neurodegenerative diseases.

Keywords: brain ischemia, progesterone, chronic cerebral hypoperfusion, neurodegeneration, neuroprotection

MOL.10 Sunday, 17 May, 12:00
[Poster section: Molecular neuroscience B]

Studies of the oxidative status in the brain of the hSOD1G93A ALS rat

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Amyotrophic lateral sclerosis (ALS) is a fatal neurodegenerative disorder characterized by death of motor neurons. 20 % of familial forms are caused by mutations in the Cu,Zn-superoxide dismutase (SOD1) forming insoluble intracellular aggregations, followed by glial activation and neuroinflammation. We examined by biochemical assays oxidative stress and by X-ray fluorescence metal imbalance in the rat brainstem and hippocampus of hSOD1 G93A ALS rats vs. nontransgenic controls, followed by in vivo studies of oxidative status in rat brains by means of Electron Paramagnetic Resonance Imaging (EPRI).

Biochemical assays detected increased presence of reactive oxygen and nitrogen species, increased index of lipid peroxidation, decreased SOD1 but increased SOD2 (MnSOD) activity, in both investigated regions. Investigation of tissue elemental composition revealed increased copper and nickel accumulation in both regions of ALS animals, while the presence of zinc was higher in brainstem but lower in hippocampus.

The EPRI measurement with the 3-CP probe revealed different reduction kinetics among presymptomatic (preALS), symptomatic (ALS) rats and nontransgenic controls. Application of a two-compartment kinetic model showed a rise in the drainage by brain bloodstream and particularly, the exchange through the blood brain barrier (BBB) in both preALS and ALS animals as compared to the control. This study thus revealed the oxidative stress occurring already in preALS rats and in line with previous studies revealing the change in the BBB also demonstrated an early hampering as a potential ALS biomarker.

These results bring new incite to the oxidative stress mechanism and early biomarker detection in ALS.

SYS.01 Saturday, 16 May, 12:00
[Poster section: Systems neuroscience A]

The relationship between parasympathetic modulation two minutes after exercise and early heart rate recovery

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In the present study, we tested the hypothesis that the HRR early after submaximal exercise is related to the post-exercise parasympathetic modulation determined by heart rate variability parameters (HRV). Thirty endurance trained athletes and thirty sedentary control subjects, performed a submaximal exercise on a cyclo-ergometer. Post-exercise (five minutes long ECG records, obtained two minutes after cessation of exercise) short-term heart rate variability (HRV) parameters in time-domains, frequency-domains and Poincare plot, 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 controls at all examination time points ($p < 0.05$). Also, SD1, TP, LF,HF, SDNN and RMSSD were significantly higher in athletes than in controls ($p < 0.005$), but other HRV parameters two minutes after recovery were not statistically different between groups. After 30 seconds, 1 and 2 minutes of recovery, HRR correlation with TP, LF, HF, SD1, SDNN and RMSSD two minutes after cessation of exercise were positive ($p < 0.018$). All correlations were linear, except the correlation between HRR and LF in which the curve was steeply rising for smaller values and significantly flattened thereafter.

These findings support the hypothesis that HRR early after submaximal exercise is related to parasympathetic modulation in the middle-aged subjects. In addition, they suggested an optimal balance between parasympathetic and sympathetic modulation for maximal HRR immediately after exercise.

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

SYS.03 Saturday, 16 May, 12:00
[Poster section: Systems neuroscience A]

Synaptotagmin VII and SYNCRIP (Heterogeneous Nuclear Ribonuclear Protein Q1) distribution and co-localization study in the adult rat brain

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Synaptotagmins are large family of transmembrane proteins involved in membrane trafficking. Synaptotagmin VII (Syt VII) is ubiquitously expressed synaptotagmin isoform that binds Ca^{2+}, yet its function and subcellular localization in neurons remain obscure. Immunoprecipitation experiments demonstrated that Syt VII interacts with SYNCRIP, cytoplasmic RNA-interacting protein, which is a component of mRNA granules that are transported to dendrites. It is speculated that SYNCRIP is implicated in mRNA turnover and/or regulation of protein synthesis in dendrites. The aim of this study was to analyse distribution of Syt VII and SYNCRIP protein in the adult rat brain by immunohistochemistry and to investigate the degree of Syt VII-SYNCRIP co-localization utilizing double immunofluorescence labeling in four selected brain areas: the hippocampus, striatum, cerebral and cerebellar cortex. We have demonstrated that Syt VII is expressed uniformly in all examined anatomical areas in neuropil. Exception was the cerebellar cortex where Syt VII was found to be expressed not only in neuropil but also in somata of Purkinje cells. SINKRIP was expressed only in somata, at high levels in the hippocampus and cerebellar cortex, at lower levels in other examined brain areas. In the hippocampus, striatum and cerebral cortex Syt VII and SYNCRIP immuofluorescent signals were mutually excluded and there was no co-localization between proteins. In somata of Purkinje cells in cerebellar cortex, where both Syt VII and SYNCRIP were expressed, we have found partial co-localization between Syt VII and SYNCRIP. We will discuss the possible role of Syt VII in mRNA granules trafficking.

Keywords: synaptotagmin VII, SYNCRIP, rat brain

SYS.05 Saturday, 16 May, 12:00
[Poster section: Systems neuroscience A]

Learning and motor performances after repetitive traumatic brain injury in the mouse

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[2]Department of Psychiatry and Neuroscience, Faculty of Medicine, University Laval, Quebec, Canada

People often sustain repetitive traumatic brain injury (rTBI), mostly in contact sports and as a result of domestic violence and military combats. It is suggested that rTBI is associated with persistent alterations in cognition, emotional functioning, behavior and motor performance. The aim of our research was to investigate cumulative effects of rTBI on learning and motor abilities in adult male C57BL/6 mice previously trained in the passive avoidance and rotarod tasks. The animals were subjected to a repetitive brain injury using a noninvasive modified weight drop model by Marmarou. Apparatus consisted of a vertical tube, box below the tube with a piece of aluminum foil on its upper side, on which the animals were situated immediately after isoflurane anesthesia, and a steel weight suspended on a nylon thread. Weight was set above the mouse head, pulled upward to a height of 1 m and dropped. rTBIs were performed twice daily, 6 hours apart, during 5 consecutive days. Sham treated, control animals were anesthetized but not subjected to the head impact. One day after the final injury or sham procedure, the mice were retested on passive avoidance task. Additionally, they were tested on the rotarod apparatus either one or three days after the last traumatic or sham injury. Mentioned preliminary results indicate no significant differences in learning or motor performances in traumatized animals compared to the mice of the control group in our experimental conditions.

This work was supported by the University of Rijeka, Croatia, project number 13.06.1.1.09 to G.Ž.

Keywords: repetitive traumatic brain injury, rotarod, passive avoidance, mouse

SYS.07 Saturday, 16 May, 12:00
[Poster section: Systems neuroscience A]

Prenatal stress affects behavior of adult male mice

Katja Kozinc, Monika Ogrizek, Tanja Španić, Gregor Majdič

Veterinary Faculty, University of Ljubljana, Slovenia

Brain development during fetal period is very sensitive to different factors. Previous studies have shown that maternal stress in mice during pregnancy could cause behavioral alterations in offspring of stressed mice. In the present study the effect of prenatal stress, caused by subcutaneous sham injection of pregnant mothers, on male sexual and aggressive behavior in adult male mice was examined. Female C57BL/6J wild type mice were mated and checked for vaginal plugs. First group of pregnant mice had skin pierced by injection needle (sham subcutaneous injection with empty syringe) on days 13, 14 and 15 of gestation, the second group on days 17 and 18 of gestation and the third group served as a control group (no injections). Adult male offspring of injected mothers were tested for sexual and intermale aggressive behavior, and their body weight was measured. Adult male mice, born to mothers receiving sham injections on days E13 – E15, had significantly higher body weights in comparison to control mice. Aggressive behavior tests revealed that male offspring from mothers receiving sham injections on days E17 and E18 displayed significantly less aggressive behavior in comparison to the other groups, while results from male sexual behavior tests did not reveal statistically significant differences between groups. These data therefore suggest that prenatal stress caused only by injection of pregnant mice affects body weight regulation and the development of capacity to display aggressive behavior in male offspring in adult life, and there might be different sensitivity to stress during different gestational periods.

Keywords: prenatal stress,adult male mice, behavior, body weight

SYS.02 Sunday, 17 May, 12:00
[Poster section: Systems neuroscience B]

Social isolation stress during puberty affects behavior in adult mice

Jasmina Kerčmar, Gregor Majdič[1] [2]

[1]Center for Animal Genomics, Veterinary Faculty, University of Ljubljana, Slovenia

[2]Institute of Physiology, Faculty of Medicine, University of Maribor, Slovenia

Exposure to different stressors during puberty can lead to long-term behavioral alterations in adult rodents. Rearing in social isolation is a stressful experience for rodents that are social animals by nature, but little is known about the effects of such stress during puberty on later social and reproductive behaviors.

In the present study we examined the social recognition in mice of both sexes and sexual behavior of ovariectomized, estradiol and progesterone primed females that were exposed to social stress during puberty. Mice were individually housed from 25 days of age, or individually housed from day 25 until day 60 (during puberty), followed by housing in social groups of 3 mice together. The control mice were group housed throughout the experiment. Using immunocytochemistry on floating brain sections the immunoreactivity for some neurotransmitters or hormone receptors, involved in the regulation of studied behaviors, were quantified.

Results of our study show that social isolation during puberty affects social recognition as well as female sexual behavior in adult mice. Mice, socially isolated during puberty thus exhibited reduced female sexual behavior and had diminished ability for social recognition in comparison to socially housed mice. Interesting, re-socialization in adulthood was insufficient to completely rescue these behaviors from the effects of social isolation during the pubertal period, suggesting long lasting effects of pubertal social isolation.

