

SCIENTIFIC COMMITTEE

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Robert Vink (Adelaide, *Australia*)
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> Workshop Organizer Nathalie Letrillard Spinelli

*sdrm@sdrmsociety.org*Phone +33 (6) 52.35.89.91

SDRM

International Society for the Development of the Research on Magnesium www.sdrmsociety.org

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Official Journal:

Magnesium Research





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Dear Colleague,

it is a pleasure for us to welcome you in KRAKOW.

In our modern society neurological disorders are becoming more and more relevant. Social challenges, carreer pressures, lifestyle, globalization, concurr in increasing stress, anxiety, depression, addiction, sleep disorders and other pathological conditions. Is there a role of Magnesium in this complex field? Can we prevent some of these conditions by an healthier lifestyle?

Our challenge this time has been to gather the latest scientific data on magnesium in the different aspects of neurosciences and provide the most scientifically sound information to the participants.

We hope that scientific contributions will stimulate questions, inspire discussions, hypotheses and hopefully will be the ground for new projects and collaborations.

We have invited young Researchers to present their work, you should support them and encourage them to further study this fascinationg cation. The future knowledge depends on this young generation, we need their efforts.

Please be an active participant, share your experience, participate to discussions, bring new ideas or suggestions in a unformal environment surrounded by the fascinating, relaxing and inspiring city of Krakow and its embracing beauty.

We are looking forward to spend two exciting days with you all.

On behalf of the Organizing Committee

Federica Wolf, PhD





Friday April 20th, 2018 - Morning

09:00 - 09:30 Registration and Welcome Coffee

09:30 - 09:45 Welcome Remark

Federica I. Wolf (Rome, *Italy*)

Magdalena Maj-Zurawska (Warsaw, Poland)

Gabriel Nowak (Krakow, Poland)

KEYNOTE LECTURE Magnesium Functions in CNS

09:45 - 10:30 Robert Vink (Adelaide, *Australia*)

SESSION 1 Magnesium intake and Health

Chairmen Andrzej Mazur (Clermont-Ferrand, France)

Federica I. Wolf (Rome, *Italy*)

10:30 - 10:55 Epidemiology of Low Magnesium Intake and Status

Andrzej Mazur (Clermont-Ferrand, *France*)

10:55 - 11:20 Low Magnesium Status and Health: an Update

Jeanette AM Maier (Milan, *Italy*)

11:20 - 11:45 Innovative approaches for Mg quantification in cells,

tissues and mini organs Stefano Iotti (Bologna, *Italy*)

11:45 - 12:15 Oral Communications

11:45 - 11:55 OC01A

Percentage of hypomagnesemia and hypermagnesemia in a hospital between 2006 and 2014. Aggravating factors and risks M. Guerra, B. Founaurd, S. Izquierdo, F. López-Alcuten,

M. Galvez, J. F. Escanero

Area of Physiology, Depart. of Pharmacology and Physiology, University of Zaragoza, Clinical Biochemistry Service, Miguel Servet University Hospital, Clinical Biochemistry Service, Lozano Blesa

University Hospital, Zaragoza, Spain

11:55 - 12:05 OC02

CellViewer, a lab-on-a-chip technology for in-vivo-like imaging

and study of biological phenomena

A. Sargenti, M. Rossi, G. Farruggia, S. Pasqua, S. Bonetti, A. Quaranta, F. Musmeci, F. Alviano, D. Gazzola and S. Iotti Department of Pharmacy and Biotechnology (FABIT), Department of Experimental, Diagnostic and Specialty Medicine (DIMES),

University of Bologna, CellDynamics SRL, Bologna, IT

12:05 - 12:15 OC03

A challenging future for magnesium research in the brain:

organoids and brain on-a-chip

A. Cazzaniga, V. Romeo, S. Castiglioni

"L. Sacco" Department of Biomedical and Clinical Sciences,

University of Milan, Milan, IT

12:30 - 14:00 Buffet Lunch



SCIENTIFIC PROGRAM Friday April 20th, 2018 - Afternoon

SESSION 2	Magnesium in Anxiety, Stress and Depression – Part I
Chairmen	Louise Dye (Leeds, <i>United Kingdom</i>) Gabriel Nowak (Krakow, <i>Poland</i>)
14:00 - 14:25	The Effects of Magnesium Supplementation on Subjective Stress and Anxiety: a Systematic Review Neil Boyle (Leeds, <i>United Kingdom</i>)
14:25 - 14:50	Magnesium in Anxiety and Depression: Lesson from a Rodent Model Ewa Poleszak (Lublin, <i>Poland</i>)
14:50 - 15:15	Low Levels of Magnesaemia Induce Psychiatric Comorbidity in Patients with Inflammatory Bowel Disease Franco Scaldaferri (Rome, <i>Italy</i>)
15:15 - 15:45	Oral Communications
15:15 - 15:25	OC04 Investigating the functional role of TRPM6 in colon mucosa F. Luongo, V. Trapani, V. Petito, G. Pietropaolo and F. I. Wolf Istituto di Patologia Generale, Facoltà di Medicina e Chirurgia "A. Gemelli", Università Cattolica del Sacro Cuore, Rome, Italy
15:25 - 15:35	OC05 Magnesium and stress in the domestic pig E. V. Bushby, L. Dye, H. M. Miller, L. M. Collins Faculty of Biological Sciences, School of Psychology, University of Leeds, UK
15:35 - 15:45	OC06 Therapeutic Drug Monitoring (TDM) of depression – augmentation by magnesium ions (NCN2012/07/B/NZ7/04375) B. Ryszewska-Pokraśniewicz, M. Skalski, P. Januszko, E. Drozdowicz-Jastrzębska, G. Nowak, A. Pilc, M. Radziwoń-Zaleska Department of Psychiatry, Medical University of Warsaw, Poland Institute of Pharmacology, Polish Academy of Sciences, Kraków, Poland
15:45 - 16:10	Coffee/Tea Break



Friday April 20th, 2018 - Afternoon

SESSION 3 Magnesium in Stress, Pain and Addiction

Chairmen Louise Dye (Leeds, *United Kingdom*) Mihai Nechifor (Iasi, *Romania*)

16:10 - 16:35 Neurophysiological mechanisms of different stress resiliance

Pavel Umriukhin (Moscow, Russia)

16:35 - 17:00 Magnesium and Pain: state of the art and therapeutic

perspectives

Gisèle Pickering (Clermont-Ferrand, *France*)

17:00 - 17:25 **Magnesium and Addiction**

Mihai Nechifor (Iasi, *Romania*)

17:25 - 17:45 **Oral Communications**

17:25 - 17:35 OC07

> Injection of magnesium sulphate induces local hyperalgesia via activation the transient receptors potential ion channels

D. P. Srebro, S. Vučković, K. Savić Vujović, B. Medić,

M. Prostran

Department of Pharmacology, Clinical Pharmacology

and Toxicology, Faculty of Medicine, University of Belgrade,

Belgrade, Serbia

17:35 - 17:45 **OC08**

The impact of magnesium prophylaxis on disability, quality

of life, and depressive and anxiety symptoms in pediatric migraine

<u>G. Kovacevic</u>, D. Stevanovic, D. Bogicevic, D. Nikolic,

S. Ostojic, B. Vucetic Tadic, B. Nikolic, I. Bosiocic, N. Ivancevic,

K. Jovanovic, J. Samardzic, J. Jancic

Mother and Child Health Institute of Serbia,

Clinic for Neurology and Psychiatry for Children and Youth,

University Children's Hospital,

Faculty of Medicine, University in Belgrade, Institute of Pharmacology, Clinical Pharmacology

and Toxicology, Belgrade, Serbia

SPONSORED SESSION - Nova Biomedical

The role of ionised magnesium – new aspects 17:45 - 18:05 Bogdan Milojkovic (Nova Biomedical, *UK*)



Saturday April 21st, 2018 - Morning

SESSION 4	Magnesium in Anxiety,		
	Stress and Depression – Part II		

Chairmen Mihai Nechifor (Iasi, *Romania*) Ewa Poleszak (Lublin, *Poland*)

08:30 - 08:55 Magnesium and depression in the context

of the Mediterranean diet: epidemiological data

Almudena Sanchez-Villegas (Las Palmas de Gran Canaria, *Spain*)

08:55 - 09:20 Magnesium and other Metal Ions in Depression

Gabriel Nowak (Krakow, *Poland*)

09:20 - 09:45 Interaction of magnesium and glutamate receptors

in the mechanism of antidepressant action

Bartłomiej Pochwat (Krakow, *Poland*)

09:45 - 10:25 **Oral Communications**

09:45 - 09:55 **OC09**

> The effects of NMDA receptor antagonists – ketamine and magnesium sulphate on the body temperature and acute nociceptive pain in rats

> K. Savić Vujović, S. Vučković, A. Vujović, B. Medić, D. Srebro,

M. Prostran

Department of Pharmacology, Clinical Pharmacology and Toxicology, Faculty of Medicine, University of Belgrade, Hospital

for ENT, Belgrade, Serbia

09:55 - 10:05 **OC10**

> Antiepileptic and antiepileptogenic effect of magnesium on nickel-induced epileptiform activity of leech Retzius neurons M. Stanojević, S. Lopicic, S. Spasic, V. Nedeljkov, I. Banjac, D. Pathak, M. Prostran

Institute for Pathological Physiology, Faculty of Medicine, Institute for Pharmacology, Clinical Pharmacology and Toxicology,

Faculty of Medicine University of Belgrade, Belgrade, Boston University School of Medicine, Boston, USA

10:05 - 10:15 OC11

> Mg and kidney: the role of hypomagnesaemia in acute kidney injury

B. Medić, K. Savić Vujović, D. Srebro, S. Vučković, M. Prostran Department of Pharmacology, Clinical Pharmacology

and Toxicology, Faculty of Medicine, University of Belgrade, Belgrade, Serbia



Saturday April 21st, 2018 - Morning

10:15 - 10:25 OC12

 $Magnesium\ modulates\ the\ permeability\ of\ the$

Blood-Brain Barrier

V. Romeo, L. Locatelli, A. Sargenti, A. Cazzaniga

"L. Sacco" Department of Biomedical and Clinical Sciences,

University of Milan, Milan, IT

Department of Pharmacy and Biotechnologies, University

of Bologna, Bologna, IT

10:25 - 10:45 Coffee Break

SESSION 5 Magnesium in Aging

Chairmen Federica I. Wolf (Rome, *Italy*)
Jeanette AM Maier (Milan, *Italy*)

10:45 - 11:10 Magnesium, Transporters and Aging:

Lesson from Molecular Genetics

Vladimir Chubanov (Munich, *Germany*)

11:10 - 11:35 Magnesium Status in Alzheimer's Disease:

A Systematic Review

Nicola Veronese (Padua, *Italy*)

11:35 - 12:00 Magnesium and muscle function

Valentina Trapani (Rome, *Italy*)

12:00 - 12:30 Oral Communications

12:00 - 12:10 OC13

Effect of inflammation on muscle function in a murine colitis

model: the contribution of Magnesium

V. Petito, V. Trapani, F. Luongo, G. Pietropaolo, C. Petito, C. Graziani, L. Lopetuso, V. Arena, A. Gasbarrini, F. Scaldaferri

and F. I. Wolf

Gastroenterological Area, Gastroenterological and

Endocrino-Metabolical Sciences Department, Institute of General

Pathology

Fondazione Policlinico Universitario Gemelli, Università Cattolica

del Sacro Cuore, Rome, Italy

12:10 - 12:20 OC14

Effects of magnesium, vitamin C and D3 on miR-1 and miR-29b expression in adipose-derived mesenchymal stem cells

