

14th ISHEN Symposium

International Society on Hepatic Encephalopathy and Nitrogen Metabolism

Val-David, Canada

September 14 -18, 2010



SCIENTIFIC PROGRAM

September 14th 2010

WELCOME RECEPTION

OPENING REMARKS

Roger F. Butterworth Ph.D., D.Sc., University of Montreal, Canada

Jacques Turgeon B.Pharm., Ph.D., University of Montreal, Canada

September 15th 2010

SESSION I: BRAIN EDEMA AND LIVER FAILURE

Brain edema: a distinct feature of acute and chronic liver failure

Juan Córdoba MD, Hospital Vall d'Hebron, Barcelona, Spain

Brain edema in cirrhosis

Radhakrishan Dhiman MD, PGIMER, Chandigarh, India

Mechanisms of brain edema in HE

Michael D. Norenberg MD, UM Miller School of Medicine & Miami VA Medical Center, USA

Blood-brain barrier in ALF

Justin Nguyen MD, Mayo Clinic, Jacksonville, USA

Localisation of osmolyte transporters in brain

Michael Moos Ph.D., Heinrich Heine University, Düsseldorf, Germany

Biexponential analysis of diffusion-tensor data from patients with liver cirrhosis suggest a mixed pattern of brain edema

Laia Chavarria Vilarasau, Hospital Vall d'Hebron, Barcelona, Spain

SESSION II: YOUNG INVESTIGATOR COLLOQUIUM #1 – BASIC RESEARCH

GABAA receptor complex in HE: an update

Samir Ahboucha Ph.D., Cadi Ayyad University, Marrakech, Morocco.

Protective effect of hypothermia in ALF: multiple mechanisms

Javier Vaquero MD, Ph.D., University of Washington, Seattle, USA

The blood-brain barrier in cirrhosis: hints from neuroimaging

Michael Sørensen, MD, Ph.D., Aarhus University Hospital, Denmark

OP substantially improves glutamine synthase and glutaminase expression and activity in multiple organs in cirrhotic rats: additional insights on mechanism of action

María Jover Cobos, Ph.D., University College London, UK

OP prevents neurophysiological abnormalities and hyperammonemia in PCA rats with gastrointestinal bleeding

Marc Oria Alonso, Hospital Vall Hebron, Barcelona, Spain

Acute effects of ingestion of branched-chain amino-acids on muscle ammonia metabolism

Gitte Dam, Aarhus University Hospital, Denmark

SESSION III: NEUROCHEMISTRY OF HE

Peripheral oxidative stress in HE

Christopher Rose Ph.D., University of Montreal, Canada

Oxidative/nitrosative stress in HE

Dieter Häussinger MD, Ph.D., Heinrich Heine University, Düsseldorf, Germany

Brain signalling in HE: 13C-NMR studies

Claudia Zwingmann Ph.D., University of Montreal, Canada

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Second messenger systems in HE

Jan Albrecht Ph.D., Polish Academy of Sciences, Warsaw, Poland

Synthesis of alanine and glutamine / hyperammonemia

Arne Schousboe, D.Sc., University of Copenhagen, Denmark

Ammonia increases nitric oxide, free zinc and metallothionein (MT)-1 mRNA expression in cultured rat astrocytes and MT-1 mRNA expression in rat brain in vivo

Freimut Schliess Ph.D., Profil Institute for Metabolic Research GmbH

ROUNDTABLE I: AMMONIA AND HE: FACTS AND FANTASY

Ammonia Transport

Christopher Rose Ph.D., University of Montreal, Canada

Ammonia Gradients

Arthur J.L. Cooper Ph.D., D.Sc., New York Medical College, Valhalla, USA

Concentrations of Ammonia in blood, brain, CSF, microdialysis

Alan H. Lockwood MD, University at Buffalo and Center for PET (115P), Buffalo, USA