Keywords: mice, social isolation, social recognition, female sexual behavior, puberty

SYS.04 Sunday, 17 May, 12:00
[Poster section: Systems neuroscience B]

Effects of pioglitazone on the cortical neurodegeneration and neuronal loss following the lateral fluid percussion brain injury in the rat

Kristina Pilipović[1], Željko Župan[2 3], Gordana Župan[1]

[1]Department of Pharmacology, Faculty of Medicine, University of Rijeka, Croatia

[2]Department of Anesthesiology, Reanimatology and Intensive Care Medicine, Faculty of Medicine, University of Rijeka, Croatia

[3]Clinics of Anesthesiology and Intensive Care Medicine, Clinical Hospital Center Rijeka, Croatia

Even though traumatic brain injury (TBI) and its consequences are a great public health concern, effective therapeutic solutions have not yet been established. In our previous studies we have found that single dose of pioglitazone, a peroxisome proliferator receptor-γ agonist, exerted limited ameliorative effects in rats with brain trauma induced by lateral fluid percussion injury (LFPI) method. The aim of this study was to test the dose-related effects of the mentioned drug on the neurodegeneration and neuronal loss and in the rat parietal cortex following moderate LFPI. Rats were craniotomized over the left parietal cortex, midway between bregma and lambda, connected to the LFPI apparatus and subjected to brain trauma. Ten minutes after the injury induction animals were injected with different doses of pioglitazone and additional applications of this drug were given at various time points post-TBI. Rats were sacrificed at 72 h after LFPI and their brains were prepared for the histological analyses. Sham-operated, vehicle-injected animals were used as the control group. Cortical neurodegeneration was evaluated using the Fluoro Jade B staining. NeuN immunohistochemistry was used for the determination of the number of neuronal cells. Brain trauma caused significant cortical neurodegeneration and neuronal cell loss. Our preliminary results showed that pioglitazone treatment did not exert significant effects on the determined histological parameters in the used experimental conditions.

This work has been supported by the University of Rijeka, Croatia, under the project number 13.06.1.1.09 to G.Ž.

Keywords: neurodegeneration, parietal cortex, pioglitazone, rat, traumatic brain injury

SYS.06 Sunday, 17 May, 12:00
[Poster section: Systems neuroscience B]

2015 Brain Awareness Week in Osijek, Croatia

Ana Bardak[1], Stjepan Kovačević[1], Amleto Tonello[1], Vedrana Ivić[1], Marta Balog[1], Irena Labak[2], Marija Heffer[1]

[1]Faculty of Medicine, Josip Juraj Strossmayer University of Osijek, Croatia

[2]Department of Biology, Josip Juraj Strossmayer University of Osijek, Croatia

Neuroscience is a scientific branch important in many aspects, from brain diseases to everlasting investigation understanding of human behavior. Faculty of Medicine Osijek has a long tradition in promoting neuroscience together with collaborators from other Croatian faculties so 14th Brain Awareness Week was held during March 16th-22nd 2015 in Osijek. This year main topics were "Brain and Communication", "Role and Positioning of Neuroscience in Society"; and "Brain Stroke". The project titled "Communicate to Connect, Connect to Communicate"; was written by collaborator from Department of Biology Osijek and funded by Federation of European Neuroscience Society.

During the promotion of this event posters were sent to all elementary and high schools and faculties in the region. Unique T-shirts were designed. Radio, web portal, newspapers and TV media covered this event. Flash mob event was organized with student wearing giant brain dancing together with whole dancing troupe. During this year's event, 52 workshops, 26 lectures, Scientific Caffe and Brian Beat Party were held. There was two art exhibitons and one theatre show. 5000 students visited 98 different Brain Awarenes Week events. During 2015 Brain Awareness Week, we fullfiled planned expectations. We talked about and trained students on different aspects of communications. During many workshops we taught students the principle of basic communication between neurons, we talked about language centers in brain, verbal and non-verbal communication and many more communication themes. Our main goal was accomplished – to spread the simple and complicated, old and new, useful and entertaining neuroscience facts to public.

Keywords: Brain Awareness Week, communication, Osijek, Croatia

Characterisation of co-culture of spinal cord explants and muscle cells after electroporation with FUS, a protein involved in ALS/FTLD

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[1]Department of Biotechnology, Jožef Stefan Institute, Ljubljana, Slovenia

[2]Group for Nano and Biotechnological Applications, Faculty of Electrical Engineering, University of Ljubljana, Ljubljana, Slovenia

[3]Institute of Pathophysiology, Faculty of Medicine, University of Ljubljana, Slovenia

[4]Biomedical Research Institute BRIS, Ljubljana, Slovenia

Decades of pathological and physiological studies have focused on neuronal abnormalities in neurodegenerative disorders, but it is becoming increasingly evident that astrocytes, oligodendrocytes microglia and skeletal muscle cells also play an important role in neurodegeneration. These cells are responsible for many functions, including maintenance of the extracellular environment, stabilization of cell–cell communications, maintenance of synaptic function, and facilitation of immune response during inflammation, all of which is important in the maintenance of the neuronal environment and the progression of the disease. In this study we employed a complex in vitro model of neuromuscular junction (NMJ) formation using rat embryonic spinal cord explants co-cultured with primary human myoblasts which might give valuable insight into abnormal accumulation and mislocalisa-tion of proteins involved in amyotrophic lateral sclerosis (ALS) and frontotemporal lobar degeneration (FTLD). Cytoplasmic inclusions in fused in sarcoma (FUS) are the hallmark of several forms of FTLD and ALS in patients with mutations in the FUS gene. Difference in neurite outgrowth and NMJ formation was observed after electroporat-ing spinal cord explants with wild type (pEGFP: FUSwt) and mutant FUS-EGFP (pEGFP: FUS Y526X and pEGFP: FUS Y526F). Cell type specific incorporation of FUS was detected by imunocytochemi-cal stains followed by confocal microscopy. All cell types present in the spinal cord were electrotransfected, namely EGFP signal was detected in neurons, astrocytes, oligodendrocytes and Schwann cells. This model might represent a platform to study the role of different ALS/FTLD related proteins in triggering and/or worsening the pathol-ogy in a complex system.

Keywords: co-culture, neuro muscular junctions, elecroporation, FUS

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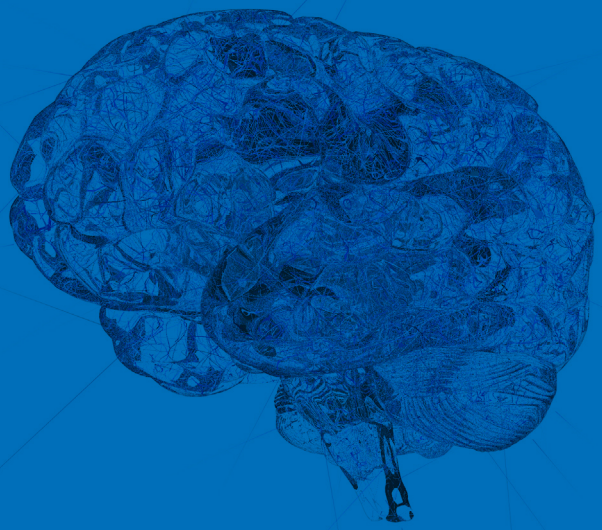

Abstracts

Educational Workshop on Addiction

Univerza *v Ljubljani*

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Cankarjev dom, Ljubljana, Slovenia
16 May 2015

Saturday, 16 May, 8:30
[Educational Workshop on Addiction, Session I: Neurobiology]

Learning mechanisms of drug dependence

Jennifer Murray

Department of Psychology at the Behavioural and Clinical Neuroscience Institute, Murray Edwards College, and Lucy Cavendish College, University of Cambridge, United Kingdom

The development of drug dependence relies heavily on an aberrant learning history. Initially, the experience of the drug itself is linked with environmental cues through a process of Pavlovian conditioning. The unconditioned drug stimulus becomes associated with conditioned stimuli that can then come to instigate goal-directed drug seeking. Over time, a shift in the circuitry maintaining the drug-seeking behaviour occurs. This transition from a dominant role of the mesolimbic dopamine system to the nigrostriatal dopamine system is reflected behaviourally in a transition to habitual drug seeking. At this stage, the drug-seeking behaviour is resistant to devaluation of the drug stimulus, indicating a loss of outcome value as the dominate source of motivation, and instead implicating the drug-associated conditioned stimulus as the driving force of the behaviour. From a clinical standpoint, increased focus on the impact of associated environmental cues in perpetuating drug habits should be of use. Unfortunately, approaches utilizing extinction processes such as cue-exposure therapy have been less than successful in prolonging abstinence. One of the factors that may contribute to that is our often narrow approach to understanding the role of the drug itself. Importantly, a drug is not only a rewarding Pavlovian unconditioned stimulus or operant reinforcer. The drug experience can also function as a conditioned stimulus, indicating the presence of another appetitive environmental stimulus, as well as set occasions for when other conditioned-unconditioned stimulus associations are available. Combined, understanding the functional significance of the impact on neural processes of the drug experience in various learning domains will provide a more solid foundation for moving forward in the development of treatment techniques.