N. Sabová, A. Samáková, O. Sprušanský, Z. Lešková,

T. Bačkayová, A. Gažová, J. Kyselovič

Department of Pharmacology and Toxicology,

Faculty of Pharmacy,

Institute of Pharmacology and Clinical Pharmacology,

Faculty of Medicine,

Clinical Research Unit, V. Internal Clinic, Faculty of Medicine,

Comenius University in Bratislava, SK



Saturday April 21st, 2018 - Morning

12:20 - 12:30

Dietary magnesium intake modifies the number of hepatic stem

cells in rat

S. Aupet, J. Gromand, L. Richert, A. Berthelot and H. Martin Faculté des Sciences Médicales et Pharmaceutiques, Besançon, FR

12:30 - 12:45 Award Nomination and Closing Ceremony

Chairman Federica I. Wolf (Rome, *Italy*)

> Jury Andrzej Mazur (Clermont-Ferrand, *France*)

> > Gabriel Nowak (Krakow, *Poland*) Robert Vink (Adelaide, *Australia*)

Prizes will be awarded by Dr. Cécile Durlach

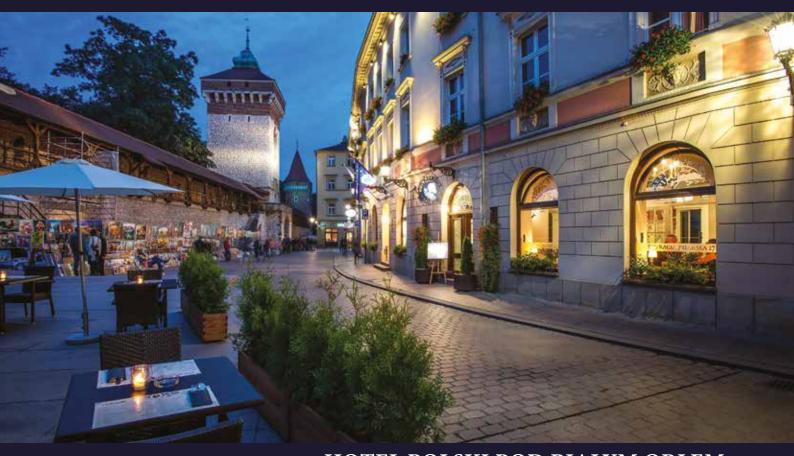
12:45 - 14:00 Farewell Lunch





GENERAL INFORMATION

CONGRESS VENUE



HOTEL POLSKI POD BIAŁYM ORŁEM

HOTEL POLSKI POD BIAŁYM ORŁEM

Donimirski Boutique Hotels ul. Pijarska 17 31-015 Kraków (Poland) www.donimirski.com

Tel: +48 12 422 11 44

Registration Fees - All fees shown are in Euro (€)

Registration categories	on site Registrations	
Delegate as SDRM member (*)	200 €	
Delegate (non member)	300 €	
Student (**)	100 €	

- (*) As an SDRM member (€ 40 regular membership € 25 for students under 30 years old), you are entitled to:

 - reduced registration fees to SDRM sponsored and organized events,
 access to the website reserved area with free download of proceedings and selected presentations from SDRM events.
- (**) As a student, you are kindly requested to send to sdrmsociety@gmail.com a copy of your student card.



GENERAL INFORMATION

REGISTRATIONS

Delegates' registration fee includes:

- Congress kit (badge, program/abstract book and bag)
- Access to the scientific sessions
- Access to the commercial exhibition
- Luncheons on Friday, April 20th and on Saturday, April 21st
- Coffee breaks on Friday, April 20th and on Saturday, April 21st
- Certificate of attendance

Please note that the certificate of attendance will be issued upon receipt of your completed workshop evaluation form. Your feedback will be highly appreciated.

The Social Dinner is not included in the Registration fee.

Certificate of Attendance

A certificate of attendance will be issued to all registered participants upon request at the Secretariat Desk at the end of the Workshop.



GENERAL INFORMATION

Social Dinner



Friday, April 20th, 2018 19:30 - 22:00

The "SDRM SOCIAL DINNER" will be held on Friday, April 20th, 2018, at 19:30 – 22:00 at :

WIERZYNEK RESTAURANT

Rynek Główny 16 - Krakow http://wierzynek.pl/en/wnetrza/

Located in the heart of Krakow's old city, Wierzynek Restaurant invites you to experience the beauty of its legendary interiors. This marvelous place is surrounded by historic buildings: Florian Gate, St. Mary's Basilica, St. Adalbert's Church, Cloth Hall and Town Hall Tower. The Restaurant itself houses eight rooms, each of different décor and size, but with common attribute exceptional atmosphere filled with royal heritage.

Please remember to book your dinner through the registration form (Social Dinner participation fee: € 50)

Wierzynek restaurant is situated at 5 minutes walking distance from the Workshop venue.

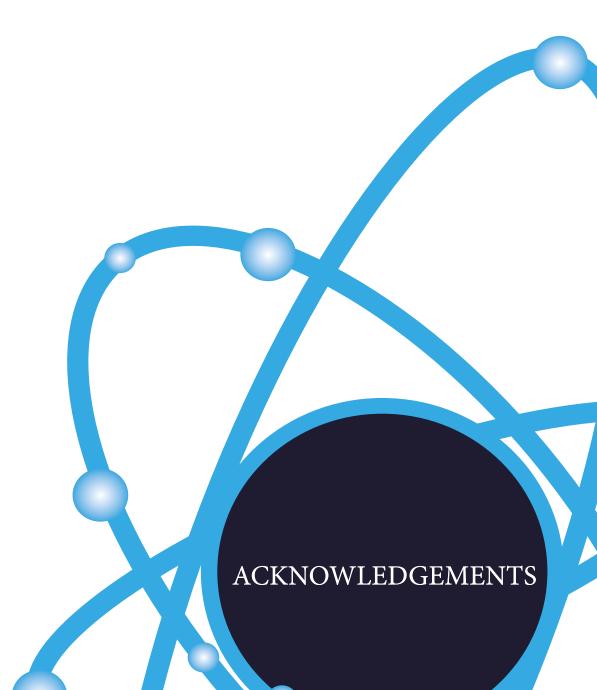
WIERZYNEK RESTAURANT

How to reach the Wierzynek Restaurant

When outside the hotel, go on your right, turn on your right on Florianska – walk straight on for a few minutes.

Across the Market Place, the Wierzynek Restaurant is situated on the other side in front of you.





ACKNOWLEDGEMENTS

The President of the Workshop

MAGNESIUM IN NEUROSCIENCE, PRECLINICAL AND CLINICAL FINDINGS

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Magnesium functions in the Central Nervous System

Robert Vink

University of South Australia, Adelaide, Australia (Adelaide, **Australia**)

Abstract

It is now well known that the tissue concentration of magnesium is highly regulated and that changes in concentration in response to stress and injury are associated with change in cell function. In the CNS, alterations in brain magnesium homeostasis have been linked to virtually every aspect of brain function throughout life and have been strongly implicated in the development of major CNS disorders. For example, acute pathological declines in brain intracellular free concentration following trauma and stroke have been linked to motor dysfunction, as well as to the development of cognitive deficits affecting learning, memory and executive function. Acute and chronic decreases in magnesium concentration have been linked to increases in blood brain barrier permeability as well as the manifestation of seizure disorders. Finally, chronic magnesium deficiency has been linked to disorders of mood as well as to neurodegenerative diseases such as Parkinson's disease and Alzheimer's disease. In contrast, administration of magnesium has been reported to be neuroprotective through a wide variety of mechanisms including effects on neuroinflammation, neurotransmitter release, glutamate receptors, brain edema, aquaporin channels, oxidative stress, mitochondria, energy metabolism, and cell proliferation, amongst others. This presentation will provide an overview of the role of magnesium in some critical aspects of brain function, using examples from pathology to illustrate the principle that magnesium is an essential nutrient in the nexus between a healthy brain and a healthy body.

Biographical Sketch

Pro Vice Chancellor and Vice President: Health Sciences at the University of South Australia in Adelaide, Australia, Bob has spent most of his scientific career studying secondary injury following traumatic brain injury, focusing on the development of novel pharmacotherapies that improve functional outcome. He is particularly noted for his characterisation of the role of magnesium in traumatic brain injury, for which he was awarded a DSc in 2012. His book entitled "Magnesium in the Central Nervous System", co-edited with Mihai Nechifor and published in 2011, has been downloaded over 150,000 times. He hosted the 10th International Magnesium Symposium in Cairns (2003) and is currently the Secretary of the International Society for Neurotrauma. Contact: Robert.Vink@unisa.edu.au









Epidemiology of Low Magnesium Intake and Status

Andrzej Mazur

Andrzej Mazur, Edmond Rock

Human Nutrition Unit, INRA/University of Clermont Auvergne, Clermont Ferrand, France (Clermont-Ferrand, **France**)

Abstract

As supported by several epidemiological studies, magnesium intake is suboptimal in a large part of the Western countries population. However, there are some discrepancies between various countries with respect to the Dietary Reference Values for magnesium. Current status of the nutritional references established by the international and national organizations will be presented. Some of them set Adequate Intake (AI) values instead of Estimated Average Requirements (EARs) and Recommended Dietary Allowances (RDAs), for all or certain age groups. This is due to the lack of an appropriate biomarker of magnesium intake or status and/or insufficient data that can be used to assess magnesium requirements. In particular, insufficient scientific evidence is available to relate magnesium intake and status to chronic disease. Severe magnesium deficiency with marked hypomagnesemia and characteristic clinical symptoms is rare. However, some studies show a significant prevalence of moderate hypomagnesemia. This supports an increased risk of chronic latent magnesium deficiency. This mild deficiency can cause a wide spectrum of health disorders, that can be considered nonspecific and to be at the origin of progressive severe health deterioration, in particular, cardio-metabolic diseases. In turn, several pathophysiological conditions e.g. metabolic syndrome, obesity, type 2 diabetes, stress and aging related dysfunctions can contribute and deepen chronic magnesium deficiency. Compared with severe magnesium deficiency, the diagnosis of latent deficiency is difficult because of nonspecific clinical symptoms and magnesemia often within reference intervals. Current knowledge and perspectives on biomarkers of magnesium status are discussed.

Biographical Sketch

Research Director and Head of the Human Nutrition Unit, INRA, Clermont-Ferrand, France, Editor-in-Chief of "Magnesium Research" - Official Journal of the International Society for the Development of Magnesium Research. His lab conducts research that aims to provide insight into the mechanisms by which nutrients, especially micronutrients, contribute to the prevention of age-related diseases. His research on magnesium is focused on its role in inflammation and the risk of cardiovascular disease as well as on the assessment of the magnesium status. Contact: <code>andre.mazur@inra.fr</code>







Low magnesium status and health: an update

Jeanette AM Maier

Università di Milano (Milan, *Italy*)

Abstract

Magnesium is vital. Indeed, ATP, the main source of energy in the cells, must be bound to magnesium to be active. Magnesium is also a cofactor of many enzymes involved in metabolism and controls several channels and transporters as well as signal transducers, among which protein kinase C and calcium/calmodulin-dependent protein kinase II. On these bases, it is not surprising that magnesium deficiency might contribute to disease. In particular, low magnesium status promotes chronic inflammation and oxidative stress, which are pathogenic factors of many disorders, from osteopenia to neuropathies, from cardiovascular diseases to diabetes.