Direct effects of Ammonia

Roger F. Butterworth Ph.D., D.Sc., University of Montreal, Canada

Ammonia permeability across BBB

Michael Sørensen, MD, Ph.D., Aarhus University Hospital, Denmark

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SESSION IV: PATHOGENESIS OF HE: INFLAMMATION

CNS effects of peripheral inflammation

Marc Swain Ph.D., University of Calgary, Canada

Pathogenesis of HE: key role of the neutrophil

Deborah Shawcross Ph.D., University College London, UK

Neuroinflammation in both acute and chronic liver failure

Roger F. Butterworth Ph.D., D.Sc., University of Montreal, Canada

Septic Encephalopathy and HE: similarities and differences

Jessy Alexander Ph.D., University of Chicago, USA

Impact of ammonia on microglia activation

Boris Görg Ph.D., Heinrich Heine University, Düsseldorf, Germany

Norfloxacin administration prevents the occurrence of LPS induced acute deterioration of cerebral edema in bile duct ligated cirrhotic rats through a TLR-4 mediated pathway

Naina Shah, Institute of Hepatology, London, UK

SESSION V: NEUROPATHOLOGY IN HE

Parkinsonism in cirrhosis

Karin Weissenborn MD, Hannover Medical School, Germany

Motor activity deficits following portal-systemic shunting

Vicente Felipe Ph.D., Centro de Investigación Príncipe Felipe, Valencia, Spain

Imaging the basal ganglia in cirrhosis

Simon Taylor Robinson MD, Imperial College London, UK

PET imaging of the dopaminergic system in HE

Akinobu Kato MD, Iwate Medical University, Morioka, Japan

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Reduced dopaminergic innervation and voluntary movements in bile duct ligated rats: effect of the neurosteroid dehydroepiandrosterone sulfate

Omar El Hiba, Cadi Ayyad University, Marrakech, Morocco

Alterations in expression of genes coding for key astrocytic proteins in frontal cortex of autopsied brain tissues of patients with ALF and of patients with liver cirrhosis and HE

Kiran K. Thumburu, PGIMER, Chandigarh, India

SOCIAL ACTIVITIES

POSTER SESSION

September 17th 2010

SESSION VI: MANAGEMENT AND TREATMENT OF HE #1

Rifaximin in the treatment of HE

Kevin Mullen MD, MetroHealth Medical Center, Cleveland, USA

Probiotics and synbiotics in HE: progress to date

Jasmohan Bajaj MD, Virginia Commonwealth University, Richmond, USA

AST-120: new kid on the block

Kevin Mullen MD, MetroHealth Medical Center, Cleveland, USA

Glutaminase inhibitors and HE: proof of principle

Manuel Romero-Gómez MD, Ph.D., Valme University Hospital, Seville, Spain

Mild hypothermia in ALF: review of the evidence

Fin Stolze Larsen MD, Ph.D., University Hospital of Copenhagen, Denmark

Post-TIPS HE: mechanisms and management

Christopher Record Ph.D., University of Newcastle upon Tyne, United Kingdom

SESSION VII: MANAGEMENT AND TREATMENT OF HE #2

OP: novel ammonia-lowering agent

Rajiv Jalan MD, Ph.D., University College London, UK

L-ornithine L-aspartate: new indications

Gerald Kircheis MD, Heinrich Heine University, Düsseldorf, Germany

L-Histidine: multiple action amino acid

Michael D. Norenberg MD, UM Miller School of Medicine & Miami VA Medical Center, USA

The Bioartificial Liver: an update

Scott L. Nyberg MD, Ph.D., Mayo Clinic, Rochester, USA

Neurological complications post-LT

Piero Amodio MD, University of Padova, Italy

Sleep disturbances in cirrhosis

Sara Montagnese MD, University College London, UK

SESSION VIII YOUNG INVESTIGATOR COLLOQUIUM #2 CLINICAL RESEARCH

Inhibitory control test for diagnosis of HE-sensitivity and specificity compared to PHEs, CFF and RBANS