Saturday, 16 May, 9:30
[Educational Workshop on Addiction, Session I: Neurobiology]

Pleasant and unpleasant effects of alcohol

Dorit Ron

Department of Neurology, University of California, San Francisco, USA

Alcohol addiction is one of the most prevailing psychiatric disorders. Alcohol abuse is associated with serious global health as well as socioeconomic consequences. Unlike most drugs of abuse alcohol does not have a single pharmacological site of action. Thus, the mechanisms that underlie the disease, e.g. the transition from recreational use to abuse are poorly understood, and thus pharmacotherapies available to treat the disorder are very limited. Dr. Ron will present two examples from her group's research showing that elucidating the molecular mechanisms by which alcohol affects the adult brain can lead to the identification of novel drug targets to treat the disease. First, using rodent models that mimic social drinking and uncontrolled excessive intake she will show that the transition from social to compulsive alcohol drinking results from the disregulation of the expression and function of the neurotrophic factor, BDNF, in a specific brain circuitry. She will then present data suggesting that restoring the normal function of the BDNF signaling pathway reverses the escalation of alcohol use. The second part of her presentation will focus on mTORC1, a kinase important for learning and memory. Dr. Ron will show that excessive drinking of alcohol leads to the activation of mTORC1 in specific brain regions, resulting in the translation of synaptic proteins. She will then describe the physiological and behavioral consequences of mTORC1 activation, and present data implicating mTORC1 in maladaptive forms of learning and memory that underlie alcohol-related behaviors. Finally, she will describe the potential use of mTORC1 as valuable target for the treatment of alcohol use and abuse disorders.

Saturday, 16 May, 14:30
[Educational Workshop on Addiction, Session II: Alcohol addiction: Stigma, ethical challenges and treatment]

How can science help explain ethical issues related to alcohol dependence syndrome?

Zdenka Čebašek Travnik

University Psychiatric Hospital Ljubljana, Slovenia

Faculty of Medicine, University of Ljubljana, Slovenia

Talking about addictions put at the forefront the type of dependence, effects of psychoactive substances and therapeutic efforts to reduce the impact of this disease. To rediscover the values of life, we increasingly deal with the ethics – in our case the ethics of addiction, particularly addiction to alcohol. Ethics is becoming an important tool to understand behavior of the addicted person and an indispensable element in all areas dealing with addiction: epidemiology, prevention, motivational processes, treatment and recovery.

Some authores claim that alcohol and drug research has a lack of scientificc production related to ethical, legal and social issues. But the advances in neuroscience are changing how mental health issues such as addiction are understood and addressed as a brain disease. Although a brain disease model legitimizes addiction as amedical condition, it promotes neuro-essentialist thinking, categorical ideas of responsibility andfree choice, and undermines the complexity involved in its emergence.

Addiction neuroethics raise important ethical questions. Some of them are: (1) Are people who use drugs or alcohol morally responsible for their behavior?, (2) Under what circumstances is it justified to test individuals for drug and alcohol use?, (3) Is it acceptable for health-care professionals to prescribe and keep people on addivtive drugs that are otherwise illegal, and if so, under what circumstances?

Saturday, 16 May, 15:00
[Educational Workshop on Addiction, Session II: Alcohol addiction: Stigma, ethical challenges and treatment]

Alcohol addiction treatment

Darja Boben Bardutzky

Department for Addiction Treatment, Psychiatric Hospital Vojnik, Slovenia

The method of treatment of alcohol addiction currently used in Slovenia can be seen as a result of rich experience and great efforts by a number of experts throughout almost fifty years. The method is based on the concept of addiction as a disease.

The treatment can be presented as a sequence of phases. The preparation phase is followed by intensive treatment phase and then maintenance phase. We always try to find for each individual a suitable combination of pharmacological, psychological and social interventions, which are needed in different phases of addiction treatment. As far as pharmacological treatment is concerned, three groups of medicaments are used: medication for the withdrawal syndrome, for abstinence maintenance and for co-morbidity treatment.

Psychotherapy in different modalities (psychodynamic, systemic, family, RT, CBT, TA …) and in different contexts (group, family, individual), sociotherapy, psychoeducation, occupational and other therapies are practiced as part of the treatment.

Considering that addiction involves problems on the level of relationships, inclusion of the patients' relatives is considered very important. Thereby, the role of the family members of the treated person changes from the role of the helper to the role of someone who needs help. Programs with a clearly defined structure are more effective as they enable managing compulsive behavior, existential emptiness, and anxiety. Combining intensive emotional support with some external control mechanisms provides the patients with the best possible opportunities to learn new ways of fulfilling their basic psychological needs without manipulations.

There is evidence to support that the duration of rehab models should be three months, and that is approximately the right time for the brain to be "reset" and get rid of the direct influence of drugs. A longer period of time is needed to establish the automatization of new, different, more self-protecting and healthy ways of patient's behavior.

Saturday, 16 May, 15:30
[Educational Workshop on Addiction, Session II: Alcohol addiction: Stigma, ethical challenges and treatment]

(Neuro)science and alcohol dependence syndrome related stigma

Mirjana Radovanović

Alcoholism Treatment Unit, University Psychiatric Hospital Ljubljana, Slovenia

Addiction as a brain disease is a broadly accepted concept. Nonetheless alcohol dependence syndrome (as defined in ICD-10) or alcohol use disorder (as defined in DSM V) is the one with the highest level of stigma among mental disorders. This finding is similar across countries and continents. The bio-psycho-social model of understanding addiction increased awareness about the disease, provided a background for securing some funding by the health insurance companies of the addiction treatment programs and is supported by the results of numerous scientific studies, particularly from the 1990s onward.
This presentation does not provide an extensive literature review. Rather, it will address some clinically relevant factors contributing to the high level of stigma attached to addiction and alcohol dependence syndrome in particular. Basic neurosciences on one end inform more clinically oriented studies on the other end of the scientific spectrum, all of which in turn provide some insight into a very complex phenomenon of stigma underpinning beliefs, attitudes and behaviors, which medical professionals bring into everyday practice.

Saturday, 16 May, 17:00
[Educational Workshop on Addiction, Session III: Addiction, ADHD and psychoactive substance abuse]

Addiction, comorbidity and new psychoactive substances

Nuša Šegrec

Center for Treatment of Drug Addiction, University Psychiatric Hospital Ljubljana, Slovenia

Patients with substance use and related addictive disorders have higher prevalence of co-morbid mental health disorders compared to general population; and vice versa, the prevalence of substance use disorders is higher among patients with other mental disorders than in general population. Un(der)treated one or both diseases lead to worse treatment outcomes and is associated with several negative physical and psycho-social consequences. However, it is known that some psychoactive substances (eg. stimulants, cannabis) can induce psychiatric side effects such as psychosis, anxiety, mood disturbances and suicidality or worsen the symptoms of previously existed mental disorder.

Further, we can monitor the occurrence of new psychoactive substances (NPS) in past few years, so called designer drugs, legal highs, herbal highs, research chemicals,… Beside mimicking the effects of illicit substances and being relatively cheap, they became highly available, mostly through internet smart shops and darknets. There are almost no existing studies about possible short and long term side effects of NPS, but we can find reports of toxicity on physical and mental health – unfortunately, some of them with fatal outcome. The author will present the most frequently used NPS (with focus on synthetic cannabinoides and synthetic cathinones), especially psychiatric side effects, which can be very miscellaneous. A case-report of synthetic cathinone - induced psychosis will be presented to.

Saturday, 16 May, 17:30
[Educational Workshop on Addiction, Session III: Addiction, ADHD and psychoactive substance abuse]

Epidemiology and clinical presentation of ADHD[a]

Differential diagnosis and comorbidity in ADHD[b]

Treatment of adults with ADHD[a]

ADHD, psychoactive substance abuse, addiction disorders and treatment[b]

[a]Mirjana Delić

[b]Andrej Kastelic

Center for Treatment of Drug Addiction, University Psychiatric Hospital Ljubljana, Slovenia

Alcohol addiction is one of the most prevailing psychiatric disorders. Alcohol abuse is associated with serious global health as well as socioeconomic consequences. Unlike most drugs of abuse alcohol does not have a single pharmacological site of action. Thus, the mechanisms that underlie the disease, e.g. the transition from recreational use to abuse are poorly understood, and thus pharmacotherapies available to treat the disorder are very limited. Dr. Ron will present two examples from her group's research showing that elucidating the molecular mechanisms by which alcohol affects the adult brain can lead to the identification of novel drug targets to treat the disease. First, using rodent models that mimic social drinking and uncontrolled excessive intake she will show that the transition from social to compulsive alcohol drinking results from the disregulation of the expression and function of the neurotrophic factor, BDNF, in a specific brain circuitry. She will then present data suggesting that restoring the normal function of the BDNF signaling pathway reverses the escalation of alcohol use. The second part of her presentation will focus on mTORC1, a kinase important for learning and memory. Dr. Ron will show that excessive drinking of alcohol leads to the activation of mTORC1 in specific brain regions, resulting in the translation of synaptic proteins. She will then describe the physiological and behavioral consequences of mTORC1 activation, and present data implicating mTORC1 in maladaptive forms of learning and memory that underlie alcohol-related behaviors. Finally, she will describe the potential use of mTORC1 as valuable target for the treatment of alcohol use and abuse disorders.