Jeanette Maier, M.D., Professor of General Pathology at the University of Milan, School of Medicine, and Head of the laboratory of Cellular and Molecular Pathology, Department of Biomedical and Clinical Sciences. Her research activity is funded by national and international agencies to study the function of the endothelium

Her research activity is funded by national and international agencies to study the function of the endothelium under various stressful conditions from metabolic disorders to alterations of mechanical forces, including microgravity onboard the International Space Station.

Invited scientist in Tsukuba Science City (Japan), Department of Cell Biology, to generate genetically modified endothelial cells.

Post-doctoral training in the USA on the pathophysiology of the endothelium, with a focus on aging and senescence M.D degree, University of Parma.

Contact: jeanette.maier@unimi.it







Innovative approaches for Mg quantification in cells, tissues and mini organs

Stefano Iotti

Department of Pharmacy and Biotechnology (FABIT), University of Bologna, Bologna, IT National Institute of Biostructures and Biosystems, Rome, IT (Bologna, **Italy**)

Abstract

Purpose: In my speech, I will talk about the different approaches and techniques employed for detecting and quantifying magnesium in cells and tissues with an update on the most innovative methods recently developed and their applications in the study of magnesium homeostasis.

Materials and methods: Different techniques will be presented: starting from the early studies employing 31P-NMR in vivo to study the Mg homestasis in vivo in th human brain and skeletal muscle, then showing the application of a novel class of fluorescend dyes capable to assess the total intracellular Mg cocncentration. New innovative approaches to quantify and mapping Mg in single cells by synchrotron-based x*-ray microscopy techniques will be also presented. Finally, some new hints on a recent project exploiting a novel lab-on-a-chip strategy aiming at monitoring the Mg fluctuations in spheroid and miniorgans will be given.

Results: Several studies will presented showing the possibilities offered by the different approaches presented to untangle at least in part the complex role of Mg in cell metabolism.

Conclusion: The involvement of Mg in the main metabolic pathway is well known. However, there is still a long way to go in the comprehension of the molecular mechanisms governing the Mg homeostasis.

Biographical Sketch

Prof. Stefano lotti, currently works at Department of Pharmacy and Biotechnology of the University of Bologna coordinating the research group of Molecular Imaging, Biosensors and Cell Biology. He has contributed to the development of in vivo NMR spectroscopy in basic research and in diagnostic applications. His scientific activity ranged from organic and physical chemistry to biochemical thermodynamics. He contributed to the development of a novel approach to simplify the treatment of the thermodynamics of complex systems. At present the research activity is devoted to the study of magnesium homeostasis in cell culture combining synchrotron X-ray fluorescence and the use of a novel class of fluorescent chemo-sensors. Contact: **stefano.iotti@unibo.it**

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The Effects of Magnesium Supplementation on Subjective Stress and Anxiety: a Systematic Review

Neil Boyle (Leeds, United Kingdom)

Abstract

There has been increasing interest in the potential efficacy of magnesium (Mg) supplementation to attenuate subjective symptoms of anxiety and stress. First, there are sufficient potential mechanistic pathways via which Mg could modulate affective states. Second, the effects of Mg on clinical affective disorders and experimental studies of anxiety in animal models provide a clear rationale to propose that Mg supplementation may have a beneficial effect on mild/moderate anxiety. Third, exposure to physical and psychological stressors deplete Mg levels which in turn exacerbates stress response reactivity, suggesting a key role for Mg in responses to stress. A systematic review was conducted to examine the available evidence on the efficacy of Mg supplementation in the alleviation of subjective measures of anxiety and stress. There is currently suggestive but inconclusive evidence of a beneficial effect of Mg on subjective anxiety. This evidence is representative of anxiety vulnerable samples only. To date the effects of Mg supplementation on subjective stress has not been rigorously examined using a recognised measure of stress. Further randomised placebo controlled trials are needed to further confirm the efficacy of Mg supplementation for the alleviation of subjective anxiety and stress states.

Biographical Sketch

I am a biological psychologist with an interest in the relationship between diet and dietary interventions on stress, cognition and health. I completed my PhD on the effects of bovine phospholipids on cognition under acute stress in 2013 at the University of Leeds. My current research interests include the potential for nutrients to moderate stress vulnerability, the effects of stress on eating behaviour and the relationship between food insecurity and health and well-being.

Contact: N.B.Boyle@leeds.ac.uk







Magnesium in Anxiety and Depression: Lesson from a Rodent Model

Ewa Poleszak

Department of Applied Pharmacy Medical University of Lublin (Lublin, **Poland**)

Abstract

Magnesium (Mg) is a most distributed cation in the body. It influences the nervous system via action on the release and metabolism of many neurotransmitters. Both, preclinical and clinical data suggest that changes in Mg homeostasis contribute to the development of affective disorders.

In animals Mg deficiency leads to anxiety- and depression-like behavior (observed in light/dark box test and forced swim test (FST) respectively). The administration of Mg produces antidepressant-like activity in FST, tail suspension test, chronic mild stress and olfactory bulbectomy. It also enhances antidepressant-like activity of imipramine, citalopram and tianeptine, but not reboxetine. The data suggest the involvement of serotonergic but not noradrenergic pathway in Mg antidepressant-like activity. Moreover, synergistic effect between magnesium and cannabinoids system was observed.

Mg enhanced the action of CB1 cannabinoid receptor ligands: oleamide - an endogenous agonist, and AM 251 - an inverse agonist/antagonist, thus suggest involvement of this system in antidepressant-like activity of magnesium. The anxiolytic-like activity of magnesium was shown in elevated plus maze. In this test Mg enhanced open arm entries and time spend in open arms. It also enhanced anxiolytic-like activity of diazepam.

It's anxiolytic-like activity was reversed by flumazenil (GABA agonist). This indicates that anxiolytic-like activity of Mg is associated with GABA-ergic system.

Moreover, this divalent cation has been shown to control the activity of the hypothalamic-pituitary adrenocortical axis (HPA), which is considered to be the main stress response system, associated with both anxiety and depression. Summarizing, supplementation of Mg exerts antidepressant and anti-anxiety effects in tests and animal models, which indicates possible antidepressant and anxiolytic activity in humans.

Biographical Sketch

Chair of Department of Applied Pharmacy at the Medical University of Lublin/Poland. Regional Consultant in the field of pharmacy. Chairman of Lublin Department of the Polish Pharmaceutical Society. The current main focus of Dr. Poleszak studies is on affective disorders and their pharmacotherapy (anxiety, depression); behavioral effects of NMDA antagonist receptor in tests and models of depressive and anxiety disorders. Additionally, her research focuses on the technology of producing solid and semi – solid forms of drugs and their quality and stability. New studies focus on the topic of pharmaceutical care in Poland.

Contact: ewapoleszak@umlub.pl







Low Levels of Magnesaemia Induce Psychiatric Comorbidity in Patients with Inflammatory Bowel Disease

Franco Scaldaferri

<u>Scaldaferri Franco</u>¹, Petito Valentina¹, Ferrarese Daniele^{1,3}, Petito Claudia^{1,3}, Trapani Valentina², Camardese Giovanni³, Gasbarrini Antonio¹, Wolf Federica I.²

¹ Gastroenterology Area, Department of Gastroenterological and Endocrino-Metabolical Sciences, ² Institute of General Pathology,

³ Psychiatric Department, Fondazione Policlinico Universitario "A. Gemelli", Università Cattolica del Sacro Cuore (Rome, *Italy*)

Abstract

A number of diseases and disorders including inflammatory bowel diseases (IBD) are characterized by chronic inflammation, malabsorption, maldigestion, increased energy expenditure, and gastrointestinal protein loss, possibly inducing a relative deficiency of energy or proteins. In addition, diarrhea and occult blood loss increase the loss of zinc, potassium, magnesium, iron.

IBD describes a group of chronic gastrointestinal tract diseases that are relapsing and remitting; the term primarily comprises Crohn's disease (CD) and Ulcerative Colitis (UC). The prevalence of these diseases has increased in the past decades, up to 120–200/100000 and 50–200/100000 persons for UC and CD, respectively.

To date, there is no certain cure for IBD, and treatment is aimed at managing the inflammatory response during flares and maintaining remission with a focus on adhering to therapy. The etiology of IBD is unknown: genetic, microbial, immune and environmental factors play a role in the onset. One environmental trigger may be psychological stress. Psychological stress can increase intestinal permeability, probably as a result of alterations in the cholinergic nervous system and mucosal mast cell function.

Indeed, anxiety and mood disorders are the most common mental health manifestations among IBD patients, decrease of serum levels of Magnesium might be one of the cause.

The aim of this study is to investigate the influence of magnesium status on sleep and mood disorders, in particular anxiety and depression. We enrolled 20 outpatients with IBD (10 CD and 10 UC); serum samples were collected to assess the magnesaemia by atomic absorption spectrometry. Each patient complete a specific questionnaire for mood disorders with 567 questions: Minnesota Multiphasic Personality Inventory- 2 (MMPI-2). All study participants gave written informed consent prior to sampling and data collection.

Biographical Sketch

Currently appointed as Associate Researcher at Catholic University of the Sacred Hearth, he got the MD degree in 2005 at Catholic University of Rome -Italy, followed by a PhD degree in Gastroenterology, in 2009. In 2007 he started a research fellowship program at Cleveland Clinic, Cleveland, OHIO, USA, under the supervision of Prof. Claudio Fiocchi. He is member of several scientific societies, including SIGE (Italian Society of Gastroenterology, since 2006), YECCO (Young European Cronh's and Colitis organization since 2007), Italian Society of Internal Medicine (since 2007). He received several awards: 2007, "Menzione d'onore, Premio Prof. Petito Petrone, Pignola (PZ), Italy" for the medical school achievements, award from SIGE "Premio Giovani Ricercatori" ("young researcher award"), in 2008 he was awarded from Italian Society of Internal Medicine. In 2010 he received the first research grant from ECCO (European Crohn's and Colitis Organization"). He was representative of the Young-ECCO committee until 2014. He won the "giovani ricercatori 2016" award, being coordinator of a research group on "personalized medicine in ulcerative colitis" from Italian Ministry of Health. He accounts for several scientific collaborations on IBD pathogenesis, colonic cancer, innate and adaptive immunity and IBD, colon cancer screening, intestinal microbiota composition and modulation.

Contact: francoscaldaferri@gmail.com







Neurophysiological mechanisms of different stress resiliance

Pavel Umriukhin

P. E. Umriukhin¹, S.V. Kostyuk², A. A. Bekker^{1,2} ¹ Sechenov University ² Research Centre for Medical Genetics (Moscow, Russia)

Abstract

Purpose: stress is a common reaction to an environmental adversity. Dysregulation of the stress response can lead to a different illnesses, like hypertension, anxiety and depressive disorders, post-traumatic stress disorder (PTSD), duodenum and stomach ulcers etc.

Yet, not all individuals exposed to stress develop such disorders; those with enhanced stress resilience mechanisms have the ability to adapt successfully without developing persistent pathology.