Anita Blanka Tryc MD, Medical School Hannover, Germany

Cognitive symptoms in chronic hepatitis C infection are associated with impaired cognitive test performance but are unrelated to peripheral markers of cellular immune activation

Markus Gess MRCP, St George's Hospital and Medical School, London, UK

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Risk of HE and death in alcoholic cirrhosis with ascites: effects of liver and kidney function, hyponatremia, alcohol, and comorbidity

Peter Jepsen MD, Ph.D., University of Copenhagen, Denmark

The development and testing of the UCL liver support device (UCL-LSD): improvement of survival in paracetamol-induced acute liver failure pigs

Nathan Davies Ph.D., University College London, UK

Electrophysiological correlates of the inhibitory control task in patients with cirrhosis: inhibition or stimulus categorization defect?

Sami Schiff Ph.D., University of Padova, Italy

Prior HE and alcohol abuse determine cognitive function after liver transplantation

Rita García-Martínez MD, Hospital Vall d'Hebron, Barcelona, Spain

ROUNDTABLE II: NUTRITION IN THE MANAGEMENT OF HE

Energy requirements

Hendrik Vilstrup MD, D.Sc., Aarhus University Hospital, Denmark

Protein/nitrogen requirements

Juan Córdoba MD, Hospital Vall d'Hebron, Barcelona, Spain

Rationale for protein selection (vegetable vs animal; meat vs milk derivatives)

Misael Uribe MD, Medica Sur Hospital & Clinic Foundation, Mexico City, Mexico

Branched chain amino acid requirements and supplementation

Akinobu Kato MD, Iwate Medical University, Morioka, Japan

Fibre requirements

Sara Montagnese MD, University College London Medical School, UK

Vitamins and carnitine requirements and supplementation

Chantal Bémour Ph.D., University of Montreal, Canada

Mineral requirements and supplementation

Piero Amodio MD, University of Padova, Padova, Italy

Rationale for nutritional assessment: when and how?