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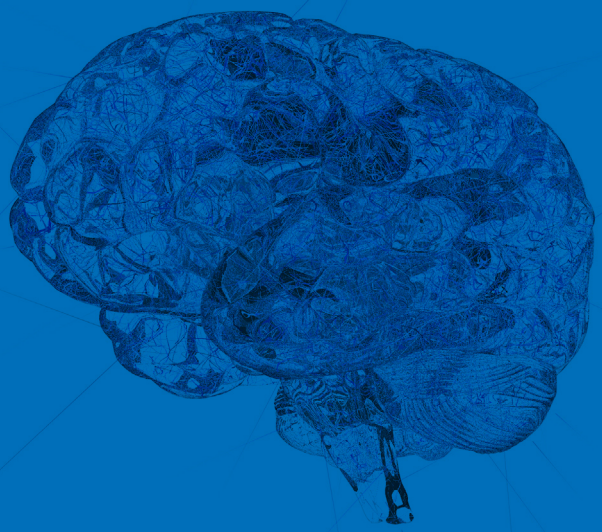

Abstracts

Educational Course on Late-onset Pompe Disease

www.sinapsa.org/SNC15/course
Cankarjev dom, Ljubljana, Slovenia
15–16 May 2015

Friday, May 15th, 14:15
[Educational Course on Late-onset Pompe Disease: Clinical reviews]

Late-onset Pompe disease - overview

Zoran Mitrović

National Center for Neuromuscular Diseases, Clinical Hospital Center Zagreb, Croatia

Late onset Pompe disease (LOPD) is the more common phenotype variant of Pompe disease (GSDII), due to the deficiency of acid α-glucosidase activity (GAA), an enzyme regulating intralysosomal glycogen breakdown. The most severe, classic or infantile form also encompasses GAA absence. Ensuing glycogen storage and/or autophagy dysfunction leads to cell death and corresponding organ failure. Skeletal, cardiac and smooth muscles are most frequently affected, featuring progressive myopathy of proximal limb girdle, the respiratory or less prominent, the bulbar muscles. Involvement of arterial walls may result with aneurisms and cerebral haemorrhage. In contrast to infantile form, LOPD commonly lacks severe cardiac involvement. The symptoms start anytime after infancy, most often presenting as muscle weakness, the exertional or spontaneous fatigue and/or dyspnoea, myalgia, cramps, low back pain, or featuring asymptomatic hyperCKaemia. Disease invariably progresses, leading to immobility and respiratory insufficiency with fatal complications. The course and clinical severity may vary, even among siblings, although their symptoms and muscle involvement follow similar profile. Full clinical picture of multisystemic disease is distinctive, yet the presentation and oligosymptomatic phenotype can be misleading toward many overlapping conditions, and could result in diagnostic delay of many years. Early diagnosis is important for timely GAA replacement therapy, shown to recuperate many patients with infantile form. In LOPD, it may halt the progression and stabilize motor symptoms. Rapid detection of GAA deficiency is possible using commonly available dry blood spot test (DBS). It should be applied in all patients with suspicious muscle symptoms, especially unexplained respiratory, particularly nocturnal complaints, exertional fatigue, myalgia or hyperCKaemia. Thorough physical examination is essential to uncover mild muscle weakness, which usually precedes symptoms for several years. Targeted work up with pulmonary tests and polysomnography can disclose orthopnea and nocturnal hypoventilation, while needle EMG may corroborate clinical findings with myopathic changes accompanied with myotonia. The diagnosis can be confirmed and ERT initiated after confirmatory GAA deficiency in fibroblasts and/or DNA findings of 2 causal GAA mutations. Disease management commonly requires coordination of multidisciplinary team. Hopefully, the rapid advances in genomics could result in better understanding of GSDII pathophysiology, giving way to personalized interventions.

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2. American Association of Neuromuscular & Electrodiagnostic Medicine: Diagnostic criteria for late-onset (childhood and adult) Pompe disease. Muscle & Nerve 2009; 40(1):149-160.

Friday, May 15th, 15:10
[Educational Course on Late-onset Pompe Disease: Clinical reviews]

Pitfalls in adult Pompe disease diagnosis

Georgios Konstantinos Papadimas

Medical School of Athens, Eginition Hospital, 1st Department of Neurology, Athens, Greece

Late onset Pompe disease (LOPD) has been recognized as a cause of proximal myopathy in adults, but despite increasing awareness, missed and/or delayed diagnosis seems to be quite common. This problem may be mainly explained by the rarity of the disease and the fact that the clinical presentation may be quite heterogeneous with symptoms, signs or laboratory findings that can be misinterpreted and may lead therefore to a wrong diagnosis.

Apart from the typical and common clinical symptoms, which are the limb girdle muscle weakness and the respiratory insufficiency that may occasionally manifest even in the absence of weakness, there are also other less frequent musculoskeletal and cardio-cerebrovascular patterns that commonly appear in conjunction with one another.

Electromyographic findings which occasionally include the presence of spontaneous activity may be also misinterpreted, while normal results do not necessarily exclude LOPD. Moreover, muscle biopsy has many limitations in the diagnostic work-up and must be cautiously analyzed. Muscle pathology in the adult form of the disease has a variable severity and may be characterized by just few vacuolated fibers or may even demonstrate only nonspecific changes without high glycogen content. Other potential misleading laboratory abnormalities are the high levels of transaminases, which may mistakenly raise the suspicion of a possible liver disease, especially in the absence of myopathic symptoms.

In an effort to facilitate a correct diagnosis, experts in Pompe disease have proposed recommendations for the evaluation of patients with symptoms suggestive of LOPD. According to their suggestions, some important key physical and laboratory findings are the proximal pattern of weakness, the electromyographic myopathic findings with increased muscle membrane irritability especially when revealed on paraspinal muscles, the diaphragmatic weakness and the increased serum transaminase levels.

The use of a very simple diagnostic algorithm that proposes DBS (dried blood spot) screening in a) patients presenting with proximal/axial weakness, with or without respiratory symptoms, b) patients affected by restrictive respiratory insufficiency and c) patients with asymptomatic hyperckemia, may help avoid LOPD misdiagnosis.

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2. Toscano A, Montagnese F, Musumeci O. Early is better? A new algorithm for early diagnosis in late onset Pompe disease (LOPD). Acta Myol. 2013;32:78-81.

Friday, May 15th, 15:30
[Educational Course on Late-onset Pompe Disease: Clinical reviews]

LGMD and GAA „pseudodeficiency": a case from Croatia

Rujana Šprljan Alfirev, Zoran Mitrović

National Center for Neuromuscular Diseases, University Hospital Center Zagreb, Croatia

The GAA gene is responsible for production of the acid alpha-glucosidase enzyme (also known as acid maltase). Allelic GAA mutations cause a rare lysosomal and also glycogen storage disease called glycogenosis type II or Pompe disease. Different forms of Pompe disease are related to excessive glycogen accumulation and disturbed autophagosome-lysosome interactions yielding to muscle tissue degradation. The patients with late-onset form of Pompe disease (LOPD) have residual enzyme activity and are typically spared of cardiomyopathy, but experience progressive leg and trunk muscle weakness, including respiratory muscles. ERT with alglucosidase alfa in LOPD could temporary stabilize motor and respiratory symptoms.

We report on an adult caucasian male from Croatia with atypical limb girdle muscle weakness of childhood onset and late onset dilatative cardiomyopathy ensuing with heart transplantation. Two siblings had a similar condition (not investigated) and died at age 27 and 60. Laboratory investigation repeatedly showed mild reduction of GAA activity on dry blood spot and lymphocytes, but normal level in fibroblast culture. Western blot analysis from fibroblasts showed normal GAA profile. Direct sequencing revealed a heterozygous common pathogenic GAA mutation c.-32-13T>G and various polymorphisms. Pseudodeficiency allele GAA2 was not seen. Histopathological and EM analysis of biopted muscles did not reveal clear glycogen deposits. CK was normal. On ERT with Myozyme no clinical improvement was observed. Atypical clinical picture and inconclusive results of laboratory investigation, rised suspicion to a coincidental muscle and heart disease conjoined with GAA „pseudodeficiency", that should be resolved with expanded molecular search.

Friday, May 15th, 16:25
[Educational Course on Late-onset Pompe Disease: Diagnostic reviews]

LOPD in EMG laboratory: Where to start? What to expect?

Ervina Bilić

University of Zagreb, School of Medicine, University Hospital Center Zagreb, Croatia

Department of Neurology, Referral Center for Neuromuscular Diseases and Clinical Electromyoneurography, University Hospital Center Zagreb, Croatia

Pompe disease (PD), also known as glycogen storage disease type II (GSD II) or acid maltase deficiency, is increasingly recognized as a cause of progressive muscle weakness in both pediatric and adult populations. In past, diagnosis required enzyme analysis in skin fibroblasts or muscle, but PD can now be readily diagnosed by analysis of enzyme activity in blood, using dried blood spot. The current challenge for clinicians is reaching the point at which PD is suspected, especially in adults. In this process of building a suspicion for late onset PD (LOPD) the clinical electromyoneurography (EMNG) could be a valuable tool.

Most of the data available on the electrodiagnostic abnormalities seen in PD were established from case reports published in the 1960's and 1970's. The most frequent finding was myotonic discharges without evidence of clinical myotonia. Sensitivity of EMG examination depends on the range of the diagnostic procedure and the muscles selected for EMG analysis. The specific complex repetitive discharges are expected to be found in patienst with LOPD in paraspinal muscles. If the paraspinal muscles are not analysed, the sensitivity of EMG in LOPD diagnostics is significantly reduced. Spontaneous EMG activity in paraspinal muscles should be analysed in any patient with clinical or laboratory signs of myopathy, respiratory weakness of unknown case, statin associated myopathy without improvement after discontinuation of statins, in patients with elevated creatin kinase levels of unknown cause and in patients with limb girdle muscle weakness. EMG in PD will show myopathic changes in almost all pediatric patients with PD, but some late onset patients may present with normal EMG examination. The mixed myopathic and neuropathic pattern could be found in glycogen storage disease type III (Cori disease), but in PD the neuropathy is not typical finding.

The presence of complex repetitive discharges or myotonic disharges isolated in paraspinal muscles is not specific for PD but should raise a suspicion in the context of above mentioned clinical or laboratory findings. More sensitive quantitative EMG methds, muscle ultrasonography or MRI may be also valuable diagnostic tool for PD patients, especially for monitoring the response to enzyme replacement therapy.

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Friday, May 15th, 16:55
[Educational Course on Late-onset Pompe Disease: Diagnostic reviews]

Detecting GAA deficiency by DBS - how sensitive and how specific is it?

Ksenija Fumić

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Pompe disease (PD) is autosomal recessive disorder of glycogen metabolism that is characterised by a deficiency of the lysosomal acid alpha-glucosidase (GAA). PD is still frequently undiagnosed, or diagnosed with a delay. Early diagnosis before the onset of irreversible pathology is critical for maximum efficacy of the enzyme replacement therapy.