Notably, the potential to enhance stress resilience in at-risk populations may prevent the onset of stress-induced disorders. This idea has prompted a number of studies probing the mechanisms of stress resilience and how it can be manipulated. Increased resiliency has been shown to improve overall health and quality of life and slow aging. We focus on a certain systemic, neurophysiological and genetic mechanisms underlying different physiological stress coping strategies.

Results: in particular, the roles of individual variability in neuronal peptidergic and glutamatergic mechanisms, different circulating free nucleic acids concentrations in blood and liquor, diverse distribution of immediate early genes expression in limbic brain structures were studied.

Recently the new data were obtained showing that circulating cell-free DNA and ionic (e.g. possibly magnesium) concentrations in blood plasma may differ in animals with different stress resilience.

We discuss stress resiliency in the context of systemic stress mechanisms applying the P.K. Anokhin and K.V. Sudakov theory of functional systems in our studies to describe possible variations in parameters of body functions and emotional reactions in different individuals.

Conclusion: in conclusion, we consider the possible methods that may be used to induce resilient phenotypes, prophylactically in at-risk populations. Research in the neurophysiological mechanisms of stress resilience may elucidate novel stress markers in population and provide novel insight about how to prevent stress induced disorders.

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Magnesium and Pain

Gisèle Pickering (Clermont-Ferrand, France)

Abstract

Chronic pain impairs dramatically the quality of life of patients. Chronic pain is associated with a variety of disorders such as chronic low back pain, chronic complex regional pain syndrome, fibromyalgia and neuropathic pain. Recommended drug treatments (including antidepressants, opioids, antiepileptics) are not always effective and withdrawals are frequent because of adverse events. Other modalities for managing pain have been sought and magnesium has been studied in the context of pain. As a modulator of ion transport by pumps, carriers and channels, magnesium impacts on signal transduction and as a physiological blocker of N-methyl-D-aspartate (NMDA) receptor may have an analgesic effect.

The presentation will discuss the use of magnesium in neuropathic migraine, pain and chronic pain in the light of recent publications and clinical trials. It will also review the clinical effectiveness of magnesium as an alternative or as an adjunct to other analgesics for controlling pain.

Biographical Sketch

Professor Gisèle Pickering (MD,PhD, DPharm) is Professor of Medicine and Clinical Pharmacology at the University Hospital of Clermont-Ferrand, France. She coordinates the Inserm CIC 1405 Clinical Research Centre and is a permanent member of the Inserm 1407 Laboratory of Fundamental and Clinical Pharmacology of Pain. Her main topics of research concern the mechanism of action of analgesics, the impact of pain on cognitive-emotional processes and pain management in older persons. She regularly contributes to peer-reviewed publications on Pharmacology and pain, to international meetings and belongs to national and international Pain, Pharmacology and Geriatrics Societies. She is the French Councillor at the European Pain Society (EFIC). She is the author of over 150 publications and the editor of several books. Her interest in Magnesium in the context of Pain has been translational for the last 15 years, and her group published on the interest of Mg on NMDA receptors from animal models of pain to patients suffering from chronic neuropathic pain. She presently coordinates clinical trials with Magnesium in cancer patients, neuropathic pain, and in fibromyalgia, with a special focus on pain relief and quality of life. Contact: <code>gisele.pickering@uca.fr</code>







Magnesium and Addiction – A General View

Mihai Nechifor

Department of Pharmacology "Gr. T. Popa" University of Medicine and Pharmacy (Iasi, **Romania**)

Abstract

Addiction is a dysregulation of brain reward systems that progressively increases, resulting in the compulsive drug use and loss of control over drug-taking. Addiction is a brain disease. There are evidences that magnesium deficit is involved in addiction to various addictive substances (heroin, morphine, cocaine, nicotine, alcohol, caffeine and others). Magnesium is involved in all stages of addiction. Magnesium deficit enhances the vulnerability to psychoactive substances addiction. Stress and trauma reduce the brain magnesium level and at the same time favors the addiction development. In our study, the heavy smokers (which are nicotine addicts) have had a lower plasma magnesium level (compared to non smokers) and magnesium daily administration 4 weeks reduced the number of smoked cigarettes. In experimental studies, administration of magnesium while inducing morphine dependence in rats reduced the dependence intensity. There are data which suggest that reducing glutamate signalling may be therapeutic strategy for treating vulnerable individuals at risk of developing substance use disorder particularly those which may have experienced stress and trauma (O'Connor RM et al 2015). Magnesium reduces the NMDA receptor activity and the glutamatergic activity. Because the stress and trauma induce hypomagnesemia while the increased vulnerability to addiction, magnesium taking in people which are subject to intense and prolonged stress could be a way to reduce this vulnerability and development of addiction to different psychoactive substances. Anxiety and depression appear to be associated with increases in drug-related harm and addictive substances use (Bertholet et al 2017, Pelloux et al. 2015). Magnesium anxiolytic effect could be important for the anti addictive action. Addiction is characterized by relapses. Magnesium deficiency may be a contributing factor to these relapses.

Biographical Sketch

Professor of Pharmacology, Director of Research Programs "Gr T Popa "University of Medicine and Pharmacy lasi Romania, President of Romanian Society of Magnesium Research. His research has focused on magnesium and other bivalent cations involvement in addiction, monopolar and bipolar disorders, schizophrenia and on interactions between magnesium and psychotropic drugs. Additionally, his research focused on collateral effects of antibiotics. He has been President of XIIth International Magnesium Symposium lasi 2009, co-editor with Robert Vink of the book: "Magnesium in Central Nervous System" 2011 and co-editor with Jean Durlach and Paul Porr of the book "Advances in Magnesium Research- New Data" 2006. Contact: *mihainechif@yahoo.com*







Magnesium and depression in the context of the Mediterranean diet: epidemiological data

Almudena Sanchez-Villegas

(Las Palmas de Gran Canaria, Spain)

Abstract

Depression is a highly prevalent disease and it is one of the leading global causes of disability-adjusted life years worldwide. So, primary prevention of depression improving the adherence to several protective factors such as physical activity or diet is essential. In this sense, magnesium intake has emerged as an important dietary factor associated with depression. However, last data suggest that magnesium intake could be associated with the prevalence of depression but not with its incidence. In this presentation we show several results obtained from the PREDIMED trial (aimed to assess the effect of the Mediterranean diet in the prevention of cardiovascular disease) and from the SUN Project (a multipurpose cohort study). In both studies, the adherence to the Mediterranean Diet was associated with a reduction in the risk of depression. The Mediterranean diet is rich several nutrients such as cereals, green vegetables or nuts, important sources of magnesium. Specifically regarding magnesium intake, the most recent analyses carried out in the SUN cohort study were published in 2016. The analyses were performed on almost 16.000 participants of the cohort followed up for a median of 10 years. Although we found a risk reduction in depression (considered as self-reported medical diagnosis of depression plus the use of antidepressants) for those participants in the upper quintiles of magnesium intake, these risk reductions were not statistical significant. The HRs for the third, fourth and fifth quintiles of magnesium intake as compare to the reference category were 0.68 (0.44-1.04), 0.70 (0.44-1.11) and 0.60 (0.35-1.02) respectively. However, we observed a dose-response relationship (p for trend=0.047). Nevertheless, when the analyses were adjusted for other dietary factors such as the adherence to the Mediterranean diet, trans fatty acids or alcohol intake, the dose-response relationship was not more statistically significant and the magnitude of effect was attenuated. The adherence to overall dietary patterns more than increasing the intake of several nutrients could be the key point to prevent depression occurrence. Larger cohort studies with sufficiently long follow-up are necessary to definitely establish the role of magnesium intake in depression risk.

Biographical Sketch

Almudena Sánchez-Villegas (25 Nov, 1975)

PhD in Pharmacy (University of Navarra, 2001). Full Professor of Preventive Medicine and Public Health at University of Las Palmas de Gran Canaria since 2016. Research Fellow in the Department of Nutrition of the Harvard T.H. Chan School of Public Health during the academic year 2005-2006. She is author of more than 90 book chapters and co-editor of several text books of Public Health (Elsevier 2013) and Biostatistics (Elsevier 2014). She is the editor of the book "The Prevention of Cardiovascular Disease through the Mediterranean Diet" published in 2017 also by Elsevier. She has authored more than 140 scientific articles, editorials or letters in international per-reviewed journals such as World Psychiatry, JAMA Psychiatry, American Journal of Clinical Nutrition, Diabetes Care or BMC Medicine (h index web of Science=39; h index Google Scholar=46, March 2018). Coordinator and principal investigator of two Spanish Projects (2005/2007; 2009/2012) sponsored by the Spanish Ministry of Health (FIS Pl042241, FIS Pl080819) to assess the role of diet and physical activity on mental disorders and quality of life. In 2016, she received a new grant (FIS Pl16/01274) for the triennium 2017/2019 to carry out a clinical trial to assess the role of the adherence to the Mediterranean diet supplemented with extra virgin olive oil in the risk of recurrence of depression. She has also participated in other Spanish or European projects related to nutritional epidemiology such as the PREDIMED clinical trial analysing the effect of Mediterranean diet on cardiovascular risk or the EURRECA project (European RECommendations Aligned Harmonising nutrient recommendations across Europe) sponsored by the European Union (FP6-0361196-2). Now part of CIBERobn (Spanish Biomedical Research Centre in Obesity Physiopathology and Nutrition network) collaborating within the PREDIMED-PLUS trial. Contact: almudena.sanchez@ulpgc.es







Magnesium and other Metal Ions in Depression

Gabriel Nowak

Institute of Pharmacology, Polish Academy of Sciences Faculty of Pharmacy, Jagiellonian University Medical College (Krakow, **Poland**)

Abstract

Antidepressant therapy exhibits low clinical efficacy and produces a variety of unwanted side effects. Treatment-resistant patients are the major problem in the therapy of depression. Therefore, the search for more effective antidepressants is continuously in progress. Antidepressant properties of magnesium, zinc and some other metal ions have been demonstrated in animal screen tests/ models and clinical studies.

Magnesium and zinc are active in the forced swim/tail suspension tests and olfactory bulbectomy, chronic unpredictable/chronic mild stress models. Moreover, these bio-elements enhances antidepressant activity of conventional antidepressants in these behavioral paradigms.

Clinical studies demonstrated equivocal results concerning supplementary effectiveness of magnesium. Generally, subgroup of depressed patients with hypomagnesia responded very well to such supplementation, while response of other patients was weaker.

Clinical data of support of the effectiveness of zinc in depression is much more robust. Most studies demonstrated enhancement of efficacy of pharmacotherapy by zinc supplementation in unipolar depression. What is important, the recent study demonstrates that zinc supplementation augments efficacy of antidepressants in treatment-resistant patients.

All the available data indicate the importance of magnesium and zinc in the therapy of depression. Partially supported by NCN2012/07/B/NZ7/04375 grant.

Biographical Sketch

Professor & Chairman of the Department of Pharmacobiology, Faculty of Pharmacy, Jagiellonian University Medical College, Kraków, Poland and Head of the Laboratory of Trace Elements Neurobiology, Department of Neurobiology, Institute of Pharmacology, Polish Academy of Sciences, Kraków, Poland.

Research Interest: General: neurochemical mechanisms of action of psychotropic drugs, mechanism of pathophysiology of depression (animal models and human studies).

Recent interest: the role of zinc (magnesium and other biometals) with relation to glutamate system in pathophysiology and treatment of depression, molecular mechanisms of antidepressant action.