Marsha Y. Morgan MD, University College London Medical School, UK

SOCIAL ACTIVITIES

SOCIETY MEETING

September 18th 2010

CLINICAL WORKSHOP: DESIGNING CLINICAL TRIALS IN HE

Episodic HE

Juan Córdoba MD, Hospital Vall d'Hebron, Barcelona, Spain

Prevention of HE

Kevin Mullen MD, MetroHealth Medical Center, Cleveland, USA

Low-grade HE

Marsha Y. Morgan MD, University College London Medical School, UK

ABSTRACTS

BASIC RESEARCH

01. *Brain toll-like receptor-4 (TLR4) is upregulated in cirrhosis and its modulation by selective gut decontamination reduces brain inflammation and edema*
N. Shah, D.K. Dhar, R.P. Mookerjee, N.A. Davies, R. Jalan
Institute of Hepatology, London, United Kingdom.
02. *The regulation of nitrogen elimination via urea during different stages of the tumor necrosis factor-alpha induced acute phase response*
K.L. Thomsen, N.K. Aagaard, T.D. Sandahl, H. Grønbaek, J. Frystyk, H. Vilstrup
Aarhus University Hospital, Denmark.
03. *Non-selective adenosine receptor antagonism aggravates intracranial hypertension in a rat model of acute hyperammonemia and systemic inflammation – a biosensor study*
P.N. Bjerring, F.S. Larsen
Rigshospitalet, Copenhagen, Denmark.
04. *Locomotor impairment and cerebrocortical oxidative stress in portal-vein ligated rats in vivo*
B. Görg, J. Brück, H.-J. Bidmonš, I. Zemtsova, N. Qvartrskhava, V. Keitel, G. Kircheis, D. Häussinger
Heinrich-Heine-University, Düsseldorf, Germany.
05. *Reduction in hyperammonemia with L-ornithine phenylacetate (OCR-002) in bile-duct-ligated (BDL) cirrhotic rats restores brain eNOS activity by modulating the DDAH-ADMA pathway*
V. Balasubramaniyan, N.A. Davies, G.A.K. Wright, V. Sharma, R.P. Mookerjee, R. Jalan
University College London, United Kingdom.
06. *Ex vivo treatment of neutrophils from patients with acute and acute-on-chronic liver failure and HE with isoproterenol improves neutrophil phagocytosis*
A. Nishtala, N. Taylor, D.L. Shawcross
King's College London School of Medicine, London, United Kingdom.
07. *Inadequate compensation by glutamine synthetase (GS) and increased glutaminase (GA) activity contributes to hyperammonemia in cirrhosis*
M. Jover-Cobos, L. Noiret, A. Habtesion, V. Balasubramaniyan, Y. Sharifi, M. Romero-Gómez, N.A. Davies, R. Jalan
University College of London, United Kingdom.
08. *Astrocyte glutamine synthetase: importance in hyperammonemic syndromes and potential target for therapy*
S.W. Brusilow, R.C. Koehler, R.J. Traystman, A.J.L. Cooper
The Johns Hopkins University School of Medicine, Baltimore, USA.
09. *The profile of gene expression of cortex microvessels suggests energy impairment in the pathogenesis of brain edema in acute liver failure*
L. Palenzuela, M. Oria, J. Romero, J. Cordoba
Hospital Vall d'Hebron, Barcelona, Spain.
10. *The impact of blood flow change on interorgan ammonia metabolism in cirrhosis: a mathematical approach*
L. Noiret, S. Baigent, M. Jover-Cobos, R. Jalan
University College of London, United Kingdom.
11. *Brain expression of NKCC1 in a mouse model with acute liver failure*
M. Eefsen, H.C. Bisgaard, F.S. Larsen
Rigshospitalet, University of Copenhagen, Denmark.
12. *Hippocampal early changes in a MHE rat model*
J.C. Perazzo, S. Tallis, L. Caltana, M.P. Aronne, A. Delfante, P. Souto, A. Reines, A. Brusco.
UBA, Buenos Aires, Argentina.
13. *An improved porto-systemic shunt technique by the use of a c-clamp in the encephalopathy-like rodent model*
M. Asgeri, N. Waghray, K. Mullen, N. Nader, H. Brunengraber, J. Sanabria
MetroHealth Medical Center, Case Western Reserve University, Cleveland, USA.