Dried blood spot (DBS) methods are currently available for identification of a range of lysosomal storage disorders (LSDs) including the GAA. DBS involves minimally invasive sample collection and samples can be shipped at room temperature. This assay provides robust, rapid and reliable first tier test for screening patients suspected of having PD. Hovewer, the activity of another alpha-glucosidase, maltase-glucoamylase, may lead to false negative test results if not inhibited by acarbose. There are also some other issues of DBS that can influence the final results as: sampling, drying, storage, shipping, haematocrit, hemoglobine, leukocythosis. Another issue is the fact that laboratories use different in-house methods, cut-off values and different units, which makes comparison of results impossible.

DBS is a reliable tool for PD screening. Hovewer, good quality of sample is essential and physicians and laboratory staff have to be aware of pitfalls. A second test should be done to confirm the diagnosis of PD. Confirmatory tests include enzyme activity assay with lymphocytes, fibroblasts or genotyping. It is important to have laboratories with expertise in the diagnosis of LSDs.

Friday, May 15th, 17:10
[Educational Course on Late-onset Pompe Disease: Diagnostic reviews]

The impact of molecular diagnosis

Karin Writzl

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Pompe disease is an autosomal recessive lysosomal glycogen storage disorder with a wide clinical variability, caused by pathogenic sequence variations in the GAA gene. Five hundred different variations, among them more than 300 pathogenic, have been identified and are catalogued by the Erasmus University Medical Centre in Rotterdam (http://www.pompecenter.nl). According to severity, they are classified into seven classes: "very severe", "potentially less severe", "less severe", "potentially mild", "presumably nonpathogenic", and "nonpathogenic" (1). Variants that prevent the formation or function of acid alpha-glucosidase (GAA) are usually associated with the classic infantile Pompe disease, whereas variants leading to residual GAA activities portend a better prognosis. However the genotype-phenotype correlation is not strict, as different phenotypes have been observed even within families, pointing to an important role of the modifying factors (2).

The diagnostic test of choice for individuals with Pompe disease is measurement of GAA enzyme activity, still genetic testing has important uses. It provides additional confirmation of the diagnosis, enables carrier testing and predictive testing for at-risk relatives, and prenatal or preimplantation genetic diagnosis for at risk pregnancies in families with known pathogenic variants.

Genetic counselling should be offered to all parents with an affected child with Pompe disease and to all adults with Pompe disease.

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Friday, May 15th, 17:25
[Educational Course on Late-onset Pompe Disease: Diagnostic reviews]

Muscle biopsy in Pompe disease

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Pompe disease is a lysosomal storage disorder, due to deficiency of enzyme which carries out the hydrolysis of glycogen at acid pH. Accumulation of undigested glycogen within lysosomes occurs in multiple tissues witch is particularly detrimental to cardiac, skeletal and smooth muscle. Severity of clinical manifestations roughly inversely correlates with residual activity of acid alpha-glucosidase.

Most of the infantile and juvenile onset forms show disease characteristic vacuoles containing basophilic amorphous material in skeletal muscle. High activity of acid phosphatase points to lysosomal origin of vacuoles. Vacuoles are usually positive with periodic acid Schiff stain for glycogen. In late-onset Pompe disease (LOPD) muscle histopathology is less uniform; it is not unusual that no vacuolar myopathy is discovered. Since muscle biopsy is used as an early evaluation tool in muscle disease, it is important to be aware of false negative results in LOPD. It was suggested that in LOPD cases with unspecific changes acid phosphatase positive globular inclusions which also faintly stain with menadione linked α-glycerophosphate dehydrogenase without substrate may be a useful diagnostic marker. Because of heterogeneity of muscle fibre damage, especially in LOPD, it is difficult to generalise observations from the single biopsy site. Considering these obstacles, and availability of non-invasive screening procedure, diagnostic muscle biopsy in Pompe disease is nowadays avoided.

However, muscle biopsy remains invaluable for the studies of the pathogenesis and mechanisms of disease. Skeletal muscle damage in Pompe disease has been traditionally attributed to lysosomal rupture and release of lysosomal enzymes into the cytoplasm. By analysing muscle biopsies Raben et al. demonstrated that lysosomal expansion is indeed the mechanism of muscle fibre destruction in patients with untreated classical infantile form; in juvenile and LOPD patients dysfunctional autophagy predominates. Interestingly, in infants on enzyme replacement therapy, lysosomal regression but autophagic accumulation, though of lesser extent than in juvenile and LOPD, occurs. It seems that the delivered enzyme digests the accumulated glycogen, but does not reverse the functional abnormality of lysosomes which are unable to fuse with autophagosomes. Another abnormality, unrelated to the phenotype, is accelerated production of lipofuscin deposits which may exacerbate lysosomal and autophagosomal abnormalities.

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Saturday, 16 May, 9:15
[Educational Course on Late-onset Pompe Disease: Patient assessment]

Patient association screening project

Lea Leonardis

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Clinically, Pompe disease exhibits a wide spectrum of phenotypes, ranging from severe, rapidly progressing infantile form with heart involvement, to slowly progressing late-onset form. The latter may also present with rather non-specific symptoms and signs, clinically indistinguishable from limb girdle muscle dystrophies or other proximal myopathies. Since the enzyme replacement therapy has become available, the correct and on-time diagnosis gained great importance. Several years ago we have had only two children diagnosed with this disease, but none in the adult population. Therefore, we started active searching in the high-risk patient populations.

The Muscular Dystrophy Association of Slovenia was established in 1969. Nowadays, it has 856 regular members. Since Slovenia is a small country, beside patients with various forms of hereditary myopathies, patients with other non-muscular hereditary diseases or autoimmune neuromuscular disorders (i.e. Charcot-Marie-Tooth, hereditary spastic paraplegia, hereditary ataxia or amyotrophic lateral sclerosis and myasthenia gravis) join the Association, as well. In summer, during their rehabilitation programs, seven lectures were organised for the audience of over 400 patients. After the lectures, every attendant had the opportunity to be tested for Pompe disease. Two hundred dry spot samples were collected indiscriminately (i.e. also from the patients with already known other genetic disorders, e.g. myasthenia gravis or amyotrophic lateral sclerosis). In spite of this, the results in two patients were positive: in a 59 years old man and in a 65 years old woman. Both had proximal muscle weakness, they could only walk with aids, and they had moderate respiratory insufficiency. In both the enzyme replacement therapy was started and their clinical status has remained stable.

Due to non-specificity of Pompe disease, screening in the high risk patient populations is essential to identify as many patients with Pompe disease as possible, since an efficient therapy is available.

Saturday, 16 May, 9:35
[Educational Course on Late-onset Pompe Disease: Patient assessment]

ALDA (Automated Limb-girdle muscle dystrophy Diagnosis Assistant)

Svetlana Tomić

Department of Neurology, University Hospital Center Osijek, Medical School of Josip Juraj Strossmayer in Osijek, Croatia

Automated limb-girdle muscle dystrophy (LGMD) Diagnosis Assistant (ALDA) is a free tool designed by Jain Foundation for clinical practice use. Before starting a test registration should be done. Tool consists of a different questions about patient`s sex, family history, ancestry, previously done genetic testings, clinical findings and symptoms (muscle involvement, other organs involvement), disease course (age of onset, speed of progresion) and examination findings (kreatin kinase and muscle biopsy findings). Pointing on each question help box appear with more detail about question or photos with specific symptom (scapular wining, skin changings, calf hypertrophy). On the right side is a diagram with muscle dystropy list and with probability scale that change after every finished question. Pointing to each disease detail about gene and protein appear. At the end, clinician got final report with results predicting the most likely type of dystrophy in a presented patient with proposals about next step in diagnostic procedure (muscle biopsy or genetic testing). Report also provide names of laboratories where this testing could be done, with prices, or available laboratory where patients could send sample with no costs for testings (sponsored by some research funds). In many countries genetic testing for muscle dystrophy is often unavailable and this information could help clinician in further diagnostic procedures. Because of it`s simplicity this tool could be used also by clinician who are not much familiar with neuromuscular disease. In conclusion, ALDA is simply and very useful tool that could help in clinical practice by pointing to most likely muscle dystrophy diagnose. This could reduce the number of potential diagnostic procedures that should be done and lower the costs till final diagnose.

ALDA (web page). http://www.jain-foundation.org/lgmd-subtyping-diagnosis-tool. Accessed on April 29, 2015.

Saturday, 16 May, 9:55
[Educational Course on Late-onset Pompe Disease: Patient assessment]

Bulgarian experience with testing high risk patient population for pompe disease

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Pompe disease is a rare autosomal-recessive lysosomal storage disorder due to a deficiency of acid alpha-glucosidase and clinically characterized by progressive damage to respiratory, cardiac, skeletal, and smooth muscles.

The rarity of the disorder, variable clinical presentation, and overlap of signs and symptoms with other neuromuscular disorders are likely sources of the typical low index of clinical suspicion for Pompe disease that often results in delays in diagnosis and treatment for many patients. In Bulgaria, whose population is 7 364 570, there weren't any patients, diagnosed with Pompe disease until the beginning of 2012.

In april 2012 a screening program, called "Prevalence study of Pompe disease" was initiated in Bulgaria. Its main aim was to determine the prevalence of Pompe disease among patients with progressive limb-girdle muscle weakness with or without respiratory insufficiency and with or without elevated creatine kinase level. The study was based on two main stand points- retrospective study of patients with undiagnosed myopathies from the registries of Bulgarian National Genetic Laboratory, Bulgarian Society of Neuromuscular diseases and Clinic of Neurology, University Hospital Alexandrovska, Sofia and prospective study of cohort of undiagnosed patients who are visiting university hospitals and electromyography centers in Bulgaria. Twenty four centers, spread throughout Bulgaria, working in close collaboration, were included in the program. For the last 3 years 250 patients were tested, by evaluating the activity of GAA on DBS and 6 patients with decreased activity were subsequently genetically verified as having Pompe disease. In four of them enzyme replacement therapy was initiated.