Contact: nowak@if-pan.krakow.pl







Potential relationship between magnesium, depression and glutamate system

Bartłomiej Pochwat

(Krakow, **Poland**)

Abstract

Major depressive disorder is a very serious medical problem for modern society. Current antidepressant drugs modulate monoaminergic systems. These compounds inhibit serotonin, dopamine or norepinephrine reuptake transporters. Unfortunately, these drugs are not effective enough. Delayed onset of action and unwanted side effects are another issues associated with monoamine reuptake inhibitors. Therefore, the novel strategies of depression treatment are still being sought. In the recent years, the compounds which modulate glutamate system have been studied widely in the context of depression treatment. The most promising results have been obtained with antagonists of glutamate NMDA receptor. These drugs, in particular ketamine, induce fast and long-lasting antidepressant-like activity after single dose in clinical and preclinical conditions. At molecular level such kind of drugs activate intracellular pathways involved in the processes of neuroplasticity. Because ketamine induces side effects alternative ways of modulation of glutamate system are taken into account. Magnesium is a natural NMDA receptor antagonist. It's potential antidepressant activity has been reported both in clinical and preclinical studies. Despite the fact that magnesium is involved in numerous functions in the body, the blockade of NMDAR and modulation of glutamate system may be the main mechanism of action engaged in magnesium antidepressant activity. This lecture focuses on the relationship between magnesium, glutamate system and depression treatment.

Biographical Sketch

I defended my PhD thesis at the Faculty of Pharmacy of the Jagiellonian University in 2014. The title of my PhD thesis was "The effect of magnesium ions on the glutamatergic system in the animal models of depression". I have been working in the Department of Neurobiology of the Institute of Pharmacology of the Polish Academy of Sciences in Cracow since 2013. In general, my primary scientific focus is an antidepressant-like activity of NM-DAR receptor antagonists (in particular antidepressant effects induced by biometals such as magnesium and zinc). Contact: <code>bartekpochwat@gmail.com</code>









Magnesium, Transporters and Aging: Lesson from Molecular Genetics

Vladimir Chubanov

(Munich, *Germany*)

Abstract

Mg²+ regulates many physiological processes and signalling pathways. However, little is known about the mechanisms underlying the organismal balance of Mg²+. Approximately 10 plasma membrane Mg²+ channels have been proposed including TRPM6 and TRPM7. TRPM6 and TRPM7 are bifunctional proteins comprising a TRP channel segment linked to an α-type protein kinase. Loss-of-function mutations in the human *TRPM6* gene cause an autosomal recessive disorder, hypomagnesemia with secondary hypocalcemia (HSH). Point mutations in the human *TRPM7* gene lead to impaired thrombopoiesis due to altered cellular Mg²+ metabolism and cytoskeletal architecture. Recently, we have defined the molecular and organismal roles of TRPM6 in mice. We showed that TRPM6 activity in the placenta and yolk sac is essential for embryonic development. In adult mice, TRPM6 is required in the intestine to maintain organismal Mg²+ balance, but is dispensable in the kidney. *Trpm6* inactivation in adult mice leads to shortened lifespan, growth deficit and impaired energy balance indicative of a progeroid-like syndrome. Dietary Mg²+ supplementation not only rescues all phenotypes displayed by *Trpm6*-deficient adult mice, but also may extend the lifespan of wildtype mice. Hence, maintenance of organismal Mg²+ balance by TRPM6 is crucial for prenatal development and survival to adulthood.

Biographical Sketch

Vladimir Chubanov, PhD

Group Leader, Walther-Straub Institute of Pharmacology and Toxicology, LMU Munich, Germany. Studies of my group are focused on TRPM6 and TRPM7, bifunctional proteins comprising a channel segment linked to an α-type protein kinase. Loss-of-function mutations in the human *TRPM6* gene cause an autosomal recessive disorder, hypomagnesemia 1, intestinal (HOMG1) also called hypomagnesemia with secondary hypocalcemia (HSH). Mechanistically, the regulation of Mg²+ homeostasis by these two channel kinases and the pathophysiological consequences of TRPM6 mutations are only poorly understood. Therefore, the major goal of our studies is to attain mechanistic knowledge about the physiological and pathophysiological roles of kinase-coupled channels using gene-modified mice and primary cells derived from TRPM6- and TRPM7-deficient animals. Contact: *vladimir.chubanov@lrz.uni-muenchen.de*







Magnesium Status in Alzheimer's Disease: A Systematic Review

Nicola Veronese

(Padua, Italy)

Abstract

Poor magnesium (Mg) status is associated with several negative outcomes. Among them, the literature regarding neurological and psychiatric diseases in of particular importance. Alzheimer's disease (AD) is the most common form of dementia in older people. In this field, the interest in poor magnesium (Mg) status as risk factor for Alzheimer's disease (AD) is increasing due to its antioxidant and neuroprotective properties. Therefore, we did a systematic literature search of studies investigating Mg status comparing AD to healthy controls (HCs) or patients with other medical illness (medical controls [MCs]). In this work, 13 studies were included (559 patients with AD, 381 HCs, and 126 MCs). Compared to HCs, patients with AD had significantly lower Mg in cerebrospinal fluid and in hair, whilst no differences between AD and controls were evident for serum and plasma Mg. In conclusion, AD seems to be associated with a lower Mg status when compared to HCs, while the scarcity of studies limited the findings about MCs.

Biographical Sketch

Researcher of Geriatric Medicine at National Research Council, Padova, Italy. He is interested in the epidemiology of magnesium deficiency in older people and its consequences in terms of major comorbidities. Contact: nicola.veronese1@aulss3.veneto.it







Magnesium and Muscle Function

Valentina Trapani

<u>Valentina Trapani</u>, Giuseppe Pietropaolo, Francesca Luongo, Federica I. Wolf *Istituto di Patologia Generale, Università Cattolica del Sacro Cuore*(Rome, *Italy*)

Abstract

The prevalence of sarcopenia, defined as low skeletal muscle mass and function, is increasing in our aging society, with its associated disabilities and costs for health and social care. Importantly, these conditions, once present, are difficult to reverse, and current treatment strategies are limited. Therefore, maintaining skeletal muscle health during aging is important, and new preventative strategies in middle and younger older ages are needed. On this regard, it is widely recognised that dietary composition can greatly contribute to healthy aging, and magnesium is a good candidate as a nutrient that is integral to muscle physiology.

The importance of magnesium (Mg) is widely acknowledged in a plethora of cellular processes. The primary energy source is the Mg-ATP complex; moreover, Mg has a key structural and functional role for hundreds of enzymes, most notably those involved in DNA replication, RNA transcription, amino acid and protein synthesis, energy metabolism and glycolysis. These processes are particularly relevant in the physiology of skeletal muscle, which in fact is one of the main Mg stores in our body, accounting for up to 30% of total body Mg. In muscle, Mg has direct metabolic roles, including maintenance of protein synthesis and turnover, and can affect performance through energy metabolism (production of ATP) and modulation of contraction/relaxation. The latest in vitro, in vivo and clinical evidence will be discussed to seek the molecular mechanisms that underlie the beneficial effects of Mg on musculoskeletal health and to explore novel preventative interventions.

Biographical Sketch

Research Fellow at the Institute of General Pathology, Catholic University School of Medicine "A. Gemelli" in Rome. Moving on from a background in biophysics and cancer biology, she is currently interested in the role of magnesium and magnesium-specific ion channels in diverse pathophysiological processes, including inflammation-driven conditions and colon carcinogenesis.

Contact: valentina.trapani@unicatt.it





OC01A

Percentage of hypomagnesemia and hypermagnesemia in a hospital between 2006 and 2014. Aggravating factors and risks

Manuel Guerra¹, Belen Founaurd², Silvia Izquierdo², Francisco López-Alcuten³, Mercedes Galvez³, Jesús F. Escanero¹

- ¹ Area of Physiology, Depart. of Pharmacology and Physiology, University of Zaragoza, Zaragoza, Sp
- ² Clinical Biochemistry Service, Miguel Servet University Hospital, Zaragoza, Sp
- ³ Clinical Biochemistry Service, Lozano Blesa University Hospital, Zaragoza, Sp.

Purpose: Analyzes the determinations of magnesium made in the HUMS between 2006-2014.

Identify the levels of Mg depending on the applicant Service, the type of patient, age and the diseases that are related to their alterations.

Materials and methods: A retrospective, observational, descriptive and transversal study was carried out. About 73,262 requests, from 34,736 patients, the origin of the request, age, type of patient, were studied. Hypomagnesemia <1.7 mg / dL, normomagnesemia between 1.7 mg / dL and 2.4 mg / dL; and hypermagnesemia > 2.4 mg / dL were considered. Finally the percentages of death were calculated in one hundred determinations.

Results: Of the requests one (84.77%) are normomagnesémicas, one (10.84%) hypomagnesémicas and one (4.39%) hipermagnesémicas. Higher hypomagnesemia rate: • Services: Hematology (31.63%) and Oncology (19.05%). • Type of patient: day hospital one (20.38%) and hospitalized (17.27%). Over 51 years (> 12%) Higher hypermagnesemia rate: • Applicant service: ICU (19.07%) and Nephrology (10.79%). • Type of patient: 10.61% hospitalized. They are young, 0-10 years old (10.38%) and older, 91-100 years old (10.41%). Higher rate of normomagnesemias: • Applicant service: Family Medicine with (95.03%) of normality rate. • Type of patient: ambulatory with a 95.03% normality rate. Between 11 and 50 years have higher normality rates.

Table 1 Aggravating factors observed in hypomagnesemias determinations=172

Factors	Oncological Pathology	Other Pathology
Arterial hypertension	29,63%	68,8%
Diabetes	18,52%	44,4%
Heart failure	14,81%	16,6%
Malnutrition	12,96%	14,8%
Renal insufficiency	9,26%	37 %
Diuretic treatment	9,26%	37 %
Hypocalcemia	7,4 %	27,7%
Hypercalcemia	7,4 %	12,9%

Table 2 Aggravating factors studied in hypermagnesemias determinations=103

Renal insufficiency	59,77%
Arterial hypertension	44,83%
Heart failure	42,53%
Malnutrition	22,99%
Hypocalcemia	20,69%
Diabetes	19,54%
Polytrauma / Postsurgical	17,24%
Hypercalcemia	9,20%
Hypokalemia	3,45%

The percentage of death in hypomagnesaemic patiens is **34.26**%, and **31.03**% in hypermagnesaemic. **Conclusion:** The percentages of exitus advise to include their determination in prognostic tests, like the APACHE.



OC01B

Clinical and alterations in the ECG of a person with a very high intake of Magnesium

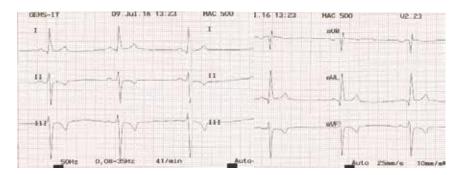
Manuel Guerra¹, Belen Founaurd², Francisco López-Alcuten³, Marta Ortin⁴, Ma Angel Julian³, Jesús F. Escanero¹

- ¹ Area of Physiology, Depart. of Pharmacology and Physiology, University of Zaragoza, Zaragoza, Sp
- ² Clinical Biochemistry Service, Miguel Servet University Hospital, Zaragoza, SP
- ³ Clinical Biochemistry Service, Lozano Blesa University Hospital, Zaragoza, SP
- ⁴ Centro de Salud de Biescas, Huesca, SP

Introduction: Patient that more than 4 times a week, runs 10 km, swims 30 minutes and does gymnastics. Go to a rural health center, (without clinical laboratory) with slight feeling of dyspnea, malaise and asthenia of 24 hours of evolution.