ABSTRACTS

CLINICAL RESEARCH

01. *HE: treat or teach?*
E. Amato, S. Facchini, S. Schiff, P. Amodio, S. Montagnese
University of Padova, Italy.
02. *Role of small intestinal bacterial overgrowth in cirrhotic patients with MHE*
S. Taneja, A. Gupta, S. Kumari, S. Rana, R. Agarwal, A. Duseja, Y. Chawla, R.K. Dhiman
Postgraduate Institute of Medical Education & Research, Chandigarh, India.
03. *Alterations in expression of genes coding for key astrocytic proteins in frontal cortex of autopsied brain tissues of patients with acute liver failure and of patients with liver cirrhosis and HE*
K.K. Thumburu, S. Goyal, A. Chakraborti, R.K. Vasishtha, Y. Chawla, A. Duseja, N. Sharma, R.K. Dhiman
Postgraduate Institute of Medical Education & Research, Chandigarh, India.
04. *Imaging interventions and neurologic outcomes in 8 ICU patients with severe hyperammonemia*
P.A. Kandiah, D. Pandya, A. Kori-Graf, R.
University of Pittsburgh, USA
05. *Brain diffusion weighted magnetic resonance imaging in liver disease*
K.K. Jain, C.C. Tchoyoson Lim
National Neuroscience Institute, Singapore
06. *Structural brain differences between patients with non hepatic liver cirrhosis and HCV-patients without liver cirrhosis*
P. Raab, K. Blum, A. Tryc, A. Goldbecker, A. Tabesh, H. Lanfermann, K. Weißenborn
Hannover Medical School, Germany.
07. *Change of cerebral glucose metabolism and neuropsychiatric symptoms in chronic hepatitis C patients with interferon therapy*
K. Sawara, T. Oikawa, R. Endo, Y. Takikawa, A. Kato, K. Suzuki
Iwate Medical University, Morioka, Japan.
08. *Usefulness of inhibitory control test for the diagnosis of MHE*
S. Taneja, A. Khatri, S. Goyal, A. Duseja, Y. Chawla, R.K. Dhiman
Postgraduate Institute of Medical Education & Research, Chandigarh, India.
09. *Computerized psychometric testing for diagnosis of MHE: progress?*
R.K. Prakash, K. Anna, R. Chikkanna, D. Gulati, P. Karanth, G. Dosanjh, S.V. Iduru, J. Wakim-Fleming, K.D. Mullen
MetroHealth Medical Center, Case Western Reserve University, Cleveland, USA.
10. *Comparison of critical flicker frequency test and continuous reaction times for identification of MHE in patients with liver disease*
M.M. Lauridsen, P. Jepsen, H. Vilstrup
Aarhus University Hospital, Denmark.
11. *Inhibitory control task for the detection of MHE*
L. Ridola, O. Riggio, S. Schiff, S. Montagnese, G. Cona, C. Pasquale, S. Nardelli, F. Pentassuglio, P. Amodio
'La Sapienza' University of Rome, Italy.
12. *The computerized diagnosis of MHE: focus on the SCAN test*
L. Ridola, O. Riggio, S. Schiff, S. Montagnese, M. Turco, C. Pasquale, S. Nardelli, F. Pentassuglio, P. Amodio
'La Sapienza' University of Rome, Italy.
13. *Number connection test-B performance accurately reflects total psychometric HE score in patients with cirrhosis*
M.J.W. McPhail, N. Senvar, M.E. Crossey, H. Marcinowski, H. Brooker, S. Khan, S.D. Taylor Robinson
Imperial College London, United Kingdom.

ABSTRACTS

14. *Animal naming test: a simple tool for the clinical assessment of HE*
F. Campagna, S. Montagnese, L. Ridola, M. Senzolo, M. Cavalletti, C. Pasquale, S. Nardelli, F. Pentassuglio, S. Schiff, P. Amodio, D. Pavanello, O. Riggio
'La Sapienza' University of Rome, Italy.
15. *Sleep EEG in patients with cirrhosis and induced hyperammonemia*
A. Bersagliere, I.D. Raduazzo, S. Schiff, P. Amodio, P. Achermann, S. Montagnese
University of Zurich, Switzerland.
16. *A multidimensional approach to the diagnosis of HE: focus on heart rate variability*
D. Pavanello, A.R. Mani, A. Biancardi, S. Schiff, P. Amodio, S. Montagnese
University of Padova, Italy.
17. *Intra-individual variability of behavioural and P300 responses in cirrhotic patients*
S. Schiff, G. Cona, C. D'Avanzo, G. Sparacino, P. Bisiacchi, P. Amodio
University of Padova, Italy.
18. *The effect of nutritional therapy on liver cirrhosis with subclinical HE: preliminary multicenter study in Japanese*
A. Kato, K. Sawara, R. Endo, K. Suzuki
Iwate Medical University, Morioka, Japan.
19. *Effect of colonic delivery of amino acid and urea challenges on blood ammonia in patients with advanced cirrhosis*
H. Mardini, C. Record
University of Newcastle, United Kingdom.
20. *Incomplete reversal of cognitive dysfunction after liver transplantation in individuals with overt HE before liver transplantation*
F. Campagna, A. Biancardi, S. Montagnese, P. Angeli, D. Mapelli, C. Poci, S. Schiff, U. Cillo, A. Gatta, P. Amodio
University of Padova, Italy.