The presence of complex repetitive discharges or myotonic disharges isolated in paraspinal muscles is not specific for PD but should raise a suspicion in the context of above mentioned clinical or laboratory findings. More sensitive quantitative EMG methds, muscle ultrasonography or MRI may be also valuable diagnostic tool for PD patients, especially for monitoring the response to enzyme replacement therapy.

Keywords: Pompe disease, selective screening, limb-girdle muscle weakness

Saturday, 16 May, 10:15
[Educational Course on Late-onset Pompe Disease: Patient assessment]

Parents refusing the child's diagnose - what's the next step? A case from Serbia

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We are reporting on the case of two sisters with Pompe disease. Now, the elder sister is a 5-year–old girl. She was examined in 9th month of her life due to elevated transaminases. Metabolic analyses and finding of liver biopsy were normal. Her earlier neurological development was normal, she only had hypomimia. Electromyography (EMG) finding: myopathic EMG with myotonic discharges in distal muscles of extremities. Ultrasound examination of the heart: mild hypertrophy of the left ventricle.

Genetic tests of Myotonic dystrophy type 1 and type 2 (DM1 and DM2) are negative.

Now, she has hypomimia, nasal speech, weakness without wasting of proximal extremities muscles more in the legs than arms. She has pseudohypertrophy of the calf muscles. She has a waddling gait. She goes up the stairs with difficulty and with assistance. CK level and transaminases in blood are elevated all the time (CK about 2,5 times increased up to 10 times now).

Her younger sister is 14 month old and has normal neurological development. She has elevated levels of CK (2-5 times).

When the elder sister was 4 years old we performed enzyme acid alpha-glucosidase assay (dried blood spot and lymphocytes, Prof dr K. Fumić, Zagreb). In the both samples, activity of acid alpha-glucosidase in the acidic area was markedly reduced. The diagnosis of Pompe disesae was confirmed at the genetic level (Prof dr B. Streubel, Vienna). The following variants were detected in heterozygous state: c.(1194+5G>A); (1716C>G).

We called the parents of our patients and explained the nature of the disease and therapeuthic plans with enzyme treatment. They didn't accept enzyme therapy because they are distrustful and afraid of the side effects of the treatment. We warned them of the importance of early enzyme therapy. Pompe disease is a rare congenital neurometabolic disease that can be treated. For this reason, the reaction of parents is totally unexpected for us.

What should we do? To what degree do parents have the right to decide about the fate of their children? The challenge for every doctor is how to convince parents of the necessity of the treatment of their children.

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Saturday, 16 May, 10:30
[Educational Course on Late-onset Pompe Disease: Patient assessment]

Pompe disease - case presentation

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Pompe disease is a metabolic inherited myopathy due to acid maltase(1,4-glucosidase) deficiency with glycogen storage.

Our case presentation: a 30-year old female patient who came to our clinic for enzyme replacement therapy.

The first symptoms occurred insidiously in 2005 with fatigability, standing and walking impairment, especially climbing stairs, frequent falls with a slowly progressive course and increasing difficulties.

The clinical exam established: underweight patient, weak connective tissue, walking impairment with bilateral assistance, proximal weakness and generalized muscular atrophies, more important at the shoulder and pelvic girdle muscles, globally abolished deep tendon reflexes.

In 2006 the EMG revealed a myopathic disorder with progressive muscular dystrophy and muscle biopsy was recommended. The muscular biopsy in 2006 showed changes compatible with glycogen metabolic myopathy.

In 2012, in the course of the disease, respiratory failure due to respiratory muscle weakness sets in. The patient undergoes pulmonary function testing and the pneumologist recommends BIPAP noninvasive ventilation, 8h daily during sleep.

In February 2013 the DNA PCR detected 2 heterozygous mutations in the GAA gene, first located in intron 1 and second in exon 15 and the likely diagnosis is Pompe disease adult form.

Since May 2013 the patient has started replacement therapy with recombinant acid α-glucosidase injected intravenously every 2 weeks with respiratory and fatigability improvement, nonprogressive motor weakness.

Saturday, 16 May, 11:10
[Educational Course on Late-onset Pompe Disease: Disease control]

Toward the therapy of late-onset Pompe disease

Danijela Petković Ramadža, Ivo Barić

University Hospital Centre Zagreb, Croatia

Pompe disease is a rare autosomal recessive glycogen storage disorder due to deficiency of lysosomal enzyme acid alpha-glucosidase. Main clinical feature of late onset Pompe disease (LOPD) is progressive muscle weakness mainly involving proximal muscles and diaphragm.

Enzyme replacement therapy (ERT) with alglucosidase alpha in LOPD patients improves motor and stabilizes or slightly improves respiratory function, and prolongs survival. It is well tolerated and most adverse events are mild or moderate, although life-threatening reactions were described. This disease-specific treatment should be started at first signs of muscle disease. Presymptomatic patients should be closely monitored until the onset of first clinical signs, when ERT should commence. Recommendations about the treatment of patients with advanced stage of disease are not so clear.

Limitations of current ERT are: relatively high doses (alglucosidase alpha is poorly targeted to the muscles and up to 80% trapped in the liver), limited clinical benefit, induction of immune response, need for lifelong intravenous therapy, quite high costs, etc.

Emerging therapies that could overcome disadvantages of current ERT are new ERT with improved uptake by muscle cells, small molecule therapies (pharmacological chaperones and substrate reduction therapy) and gene therapy.

Respiratory complications are the common cause of death. Therefore, one of the most important aspects of management is a close monitoring of respiratory function and timely interventions which include aggressive treatment of infections, regular vaccinations, respiratory therapy for adequate clearance of airway secretions, non-invasive (CPAP or BiPAP) and invasive ventilatory support, etc.

Regular physical therapy with sub-maximal aerobic exercise may increase muscle strength and gentle daily stretching may prevent contractures and deformities. As low bone mineral density is a common feature, all patient should be annually screened with DEXA. In case of abnormal finding they should have vitamin D and calcium supplementations, and ones with osteoporosis might be considered for bisfosfonate therapy. Patients are recommended to have protein rich diet and in case of feeding and swallowing difficulties they may benefit from various forms of tube feeding.

Considering all mentioned LOPD patients should be managed by a multidisciplinary team in a specialized metabolic centre.

Saturday, 16 May, 11:30
[Educational Course on Late-onset Pompe Disease: Disease control]

A case of a patient refusing treatment

Lea Leonardis

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A 10-year old girl was admitted to the hospital due to gastrointestinal problems. Coincidentally, her serum transaminases and creatine kinase levels were found increased. The results of conventional EMG conduction studies were normal, but needle electromyography revealed some small, short and polyphasic (myopathic), and some high and prolonged (neurogenic) motor unit potentials. Clinically, the girl's muscular status at that time was unremarkable. Testing with blood dry spot showed that acid alpha glucosidase activity was decreased. Pompe disease was genetically confirmed. The patient and her parents were fully informed about the disease, including about its progressive nature, but they refused treatment.

Six years later the patient had an epileptic generalised tonic-clonic seizure late at night in a disco. In her EEG, generalised spikes and spike-waves during rest and to photostimulation could be seen. The results of brain MRI and MRA were normal.

In the following two years she became awkward in gym. In her muscular status on examination at 18 years of age, weakness of several muscle groups could be detected: slight weakness of facial muscles, moderate weakness of hip flexors and extensors, knee flexors weakness, and slight dorsal flexors weakness. She couldn't rise from a supine position without using arms for the support. Respiratory functions and the results of arterial gas analyses were normal.

Asymptomatic patients should be followed-up regularly to start treatment on time. Although our patient's proximal muscles are evidently weak, she denies the diagnosis and refuses the enzyme replacement therapy which – as explained also to the patient – is most efficient if started as early as possible after the diagnosis when muscular impairment is still small.

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Saturday, 16 May, 11:40
[Educational Course on Late-onset Pompe Disease: Disease control]

Pompe disease – internist check up

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Late onset Pompe disease present with broad spectrum of clinical manifestations (phenotypical spectrum). Therefore the only right way to approach Pompe patient is multidisciplinary. Neurologists are mostly the first experts that will contact with LOPD patient. Because of the influence of the disease on pulmonary, cardiologic, gastrointestinal organs and metabolic processes (osteopenia and osteoporosis) internist assessment is often necessary. Several other tissues may be involved in the course of disease beside skeletal and smooth muscle (brain, liver, spleen, salivary glands, kidney and blood vessels. Internist different specialities also have a chance to detect LOPD patient if they are aware of it. In patients with late onset Pompe disease cardiomyopathy is exceptional finding while heart rhythm disorders seem to be more frequent. Therefore cardiac follow up in patients with LOPD should include periodical Holter-EKG monitoring. Pulmonary involvement present with broad spectrum of respiratory insufficienty (even sleep apnea), frequent respiratory tract infections require involvement of internist-pulmologist. Gastrointestinal tract involvement (swallowing assessment and evaluation for gastroesophageal reflux; nutritional problems (vitamins and minerals)) seek care of internist-gastroenterologist. Osteopenia and osteoporosis seek for endocrinologist. Enzyme replacement therapy (ERT) is availabe for Pompe disease and drug instillation can be potentially challenging. Internist will mostly deal with potential side effects which some of them can be life threating. This lecture will bring essentials of internist check up for patient with LOPD.