Materials and methods: They made a physical examination, an electrocardiogram, a glucose and a clinical history.

Results: Exploration presents a decrease in the osteotendinous reflexes, hypoesthesia in the left arm. No pain or vegetative courtship own infarction. Pulse 46 bpm, BP 120/60 mmHg, glucose 100mg/dL. Figure 1ECG.



The ECG shows a bradycardia of 41 beats per minute, the rest of the results are shown in table 1.

Wave P Interval P-Q Complex QRS Interval QT Interval PP Duration ms 126 200 144 548 1456-1460 Average value 80 160 80 / o >100 50-100 120-200 120 in a 25% Normal range ms population >390 Result T. Increased T. Normal T. Increased T. Increased T. Bradycardia

Table 1. Patients wave duration and intervals

Clinical history he said that lately he has taken three different Magnesium preparations each day:

- 1.- Calcium-Magnesium daily intake 300 mg of Mg carbonate.
- 2.- Magnesium Carbonate daily intake 400 mg of Mg carbonate.
- 3.- Collagen with Mg daily intake 185 mg of Mg carbonate.

Discussion: The main manifestations of hypermagnesemia are disappearance of the osteotendinous reflexes, depression of the cardiac conduction excito system, electrocardiographic alterations such as bradycardia, increase of the intraauricular conduction time, widening of the QRS complex, increase of the PQ and QT intervals, alterations of the ST segment, even T wave inversions.

After the suppression of the Mg intake, the clinical alterations were suppressed before 48 hours, and the pulse was increased until 54 pulsations.

Conclusion: The results are agreed with the clinical signs of hypermagnesemia. Financed with the project PRAUZ 17 375.



OC02

CellViewer, a lab-on-a-chip technology for in-vivo-like imaging and study of biological phenomena

<u>Azzurra Sargenti</u>¹, Martina Rossi², Giovanna Farruggia¹, Simone Pasqua³, Simone Bonetti³, Andrea Quaranta³, Francesco Musmeci³, Francesco Alviano², Daniele Gazzola³ and Stefano lotti¹

- ¹ Department of Pharmacy and Biotechnology (FABIT), University of Bologna, Bologna, IT
- ² Department of Experimental, Diagnostic and Specialty Medicine (DIMES), University of Bologna, Bologna, IT
- ³ CellDynamics SRL, Via Gobetti 101, Bologna, IT

Purpose: Single-cell analysis is a fast growing field with a high impact in the research community owing to its numerous applications including cancer research, diagnostic, and drug discovery. In this context, microfluidics and labon-a-chip technology have emerged as the most promising avenue to address these challenges. Here, we used Cel-IViewer, an innovative laboratory bench prototype designed for continuous observation of floating cells, to monitor single cells and tumor spheroids.

Materials and methods: The device is a Lab-on-a-Chip platform based on the combination of optics, electronics and microfluidic technologies together with disposable modules, resulting in imaging tool. The sample is continuously monitored via an optical system, which detects its position, and a feedback mechanism within the optical and microfluidic systems adjusts cell position to the desired location. Moreover, intermittent light is used to reduce photodamage by prolonged exposure.

Results: By combining fluorescence time-lapse imaging, automated focal adjustment, culture media control technologies, CellViewer allows us to perform uninterrupted observations of tumor single cells (HL60 and Jurkat) in conditioned medium, and of human osteosarcoma spheroids. Moreover, we are performing ongoing imaging tests of intracellular magnesium in cells and in spheroids of various origins by using a fluorescent dye (DCHQ5), which is able to assess total intracellular magnesium.

Conclusion: CellViewer could be the proper tools to entrap floating organoids and 3D-cell aggregates for cell culture, imaging and study of biological phenomena. In particular, the application of this lab-on-a-chip technology in the study of magnesium distribution in 3D cellular models, could shed new lights in the comprehension of magnesium homeostasis in organoids.

$\overline{OC03}$

A challenging future for magnesium research in the brain: organoids and brain on-a-chip

Cazzaniga A.1, Romeo V.1, Castiglioni S.1

1 "L. Sacco" Department of Biomedical and Clinical Sciences, University of Milan, Via G.B. Grassi 74, 20157 Milan, IT

Purpose: 2D cell cultures are widely used and importantly contributed to our knowledge about the biology and pathophysiology of the nervous cells. However, this approach does not reflect tissue specificity and functions and, in particular, do not take into account the extreme complexity of the nervous system. To overcome the limits of 2D system, spheroids were proposed as an alternative but this technique does not consider the in vivo cellular compartmentations and cell–cell interactions.

Recently, an innovative stem-cell-based 3D tissue model has been developed, termed "organoid", which miniaturizes and simplifies an organ. Cerebral organoids allow to study the function of networks of human brain cells and how they are affected by genetic modifications or drugs. Moreover, "brain-on-achip" is another emerging experimental model which has been utilized to measure different parameters and to investigate the toxicity of drugs and chemicals.

Materials and methods: The organoid is generated by induced human pluripotent stem cells, which lead to the generation of a number of mini—brains. Organoids can be studied in static conditions or under flow on-a-chip: The silicon chip is biocompatible and continuously perfused in order to model physiological functions of tissues and organoids.

Results: These unprecedentedly accurate models optimize in vitro studies on the nervous system. They can be used to study the role of magnesium and its transporters in the differentiation, function and long term survival of nervous cells.

Conclusion: These highly technological approaches might help to disclose the basis of brain disorders.



OC04

Investigating the functional role of TRPM6 in colon mucosa

<u>Francesca Luongo</u>¹, Valentina Trapani¹, Valentina Petito¹, Giuseppe Pietropaolo¹ and Federica I. Wolf¹

¹ Istituto di Patologia Generale, Facoltà di Medicina e Chirurgia "A. Gemelli", Università Cattolica del Sacro Cuore, Largo Francesco Vito, 1, 00168, Rome, Italy

Purpose: Intestine is responsible for systemic Mg homeostasis. Transcellular transport occurring in the cecum and colon, is driven primarily by transient receptor potential melastatin TRPM6 and 7 cation channels. In a mice model of colitis, we found that following inflammation (DSS), which destroys the mucosa and impairs magnesium absorption, TRPM6 and TRPM7 are severely down-regulated accounting for hypomagnesaemia. We also observed that during recovery and upon magnesium supplementation,TRPM6 but not TRPM7 is significantly upregulated. To understand the functional role of TRPM6 in the colon, we studied Mg and Ca influx in colon cancer cells.

Materials and methods: The expression of TRPM6 and 7 was evaluated by RT-PCR and Western Blotting in colon carcinoma cell lines (HCT116, HT29). In order to study the functional role of the two TRPMs channels, we have silenced either TRPM6 or TRPM7 expression by RNA interference. Proliferation and migration were assessed and intracellular influx of cationic species (Ca and Mg) were evaluated by confocal microscopy using the fluorescent probe Fura-2 and Mag-Fluo respectively.

Results: Both cell lines express TRPM7 and TRPM6. However, RNA interference suggest that the roles of TRPM7 and TRPM6 on proliferation and migration are unusual. Upon TRPM7 silencing we observed an increase in cell proliferation and migration in HCT116 cells. We also found that TRPM7 silenced cells are more efficient in taking up magnesium than control or TRPM6-silenced cells.

Conclusion: Colon cells display and unusual behavior regarding the role of TRPM7 and TRPM6 expression in the regulation of cell proliferation and cation transport. The expression of TRPM6 rather than that of TRPM7 promotes cell proliferation and migration. When TRPM6 exceeds the expression of TRPM7 we also observe a potentiation of cation influx (Mg and Ca) which is consistent with the increased proliferation rate. Further study is necessary to fully clarify this peculiar behavior.

OC05

Magnesium and stress in the domestic pig

E. V. Bushby¹, L. Dye², H. M. Miller¹, L. M. Collins¹

¹ Faculty of Biological Sciences, University of Leeds, UK

Purpose: A systematic review of the current literature investigating the effects of magnesium on reducing aggression and stress in the pig.

Materials and methods: Magnesium is often added to pig feed in order to alleviate outbreaks of aggression. However, the scientific evidence to support this strategy has not been systematically reviewed. Our aim was to perform a systematic review of studies in which magnesium was given to pigs to examine the effects on measures of stress and aggressive behaviour. A search was performed using Web of Science with the search terms "magnesium", "pig, "swine", "livestock", "stress", "aggression" and "behaviour". Inclusion criteria were any whole animal magnesium studies after 1990 with a focus on aggression, behaviour or stress. The study species must be the domestic pig.

Results: 1,434 papers were identified by the initial search. After excluding studies based on the title and abstract, 28 were retained for method review. Eleven studies met our criteria. Two studies investigated the effect of magnesium on aggression in pigs and showed magnesium had a moderate effect on reducing aggressive behaviours. Eight studies investigated stress in relation to transportation and slaughter, with six reporting that magnesium supplemented before transport reduced stress during transport and slaughter. In four studies focusing on halothane gene positive pigs susceptible to porcine stress syndrome, stress was not alleviated by magnesium. Overall, studies that have been conducted using behavioral measures indicate magnesium may have a calming effect and in four studies cortisol indicated stress was reduced. However, not all studies use the same magnesium compound or dose.

Conclusion: There are a limited number of studies investigating the effect of magnesium on reducing stress and aggression in pigs. This area would benefit from further research so that use of magnesium in animal production is evidence-based.

² School of Psychology, University of Leeds, UK

OC06

Therapeutic Drug Monitoring (TDM) of depression – augmentation by magnesium ions (NCN2012/07/B/NZ7/04375)

Beata Ryszewska-Pokraśniewicz³, Michał Skalski¹, Piotr Januszko¹, Ewa Drozdowicz-Jastrzębska¹, <u>Gabriel Nowak</u>², Andrzej Pilc², Maria Radziwoń-Zaleska¹

- ¹ Department of Psychiatry, Medical University of Warsaw, Poland
- ² Institute of Pharmacology, Polish Academy of Sciences, Kraków, Poland
- ³ Nowowiejski Hospital in Warsaw, Poland

TDM allows for individualizing and optimizing the pharmacotherapy basing on the clinical pharmacokinetics.

The aim of the studies was to assess the efficacy and the safety of the therapy of depression with the amplification of the therapy by magnesium ions .

The research was conducted in the Clinical Wards of the Chair of Psychiatry, Medical University of Warsaw, 37 patients who were on the fluoxetine therapy due to a depression episode were included in the trial. The trial was conducted on the double blind methodology with addiction of either magnesium ions or placebo. During an 8 week observation, using the psychometric scales, the clinical status of the patients was assessed, the levels of fluoxetine and magnesium in blood was controlled and the pharmaco-EEG was conducted with the analysis of the obtained results.

During all stages of the therapy there were no significant differences between patients treated with magnesium ions or with placebo, concerning either the efficacy of the treatment or its safety. There were no statistically significant differences in the pharmaco-EEG profile in both groups.

In the multidimensional statistical analysis of the whole investigated group, it has been shown that: the lower output values of HDRS, the female gender, the fact of smoking cigarettes and the supplementation with Mg ions were the factors which increased the chance of treatment effectiveness. The factors increasing the chances of remission (HDRS < 6) were: the lower HDRS values at the beginning of the therapy, to shorter duration of disease, the occurrence of positive profile of pharmaco-EEG after 3 h of drug administration and the potencialization of treatment by Mg ions.

OC07

Injection of magnesium sulphate induces local hyperalgesia via activation the transient receptors potential ion channels

<u>Dragana P. Srebro</u>, Sonja Vučković, Katarina Savić Vujović, Branislava Medić, Milica Prostran Department of Pharmacology, Clinical Pharmacology and Toxicology, Faculty of Medicine, University of Belgrade, Belgrade, Serbia

Purpose: Beside antinociceptive activity, magnesium may also have local pronociceptive action. This study aimed to asses the pro-/anti-nociceptive effect and mechanism of action of intraplantar (i.pl.) administration of magnesium sulfate (MS) in rats.

Materials and methods: In male Wistar rats the paw withdrawal threshold to mechanical stimuli was evaluated by the electronic von Frey test. MS was administered i.pl. with/without tested antagonist of the transient receptor potential ion channels ankyrin type (TRPA1) or vanilloid types (TRPV1 and TRPV4) or acid-sensing ion channels (ASIC).

Results: MS at doses of 0.5 - 6.2 mg/paw (i.pl.) induced local and dose-dependent mechanical hyperalgesia. Isotonic MS (6.2 mg/paw) induced mechanical hyperalgesia that lasted at least six hours. Isotonic pH-adjusted (7.4) MS-induced mechanical hyperalgesia was reduced by co-injection of HC-030031, a selective TRPA1 antagonist (140 nmol/paw), capsazepine, a selective TRPV1 antagonist (500 pmol/paw) or RN-1734, a selective TRPV4 antagonist (6.2 μmol/paw). Amiloride hydrochloride, a non-selective ASIC inhibitor (7.55 μmol/paw) did not change MS-induced hyperalgesia.

Conclusion: Local injection of isotonic pH-adjusted solution of MS (6.2%; pH 7.4) induces local peripheral pain to mechanical stimuli. This effect is mediated via activation of TRPA1, TRPV1 and TRPV4 receptors probably in primary afferent fibers.



OC08

The impact of magnesium prophylaxis on disability, quality of life, and depressive and anxiety symptoms in pediatric migraine

<u>Gordana Kovacevic</u>, Dejan Stevanovic, Dragana Bogicevic, Dimitrije Nikolic, Slavica Ostojic, Biljana Vucetic, Ivana Bosiocic, Kristina Jovanovic, Janko Samardzic, Jasna Jancic *Mother and Child Health Institute of Serbia*, *R. Dakica St. 6-8*,

Clinic for Neurology and Psychiatry for Children and Youth Dr Subotic 6a, University Children's Hospital, Tirsova 10, Faculty of Medicine, University in Belgrade, Dr Subotic 2, Institute of Pharmacology, Clinical Pharmacology and Toxicology, Dr Subotic 1/3, Belgrade, Serbia

Objective: The aim of this study was to evaluate to which extent disability levels, quality of life (QOL), and depressive and anxiety symptoms change after 6-month magnesium prophylaxis in pediatric migraine.

Methods: This is a follow-up study of 34 children aged 7-17 years with migraine treated with oral magnesium. Disability due to migraine was assessed by the Pediatric Migraine Disability Assessment tool (PedMIDAS), QOL was assessed by the KIDSCREEN-27 and depressive and anxiety symptoms by the Revised Child Anxiety and Depression Scale (RCADS).

Results: PedMIDAS scores significantly decreased from baseline to end-point (F (df, dferror) = 11.10 (1.63, 50.49), p< 0.001), as well as anxiety (F (df, dferror) = 8.95 (1.64, 50.67), p = 0.001) and depressive symptoms also (F (df, dferror) = 8.91 (1.59, 49.29), p = 0.001). Considering the KIDSCREEN-27, scores for physical and psychological well-being and social support domain significantly increased from baseline to end-point (p \leq 0.01).

Conclusion: After six months of magnesium prophylaxis, the disability due to pediatric migraine significantly decreased, while physical and psychosocial well-being improved. Children also reported fewer anxiety and depressive symptoms. More follow-up and randomized controlled clinical trials are needed in order to propose clinical recommendations for magnesium prophylaxis in pediatric migraine.

OC09

The effects of NMDA receptor antagonists – ketamine and magnesium sulphate on the body temperature and acute nociceptive pain in rats

<u>Katarina Savić Vujović</u>¹, Sonja Vučković¹, Aleksandar Vujović², Branislava Medić¹, Dragana Srebro¹, Milica Prostran¹ Department of Pharmacology, Clinical Pharmacology and Toxicology, Faculty of Medicine, University of Belgrade, Belgrade, Serbia

Purpose: Study is aimed at evaluating the effects of NMDA antagonists ketamine and magnesium sulphate on body temperature and acute nociceptive pain in rats and examination whether magnesium sulfate added to ketamine produces higher level of analgesia and higher effect on body temperature.

Materials and methods: Analgesic activity was assessed by tail-immersion test in male Wistar rats (200-250 g). The body temperature was measured by insertion of a thermometer probe 5 cm into the colon of unrestrained rats.

Results: Magnesium sulphate (5 and 60 mg/kg, sc) showed no influence on baseline body temperature. Subanesthetic doses of ketamine (5-30 mg/kg, ip) given alone, produced significant dose-dependent reduction in baseline colonic temperature. Analysis of the log dose–response curves for the effects of ketamine and ketamine-magnesium sulphate combination revealed synergistic interaction, and about 5.3 fold reduction in dosage of ketamine when the drugs were applied in fixed ratio (1:1) combinations. Magnesium sulfate (2.5-60 mg/kg, s.c.) and ketamine (2.5-30 mg/kg, i.p.) given alone did not produce any effect on antinociception. There is a synergistic interaction between ketamine (2.5, 5 and 10 mg/kg) and magnesium sulfate (5 mg/kg).

Conclusion: This study revealed potentiation of ketamine by magnesium sulphate in tail-immersion test in rats with higher activity when ketamine is given before magnesium sulfate. It is first time to demonstrate the synergistic interaction between magnesium sulphate and ketamine in lowering body temperature and in antinociception with statistical confirmation.

² Hospital for ENT, KBC Dragiša Mišović, Belgrade, Serbia Belgrade, Serbia

OC10

Antiepileptic and antiepileptogenic effect of magnesium on nickel-induced epileptiform activity of leech Retzius neurons

Marija Stanojević¹, Srdjan Lopicic¹, Svetolik Spasic¹, Vladimir Nedeljkov¹, Isidora Banjac¹, Dhruba Pathak², Milica Prostran³

¹ Institute for Pathological Physiology, Faculty of Medicine, University of Belgrade, Belgrade, RS

Purpose: Animal models of epileptiform activity induced by blocking active chemical synaptic transmission in both invertebrate and mammalian neurons stress the importance of nonsynaptic mechanisms in cellular basis of epilepsy. Magnesium is an element bioessential for normal function of excitable membranes. Anticonvulsive effect of magnesium is clinically used to control several specific seizure types (in eclampsia, uremia and porphyria). However, mechanisms of antiepileptic Mg2+ action and its therapeutic potential are still not well understood. This study examines the effects of Mg2+ application on epileptiform activity experimentally induced in Retzius neurons of the leech H. sanguisuga by Ca2+ channel blockade with nickel. Furthermore, the effects of exposure to Mg2+ prior to induction of epileptiform activity by Ni2+ are tested for.

Materials and methods: Classical intracellular electrophysiological recording was used. All data are represented as average±SEM.

Results: Superfusion by 3 mM NiCl2 saline induces epileptiform activity represented by rhythmical generation of paroxysmal depolarization shifts (PDSs) with a mean frequency of 5.92±0.28 min-1 (n=39). Introducing increasing concentrations of MgCl2 (1 mM, 3 mM, 7 mM, 10 mM and 20 mM Mg2+) into Ni2+ saline in separate trials of experiments suppresses epileptiform activity in a dose-dependent manner, reducing PDS frequency to 4.51±0.38 min-1 (n=5, p<0.05), 3.52±0.32 min-1 (n=7, p<0.001), 2.57±0.45 min-1 (n=8, p<0.001), 1.15±0.45 min-1 (n=11, p<0.001) and 0.00±0.00 min-1 (n=8, p<0.001), respectively. Finally, PDS frequency of epileptiform activity induced after 7 min pre-exposure to 10 mM Mg2+ saline was 1.73±0.26 min-1 (n=11).

Conclusion: Magnesium shows significant antiepileptic and antiepileptogenic effect on nonsynaptic epileptiform activity on our cell model. We conclude that increasing extracellular Mg2+ concentration can protect against non-synaptic epileptic activity. The underlying mechanism of this Mg2+ action needs to be investigated in detail.

Acknowledgement: This work was supported by Republic of Serbia Ministry of Education, Science and Technological Development, grant number 175023.

OC11

Mg and kidney: the role of hypomagnesaemia in acute kidney injury

<u>Branislava Medić</u>, Katarina Savić Vujović, Dragana Srebro, Sonja Vučković, Milica Prostran Department of Pharmacology, Clinical Pharmacology and Toxicology, Faculty of Medicine, University of Belgrade, Belgrade, Serbia

Purpose: Acute kidney injury (AKI) represents a heterogeneous process that remains an unresolved problem in pharmacotherapy with high mortality rate, especially in critically ill patients. It is known that hypomagnesemia is a common disorder in intensive care unit (ICU) patients who suffered from renal failure, but the link between levels of magnesium and prognosis of AKI is still not clarified.

The aim of our study was to analyze magnesium concentrations with severity and prognosis of different types of AKI.

Materials and methods: We searched MEDLINE from 1990 to 2017. for English language articles including following key words: magnesium, kidney, acute kidney injure, critically ill patients, clinical trials etc. Hypomagnesemia was defined as an episode of serum magnesium concentration of <0.70 mmol/L during ICU stay. The Risk, Injury, Failure, Loss and End-stage kidney disease (RIFLE) criteria were used to define AKI. We identified more than 30 relevant articles.

Results: According to the available data, hypomagnesemia seems to alter negatively prognosis in patients suffered from acute kidney injury. Hypomagnesemia was associated with higher mortality and worse prognosis, although there was no statistically significant occurrence of hypomagnesemia in AKI patients in comparison with control group (P>0.05). Limitations of our study: examined populations were heterogeneous regarding type and severity of AKI, most of the data was only observational and we were not able to exclude confounding factors.

Conclusion: Hypomagnesemia is non-dependent factor in worsening prognosis of AKI. Before definitive therapeutic recommendations, more detailed studies need to be conducted.



² Boston University School of Medicine, Boston, USA

³ Institute for Pharmacology, Clinical Pharmacology and Toxicology, Faculty of Medicine, University of Belgrade, Belgrade, RS

OC12

Magnesium modulates the permeability of the Blood-Brain Barrier

Romeo V.1, Locatelli L.1, Sargenti A2, Cazzaniga A.1

- ¹ "L. Sacco" Department of Biomedical and Clinical Sciences, University of Milan, Via G.B. Grassi 74, 20157 Milan, IT
- ² Department of Pharmacy and Biotechnologies, University of Bologna, Via San Donato 19/2, 40127 Bologna, IT

Purpose: The Blood-Brain Barrier (BBB), a dynamic structure primarily constituted by a tightly sealed monolayer of endothelial cells in concert with astrocytes, has the crucial role of separating the systemic circulation from the central nervous system (CNS), thus protecting the brain tissue from harmful substances, yet allowing the passage of substances necessary for metabolic functions. Changes in the BBB's permeability are associated with various neurological disorders and might be associated with chronic pain. The aim was to evaluate the effect of different magnesium salts on the BBB permeability.