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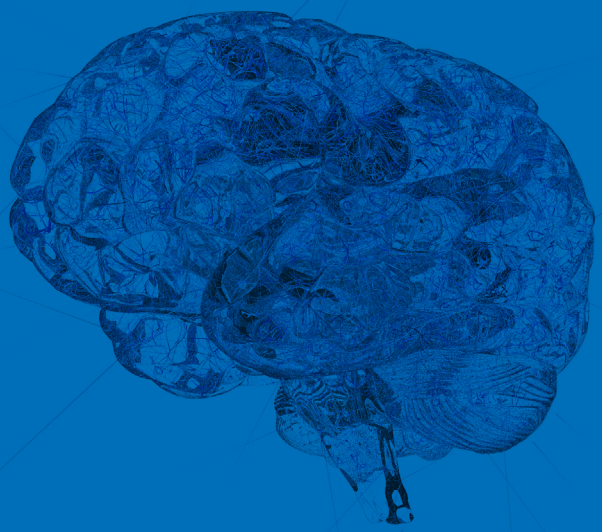

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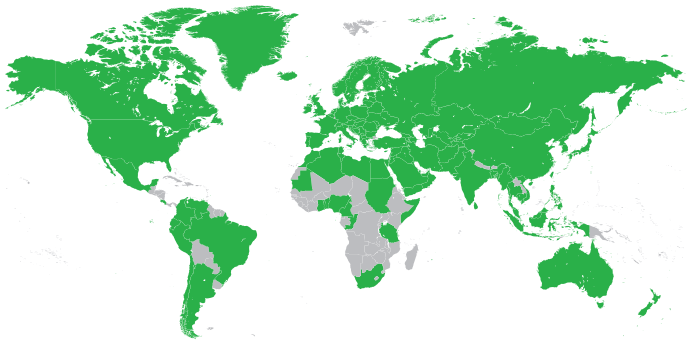

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INDIKACIJE: Zdravljenje shizofrenije; učinkovito preprečuje relapse pri shizofrenih bolnikih v stabilni remisiji, ki so na vzdrževalnem zdravljenju s Seroquelom SR; zdravljenje zmernih do hudih maničnih epizod pri bolnikih z bipolarno motnjo; zdravljenje depresivnih epizod pri bolnikih z bipolarno motnjo; preprečevanje ponavljanja epizod pri bipolarni motnji pri bolnikih, katerih manične ali depresivne epizode so bile odzivne na zdravljenje s kvetiapinom; kot dodatno zdravljenje velikih depresivnih epizod pri bolnikih z veliko depresivno motnjo (MDD - Major Depressive Disorder), ki so imeli suboptimalni odziv na antidepresivno monoterapijo.
ODMERJANJE IN NAČIN UPORABE: Seroquel SR jemlje bolnik enkrat na dan, brez hrane (vsaj eno uro pred obrokom). Bolnik mora tablete s podaljšanim sproščanjem pogoltniti cele in jih ne sme lomiti, žvečiti ali drobiti.
Odrasli: ***Zdravljenje shizofrenije in zmernih do hudih maničnih epizod pri bipolarni motnji:*** Dnevni odmerek na začetku zdravljenja je 300 mg 1. dan in 600 mg 2. dan. Priporočeni dnevni odmerek je 600 mg, vendar se lahko, če je klinično upravičeno, odmerek poveča do 800 mg. Odmerek je treba prilagoditi v učinkovitem razponu odmerkov od 400 mg do 800 mg na dan, odvisno od kliničnega odziva in bolnikovega prenašanja. Za vzdrževalno zdravljenje shizofrenije odmerka ni treba prilagajati. ***Zdravljenje depresivnih epizod, povezanih z bipolarno motnjo:*** Odmerek se vzame pred spanjem. Dnevni odmerki prve štiri dni zdravljenja so 50 mg (1. dan), 100 mg (2. dan), 200 mg (3. dan) in 300 mg (4. dan). Priporočeni dnevni odmerek je 300 mg. Glede na bolnikov odziv je mogoče Seroquel SR pri posameznih bolnikih titrirati do odmerka 600 mg na dan. ***Za preprečevanje ponavljanja epizod bipolarne motnje:*** Odmerek zdravila Seroquel SR je mogoče prilagoditi glede na klinični odziv in prenašanje posameznega bolnika v razponu od 300 do 800 mg/dan. ***Kot dodatno zdravljenje velikih depresivnih epizod pri veliki depresivni motnji:*** Odmerek se vzame pred spanjem. Dnevni odmerek na začetku zdravljenja je 50 mg 1. in 2. dan ter 150 mg 3. in 4. dan. Zdravnik mora poskrbeti, da je za zdravljenje uporabljen najmanjši učinkoviti odmerek, začenši s 50 mg/dan. Potreba po povečanju odmerka s 150 na 300 mg/dan mora temeljiti na oceni posameznega bolnika. ***Starejši:*** Tako kot druga antipsihotična in antidepresivna zdravila je treba tudi Seroquel SR pri starejših bolnikih uporabljati previdno, še posebej v začetnem obdobju uporabe. Potrebno utegne biti počasnejše titriranje Seroquela SR, dnevni terapevtski odmerek pa je lahko nižji kot pri mlajših bolnikih. Povprečni plazemski očistek kvetiapina je bil pri starejših bolnikih za 30 do 50 % manjši kot pri mlajših. Pri starejših bolnikih je treba zdravljenje začeti s 50 mg/dan. Odmerek je mogoče povečevati po 50 mg/dan do učinkovitega odmerka, odvisno od bolnikovega individualnega kliničnega odziva in prenašanja. Pri starejših bolnikih z velikimi depresivnimi epizodami, je treba odmerjanje začeti s 50 mg/dan od 1. do 3. dne, nato je treba odmerek povečati na 100 mg/dan 4. dan in na 150 mg/dan 8. dan. Uporabiti je treba najmanjši učinkoviti odmerek, začenši s 50 mg/dan. Če je na podlagi ocene posameznega bolnika odmerek treba povečati na 300 mg/dan, se tega ne sme narediti prej kot 22. dan zdravljenja. Učinkovitost in varnost nista ocenjeni pri bolnikih, starejših od 65 let, z depresivnimi obdobji v okviru bipolarne motnje. ***Otroci in mladostniki:*** Zdravila Seroquel SR ni priporočljivo uporabljati pri otrocih in mladostnikih, mlajših od 18 let, ker ni podatkov, ki bi podpirali njegovo uporabo v tej starostni skupini. ***Okvara jeter:*** Kvetiapin se obsežno presnovi v jetrih. Pri bolnikih z znano okvaro jeter je zato treba Seroquel SR uporabljati previdno, še posebej v začetnem obdobju zdravljenja. Pri bolnikih z okvaro jeter je treba zdravljenje začeti s 50 mg/dan. Odmerek je mogoče povečevati po 50 mg/dan do učinkovitega odmerka, odvisno od bolnikovega individualnega kliničnega odziva in prenašanja.
NEŽELENI UČINKI: ***zelo pogosti:*** omotica, zaspanost, glavobol, ekstrapiramidni simptomi, suha usta, odtegnitveni sindrom, zvišanje koncentracije serumskih trigliceridov, zvišanje koncentracije celokupnega holesterola, znižanje holesterola HDL, povečanje telesne mase, znižanje hemoglobina, odtegnitveni sindrom; ***pogosti:*** levkopenija, povečano število eozinofilcev, hiperprolaktinemija, znižanje celotnega T4, znižanje prostega T4, znižanje celotnega T3, zvišanje TSH, večji apetit, nenavadne sanje in nočne more, samomorilno razmišljanje in samomorilno vedenje, dizartrija, tahikardija, palpitacije, zamegljen vid, ortostatska hipotenzija, dispneja, zaprtje, dispepsija, bruhanje, blaga astenija, periferni edemi, razdražljivost, pireksija, zvišanje vrednosti serumskih transaminaz (ALT), zvišanje ravni gama GT, zmanjšanje števila nevtrofilcev, zvišanje glukoze v krvi do hiperglikemične ravni; ***otroci in mladostniki (neželeni učinki, ki se pojavljajo bodisi v višji kategoriji ali niso bili ugotovljeni v odrasli populaciji): zelo pogosti:*** večji apetit, zvišanje prolaktina, zvišanje krvnega tlaka, ekstrapiramidni simptomi pogosti: razdražljivost; Poročanje o domnevnih neželenih učinkih zdravila po izdaji dovoljenja za promet je pomembno. Omogoča namreč stalno spremljanje razmerja med koristmi in tveganji zdravila. Od zdravstvenih delavcev se zahteva, da poročajo o katerem koli domnevnem neželenem učinku zdravila na: Univerzitetni klinični center Ljubljana, Interna klinika, Center za zastrupitve, Zaloška cesta 2, SI-1000 Ljubljana, Faks: + 386 (0)1 434 76 46, e-pošta: farmakovigilanca@kclj.si.
POSEBNA OPOZORILA IN PREVIDNOSTNI UKREPI: Ker je zdravilo Seroquel SR indicirano za zdravljenje shizofrenije, bipolarne motnje in kot dodatno zdravljenje velikih depresivnih epizod pri bolnikih z veliko depresivno motnjo, je treba njegove varnostne značilnosti upoštevati glede na diagnozo posameznega bolnika in uporabljeni odmerek. Dolgoročna učinkovitost in varnost pri bolnikih z veliko depresivno motnjo (MDD) nista ocenjeni v primeru, ko se uporabi kot dodatno zdravilo, vendar pa sta bili dolgoročna učinkovitost in varnost ocenjeni pri odraslih bolnikih v monoterapiji. Klinična preskušanja zdravila Seroquel so pokazala, da so poleg znanih varnostnih značilnosti, ugotovljenih pri odraslih, nekateri neželeni učinki pri otrocih in mladostnikih pogostejši kot pri odraslih (večji apetit, zvišanje prolaktina v serumu in ekstrapiramidni simptomi), pojavil pa se je tudi neželen učinek, ki pred tem ni bil zabeležen v študijah pri odraslih (zvišan krvni tlak). Pri otrocih in mladostnikih so opazili tudi spremembe v preiskavah delovanja ščitnice. Depresija je povezana z večjim tveganjem za pojav samomorilnih misli, samopoškodovanja in samomorilnosti (s samomorom povezani dogodki). Takšno tveganje obstaja, vse dokler ne pride do popolnega umika bolezni. V kliničnih, s placebom kontroliranih preskušanjih pri odraslih bolnikih je bil kvetiapin med zdravljenjem depresivnih epizod pri bipolarni motnji in MDD povezan z večjo incidenco ekstrapiramidnih simptomov kot placebo. Zdravljenje s kvetiapinom je bilo povezano z zaspanostjo in sedacijo. Kvetiapin je treba uporabljati previdno pri bolnikih s srčno-žilnimi boleznimi, možgansko-žilnimi boleznimi in drugimi stanji, ki povzročajo nagnjenost k hipotenziji. Kvetiapin lahko povzroči ortostatsko hipotenzijo, še posebej med začetnim titriranjem odmerka; v takem primeru zmanjšamo odmerek ali uvedemo postopnejše titriranje. Priporočljiva je previdnost pri zdravljenju bolnikov z anamnezo konvulzij. Če se pojavi maligni nevroleptični sindrom, je treba zdravljenje s kvetiapinom prekiniti in poskrbeti za ustrezno terapijo. Občasno so v kliničnih preskušanjih kvetiapina opažali hudo nevtropenijo. Sočasna uporaba kvetiapina z močnim induktorjem jetrnih encimov bistveno zmanjša koncentracijo kvetiapina v plazmi. Pri bolnikih, zdravljenih s kvetiapinom, je bilo opisano povečanje telesne mase. Bolnike, ki dobivajo katerikoli antipsihotik, vključno s kvetiapinom, je treba spremljati glede znakov in simptomov hiperglikemije. V kliničnih preskušanjih s kvetiapinom so opazili porast trigliceridov, LDL in celokupnega holesterola ter znižanje HDL. Če kvetiapin predpišete skupaj z zdravili, ki podaljšujejo interval QTc, ali z drugimi nevroleptiki, zlasti pri starejših in pri bolnikih s prirojenim sindromom dolgega QT, kongestivnim srčnim popuščanjem, hipertrofijo srca, hipokaliemijo ali hipomagneziemijo, je potrebna previdnost. Akutni odtegnitveni simptomi kot so nespečnost, slabost, glavobol, diareja, bruhanje, omotica in razdražljivost so bili opisani po takojšnjem prenehanju zdravljenja s kvetiapinom. Priporočeno je postopno, najmanj eno ali dvotedensko, prenehanje zdravljenja. Kvetiapin ni odobren za zdravljenje psihoze, povezane z demenco. Med uporabo kvetiapina je bila zabeležena disfagija. Med uporabo kvetiapina sta bili opisani zaprtost in zapora črevesa. Pri uporabi antipsihotičnih zdravil so poročali o primerih venske tromboembolije. O pankreatitisu so poročali v kliničnih raziskavah in v obdobju trženja.Tablete Seroquel SR vsebujejo laktozo. Bolniki z redko dedno intoleranco za galaktozo, laponsko obliko zmanjšane aktivnosti laktaze ali malabsorbcijo glukoze/galaktoze ne smejo jemati tega zdravila. Podatki o uporabi kvetiapina v kombinaciji z valproatom ali litijem pri zdravljenju akutnih epizod zmerne do hude manije so omejeni.
KONTRAINDIKACIJE: Preobčutljivost za zdravilno učinkovino ali katerokoli pomožno snov v zdravilu. Sočasna uporaba zaviralcev citokroma P450 3A4, npr. zaviralcev proteaz HIV, azolskih antimikotikov, eritromicina, klaritromicina in nefazodona.
MEDSEBOJNO DELOVANJE Z DRUGIMI ZDRAVILI IN DRUGE OBLIKE INTERAKCIJ: Ker kvetiapin deluje v prvi vrsti na osrednje živčevje, ga je treba previdno uporabljati v kombinaciji z drugimi centralno delujočimi zdravili in alkoholom. Sočasna uporaba kvetiapina z zaviralci CYP3A4 je kontraindicirana. Prav tako kvetiapina ni priporočljivo jemati z grenivkinim sokom. Sočasna uporaba karbamazepina, fenitoina in tioridazina je pomembno povečala očistek kvetiapina. Pri bolnikih, ki dobivajo induktor jetrnih encimov, naj bi zdravljenje s kvetiapinom uvedli le, če koristi terapije s kvetiapinom po zdravnikovi presoji odtehtajo tveganja zaradi opustitve induktorja jetrnih encimov. Potrebna je previdnost, če se kvetiapin uporablja sočasno z zdravili, za katere je znano, da povzročijo elektrolitsko neravnovesje ali podaljšajo QTc interval.
NOSEČNOST IN DOJENJE: Kvetiapin naj bi med nosečnostjo uporabili le, če koristi upravičujejo možna tveganja. Ženskam, ki dojijo, je treba svetovati, naj med uporabo kvetiapina ne dojijo. Pri novorojenčkih, ki so bili v tretjem tromesečju nosečnosti izpostavljeni antipsihotikom (tudi kvetiapinu) se lahko pojavijo neželeni učinki, vključno z ekstrapiramidnimi in/ali odtegnitvenimi simptomi, ki se lahko razlikujejo glede na resnost in trajanje po porodu. Poročali so o agitaciji, hipertoniji, hipotoniji, tremorju, zaspanosti, dihalni stiski in motnjah hranjenja. Zato je treba novorojenčke skrbno spremljati.
IMETNIK DOVOLJENJA ZA PROMET: AstraZeneca UK Limited, 2 Kingdom Street, London, W2 6BD, Velika Britanija
REŽIM IZDAJE: Rp – Zdravilo se izdaja le na zdravniški recept.
DATUM PRIPRAVE INFORMACIJE: avgust 2014
Pred predpisovanjem, prosimo, preberite celoten povzetek glavnih značilnosti zdravila.
Dodatne informacije so na voljo pri AstraZeneca UK Limited, MAT047/15 v Sloveniji, Verovškova 55, 1000 Ljubljana.
INFORMACIJA PRIPRAVLJENA: april 2015.
Samo za strokovno javnost.