Materials and methods: We developed an in vitro BBB model by co-culturing endothelial cells and astrocytes using a transwell system. Astrocytes were cultured in the lower part of the transwell and endothelial cells on the upper side. We compared the effects of MgSO4 and Mg pidolate. Permeability was measured using bovine serum albumin-fluore-scein isothiocyanate conjugate (BSAFIT). We also measured Mg levels in the lower chamber using the DCHQ5 fluorescent probe.

Results: Preliminary results show that the passage of Mg through the in vitro BBB model takes place in a timeand dose-dependent manner. No significant differences were observed using MgSO4 and Mg pidolate. Moreover, high concentrations of Mg salts reduced permeability of the BBB to fluoresceinated albuminMg pidolate being significantly (P< 0,01) ore effective than MgSO4.

Conclusion: Our results can be summarized as follows: i) Mg is involved in the modulation of BBB's permeability, thereby indicating that high Mg might prevent the accumulation of toxic molecules in the brain; ii) Mg pidolate is more active than MgSO4 in reducing BBB permeability and iii) MgSO4 and Mg pidolate are transported through the BBB to a similar extent. Further studies are required to better define these events. Sanofi has sponsored this study.

OC13

Effect of inflammation on muscle function in a murine colitis model: the contribution of Magnesium

<u>Valentina Petito</u>¹, V. Trapani², F. Luongo², Giuseppe Pietropaolo², Claudia Petito¹, C. Graziani¹, L. R. Lopetuso¹, V. Arena², A. Gasbarrini¹, F. Scaldaferri^{1#} and F. I. Wolf^{2#}

¹ Gastroenterological Area, Gastroenterological and Endocrino-Metabolical Sciences Department Fondazione Policlinico Universitario Gemelli, Catholic University of the Sacred Heart, Rome, Italy

² Institute of General Pathology, Catholic University of the Sacred Heart, Rome, Italy

Purpose: Inflammation is an important contributor to the etiology of diseases implicated in skeletal muscle dysfunction. A number of diseases and disorders including inflammatory bowel diseases (IBD) are characterized by chronic inflammation, malabsorption, maldigestion, increased energy expenditure, and gastrointestinal protein loss, that may induce a relative deficiency of energy or proteins. Diarrhoea and occult blood loss increase the loss of zinc, potassium, magnesium, iron. The aim of this study is to investigate the influence of magnesium intake on muscular activity, and to assess whether expression of the magnesium channels TRPM7 and MAGT1 could be correlated with muscular function in an experimental colitis model.

Materials and methods: Mice were exposed for 5 days to 2.5% dextran sodium sulphate (DSS), followed by 7 days of recovery without DSS, and fed with three different diets (low (30mg/kg), normal (1000mg/kg) and high (4000mg/kg) Mg2+ content). The severity of the colitis was scored daily using the four points Disease Activity Index (DAI). The rota rod performance test was used to evaluate the effects of colitis on skeletal muscle dysfunction. Colon, muscle and serum were collected at the sacrifice. Magnesaemia was analysed using atomic absorption spectrometry. Muscle morphology was assessed by immunohistochemistry. Channel expression was assessed by real time RT-PCR.

Results: Dietary Mg2+ deficiency increased the severity of the DSS-induced colitis. Low Mg2+ diet enhanced muscular damage, assessed as loss of skeletal muscle mass and a deregulated skeletal muscle physiology; conversely, Mg2+ supplementation showed protective effects. Magnesium channels were modulated both by diet and DSS treatment in muscle tissues.

Conclusion: Muscle activity is compromised during colitis, probably due to inflammatory cytokines. Our results show a protective effect exerted by dietary magnesium on muscle function in this condition. Further studies are in progress to identify the underlying molecular mechanisms linking expression of the magnesium channels to intracellular signal transduction.

OC14

Effects of magnesium, vitamin C and D3 on miR-1 and miR-29b expression in adipose-derived mesenchymal stem cells

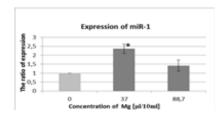
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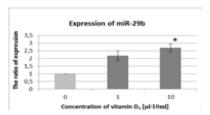
- ¹ Department of Pharmacology and Toxicology, Faculty of Pharmacy, Comenius University in Bratislava, SK
- ² Institute of Pharmacology and Clinical Pharmacology, Faculty of Medicine, Comenius University in Bratislava, SK
- ³ Clinical Research Unit, V. Internal Clinic, Faculty of Medicine, Comenius University in Bratislava, SK

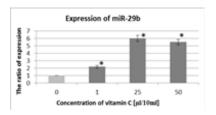
Purpose: Mesenchymal stem cells (MSCs) are an important tool in tissue engineering and regenerative cell therapy thanks to their unique ability to self-renew and differentiation. In addition to bone marrow, adipose tissue is also an important source of these cells. Under suitable culture conditions these cells can differentiate into various specialized cells. Many studies have been aimed at monitoring the effect of various growth factors, cytokines and hormones on the differentiation potential of stem cells. Our goal was to gain new insight into the impact of multiple clinicaly-used medicines, focusing on the effect of magnesium, vitamin C and vitamin D3 on potential changes in the cultivation and differentiation of MSCs.

Materials and methods: MSCs isolated from adipose tissue were incubated and grown at 37°C in a 5%CO2 humidified incubator. Expression of surface markers characteristic of MSCs was determined by the flow cytometry method. Then the individual samples were cultivated for 24 hours in media with the addition of various concentrations of magnesium, vitamin C and vitamin D3. Possible structural and morphological changes on cells were recorded under an inverse microscope. Changes in the expression of selected cardio-specific miRNAs (miRNA-1, miRNA-133a, miR-NA-499 and miRNA-29b) were determined using real-time PCR.

Results: The number of all cells was determined by flow cytometry: 1,94.107 after the treatment with vitamin C; 2,48.107 after the treatment with vitamin D3 and 8,41.107 after the treatment with magnesium. MSCs were characterized by positive staining for markers CD90, CD105 and CD73, and negative staining for markers CD14, CD20, CD34 and CD45. The viability of our cells was more than 90% in all treated cells. There was measured and detected the number of MSCs: 0,06% of MSCs in a group treated with vitamin C; 0,10% in a group treated with vitamin D3 and 0,14% MSCs in a group treated with magnesium. After the pharmacological influence of the cells by the addition of vitamin D3, the expression of all the miRNAs observed was significantly increased. Under the influence of magnesium in miRNA-1 and miRNA-29b expression was recorded a statistically significant increase compared to the control sample. Increased concentrations of vitamin C significantly affected the structure and morphology of the monitored cells and there were significant changes in the expression of miRNA-29b and miRNA-499.







Conclusion: Our work has confirmed the possibility of influencing stem cells not only by altered conditions, but also by pretreatment of incubated cells with medicines. Above all, the significant effect have been shown by magnesium, but potential for the further experiments has also vitamin D3 and vitamin C.

Acknowledgement: FaF UK/34/2015, VEGA 1/0905/14, APVV-14-0416



OC15

Dietary magnesium intake modifies the number of hepatic stem cells in rat

Sophie Aupet, Jessica Gromand, Lysiane Richert, <u>Alain Berthelot</u> and Hélène Martin EA4267 PEPITE, Faculté des Sciences Médicales et Pharmaceutiques, 25030 Besançon, FR

Purpose: Previous studies have demonstrated that Mg deficiency led to oxidative stress and apoptosis in rat livers and in rat and human hepatocytes in culture. Considering that liver tissue can regenerate in some conditions, we have hypothesized that Mg concentration could modify the number of hepatic stem cells (named oval cells in rat liver). In the present study we have isolated, counted and characterized liver stem cells (Thy-1+cells) from rats receiving different dietary intake of Mg.

Materials and methods: Male rats were randomly divided into three groups (n=3 rats/group) and were fed for 5 weeks with a normal semisynthetic diet that corresponds to 0.9 g/kg Mg (Std group), with a Mg-deficient diet that corresponds to 0.15 g/kg Mg (Def group) or with a Mg-supplemented diet that corresponds to 4.5 g/kg Mg (Suppl group). Thy-1+ (CD-90) cells were immunoselected from rat livers after cell dissociation (MACS technology, Milteny biotech). These cells were characterized by measuring the mRNA expression of different cellular markers and also cultured for up to ten days in RPMI medium.

Results: We obtained a negative correlation between the intake of Mg in the different diets and the number of Thy-1+cells present in rat liver; indeed, Mg deficiency led to a statistically significant increase in Thy-1+ cells (P<0.05). In these cells, the expression of CD-44 at the mRNA level was increased in Mg deficient group, as compared to the standard group, whereas CD-133, HNF1, c-met, AFP and CYP3A1 mRNA expressions were decreased. Moreover, when placed in culture, small colonies of cells which were adherent to the culture support appeared and proliferated over culture time.

Conclusion: we suggested that liver regeneration can occur in rat liver submitted to a deficient dietary Mg condition, as suggested by the increase in oval cells in rat liver and their growth when cultured.





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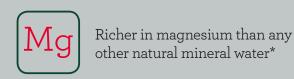
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lonised magnesium (iMg): An essential electrolyte for managing critically ill patients

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The need for iMg testing

- Dysmagnesaemia is common in critically ill patients. 1-4
- Dysmagnesaemia is associated with increased mortality, morbidity, and length of stay in critically ill patients.⁴⁻¹⁰
- iMg is the only marker that specifically identifies patients with dysmagnesaemia. 11,12
- iMg monitoring of patients treated with Mg sulfate improves clinical outcomes and can reduce length of stay. 12-14
- iMg monitoring reduces the risk of Mg toxicity in patients treated for Mg deficiency.¹¹⁻¹³
- iMg is essential for intracellular regulation and transport of Na, K, and iCa.1,3,7,10,14
- Rapid serial measurement of iMg is essential for the management of electrolyte deficiencies.¹³

iMg is part of the extensive critical care panel available on Stat Profile Prime Plus

Stat Profile Prime Plus is a comprehensive, whole blood critical care analyser that combines blood gases, electrolytes, metabolites, co-oximetry, and 32 calculated results in a simple, compact device. Prime Plus features maintenance-free biosensor technology for all tests and new, maintenance-free and non-lysing whole blood co-oximetry technology, along with comprehensive data management, bidirectional connectivity, and extensive cybersecurity protection. Prime Plus's results are produced very rapidly, a complete test menu panel in about one minute.

Comprehensive 22-Test Critical Care Menu

pH, PCO2, PO2, Na, K, Cl, iCa, iMg, Glu, Lac, Urea (BUN), Creat, Hct, TCO2, SO2%, O2Hb, COHb, MetHb, HHb, tBil, tHb, HbF

Maintenance-Free Cartridge Technology

Replacement in half the time needed by other analysers.

Automated, True Liquid QC

Liquid QC levels are coupled with continuous electronic self-monitoring (SQM).

Clot Block™ Protection

Unique probe and flow path protects the analyser from blood clots.

For further information please email info@novabiomedical.co.uk



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