1. Povzetek glavnih značilnosti zdravila Seroquel SR, avgust 2014.

AstraZeneca

MAT047/15

Reference: 1. Davidson MA, J Allen Disord 2008; 11: 628-41; 2. Asherson Pet al. Curr Med Res Opin 2014:30(8):1657-72; 3. Strattera Povzetek glavnih značilnosti zdravila, januar 2015

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POMPEJEVA BOLEZEN JE PROGRESIVNA, ŽIVLJENJSKO OGROŽUJOČA, VENDAR OZDRAVLJIVA ŽIVČNOMIŠIČNA BOLEZEN[1-4]

Pri bolnikih s poznim (adultnim) začetkom Pompejeve bolezni so najpogosteje prisotni naslednji znaki in simptomi:

- Napredujoča šibkost proksimalnih mišic, ki je najbolj izrazita v spodnjih okončinah[3,5]
- Dihalna odpoved[1,6,7]
- Rahlo do zmerno zvečane vrednosti CK (2-5x vrednosti normale)[1,4,8]

Pozno prepoznavanje Pompejeve bolezni poveča tveganje za hudo invalidnost in zgodnjo zmrt.

Pravočasna diagnoza in zdravljenje lahko stabilizirata ali izboljšata mišično moč in stabilizirata pljučno funkcijo.[1,2,9-11]

Zdravljenje je na voljo – testirajte bolnike z neopredeljeno ramensko medenično šibkostjo, restriktivnimi motnjami dihanja, oslabelimi proksimalnimi mišicami in/ali povišanimi vrednostmi CK. [5,12,13]

CK - encim kreatin kinaza

Viri:
1. American Association of Neuromuscular & Electrodiagnostic Medicine. Diagnostic criteria for late-onset (childhood and adult) Pompe disease. *Muscle Nerve.* 2009;40(1):149-160. **2.** Hagemans MLC et al. Disease severity in children and adults with Pompe disease related to age and disease duration. *Neurology.* 2005;64(12):2139-2141. **3.** Hirschhorn R et al. Glycogen storage disease type II: acid α-glucosidase (acid maltase) deficiency. In: Scriver CR et al, eds. *The Metabolic & Molecular Bases of Inherited Disease.* 8th ed. New York, NY: McGraw-Hill; 2001:3389-3420. **4.** Kishnani PS et al. Pompe disease diagnosis and management guideline. *Genet Med.* 2006;8(5):267-288. **5.** van der Beek N et al. Clinical features and predictors for disease natural progression in adults with Pompe disease: a nationwide prospective observational study. *Orphanet J Rare Dis.* 2012;7:88. **6.** Mellies U et al. Sleep-disordered breathing and respiratory failure in acid maltase deficiency. *Neurology.* 2001;57(7):1290-1295. **7.** Mellies U et al. Pompe disease: a neuromuscular disease with respiratory muscle involvement. *Respir Med.* 2009;103(4):477-484. **8.** Tinkle B et al. Glycogen Storage Disease Type II (Pompe Disease). *GeneReviews.* 1993. www.ncbi.nlm.nih.gov/books/NBK1261. **9.** van der Ploeg AT et al. A randomized study of alglucosidase alfa in late-onset Pompe's disease. *N Engl J Med.* 2010;362(15):1396-1406. **10.** Güngör D et al. Impact of enzyme replacement therapy on survival in adults with Pompe disease: results from a prospective international observational study. *Orphanet J Rare Dis.* 2013;8:49. **11.** Cupler EJ et al; AANEM Consensus Committee on Late-onset Pompe Disease. Consensus treatment recommendations for late-onset Pompe disease. *Muscle Nerve.* 2012;45(3):319-333. **12.** Winchester B et al; Pompe Disease Diagnostic Working Group. Methods for a prompt and reliable laboratory diagnosis of Pompe disease: report from an international consensus meeting. *Mol Genet Metab.* 2007;93(3):275-281. **13.** Hobson-Webb LD, Kishnani PS. How common is misdiagnosis in late-onset Pompe disease?*Muscle Nerve.* 2012;45(2):301-302.

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