27th INTERNATIONAL MONDSEE MEDICAL MEETING

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IMMM Report | 21–22 September 2023 | Salzburg, Austria

Advances in the clinical treatment of TBI and stroke

Advances in the clinical treatment of TBI and stroke

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Introduction

As organisers of the 27th International Medical Mondsee Meeting (IMMM), the Austrian Society for Neurointensive Medicine welcomed around 280 delegates to Salzburg.

IMMM 2023 focused on the management of two medical emergencies, stroke and neurotrauma. 14 speakers from 8 different countries provided lively panel discussions, exciting case presentations and the latest data from new and ongoing studies.

We have summarised the highlights of this scientific event.

The event began with a panel discussion on "Stroke Management and Guidelines", moderated by Professor Valeria Caso from Perugia, Italy. Each panellist had the opportunity to present a topical issue for the general discussion that followed.

Rich Leigh

Associate Professor of Neurology,
Johns Hopkins University
Baltimore, MD, USA

Blood brain barrier integrity in patients with emergent stroke – an MRI study

ABSTRACT

The use of Cerebrolysin has become a part of routine clinical care for patients with acute ischemic stroke treated with thrombolysis in many countries globally. Animal data suggest that one of the mechanisms by which Cerebrolysin may exert its benefit is on stabilization of the blood brain barrier (BBB). The BBB controls the movement of molecules and cells from the systemic circulation into the brain.

Acute ischemia can cause disruption of the BBB, and in the setting of severe ischemia the BBB can rupture leading to intracranial hemorrhage. Additionally, in the post-stroke brain, the BBB can become further disrupted due to inflammation. This type of inflammation has been associated with worse functional outcome after stroke. It is hypothesized that post-stroke inflammation may inhibit recovery and could be associated with cognitive decline.

Thus, if Cerebrolysin acts to stabilize the BBB, this may be one mechanism through which it improves recovery after stroke. To test this hypothesis, we will collect MRI scans on patients from two different stroke centers; one that routinely uses Cerebrolysin, and one that does not. BBB disruption will be measured for each population and compared to see if differences in BBB stability post-stroke can be detected.

We hypothesize that BBB disruption will be attenuated in the population treated with Cerebrolysin when compared to the population not treated with Cerebrolysin.

LECTURE SUMMARY

The session was opened by Professor Dr. Rich Leigh from Johns Hopkins University Hospital, Baltimore, USA.

As one of the investigators, Professor Dr. Leigh would like to investigate whether Cerebrolysin can improve the integrity of the blood-brain barrier (BBB) or stabilise the BBB after stroke.

His proposal is to incorporate the results of BBB imaging into the clinical decision-making process for recanalisation treatment. His hypothesis is that patients who are prone to haemorrhagic transformation but benefit from BBB-stabilising agents such as Cerebrolysin would also be candidates for recanalisation treatment *(figure 1)*.

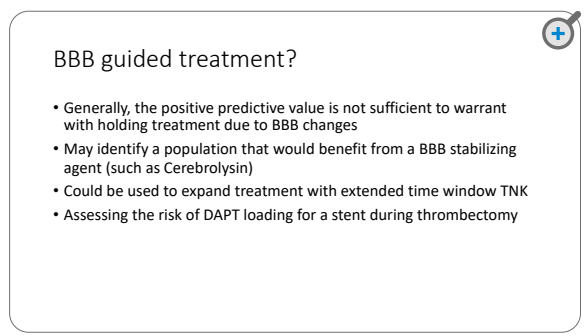

Figure 1

Professor Leigh also highlighted the benefits of BBB imaging in vascular dementia *(figure 2)*, another indication where Cerebrolysin has been shown to reduce cognitive impairment following stroke.

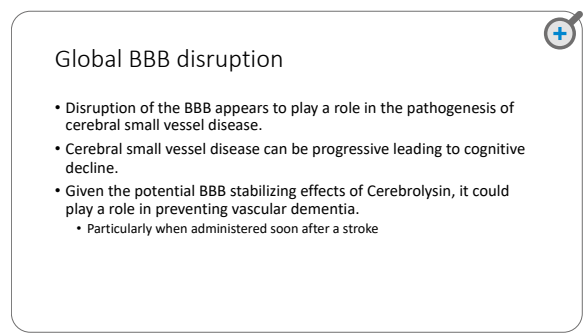

Figure 2

WATCH THE WHOLE SESSION NOW!
webinar.everpharma.com/leigh/

Jacek Staszewski

Military Institute of Medicine –
National Research Institute
Warsaw, Poland

Cerebroprotection for Acute Ischemic Stroke

ABSTRACT

The availability of mechanical thrombectomy (MT) in clinical practice has improved acute stroke outcome and allowed to understand the role played by reperfusion in mediating brain injury. Rapid reperfusion of ischemic penumbra is critical to neurological recovery, however, it can also lead to reperfusion injury induced by high levels of free oxygen radicals, reactive hyperemia and proinflammatory state thrombosis.

Therefore, the rates of excellent outcome or functional independence following MT performed in both the early and late time window, in clinical trials, or in clinical practice are far from satisfactory compared with the very high rates of successful recanalization which implies the need to further improve recovery of patients.

Recanalization therapy constitutes a novel opportunity for cytoprotective agents due to a higher chance to reach the ischemic penumbra and to protect from the injury and death of neurons after ischemia-reperfusion. Success in developing cerebroprotection, either as an adjunct to recanalization or as stand-alone treatment will require new focus on pleiotropic agents that act via multiple mechanisms of action and target different components of the neurovascular unit.

Cerebrolysin is a neurotrophic peptidergic preparation with broad cytoprotective properties, recommended by the European Academy of Neurology and European Federation of Neurorehabilitation Societies for both the acute- and poststroke rehabilitation.

Preclinical and clinical studies suggest that Cerebrolysin as an add-on therapy to reperfusion therapy may improve stroke outcome by initiating cytoprotective effects and preventing reperfusion injury. Potential targets for cerebroprotection and preliminary data of Cerebrolysin in acute stroke treatment will be discussed during the presentation.

LECTURE SUMMARY

The second panellist, Professor Dr. Jacek Staszewski from Warsaw, Poland, briefly presented his ongoing study using Cerebrolysin as an add-on to full recanalisation therapy. He made a strong case for effective add-on treatments, as thrombolysis and thrombectomy alone do not achieve an excellent outcome as measured by mRS at day 90 in more than 55% of patients treated *(figure 3)* .

He shared with the audience the interim results of his study, which has enrolled 80% of the planned number of participants (n=100) as of September 2023. In the Cerebrolysin treatment group, significantly fewer patients experienced haemorrhagic transformation (HT) *(figure 4)* and showed a significantly better clinical outcome at day 90 *(figure 5)*, despite the small sample size of patients observed. He gave the following messages to the audience *(figure 6)*.

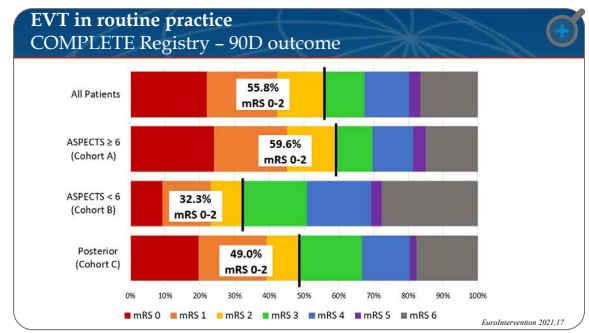

Figure 3

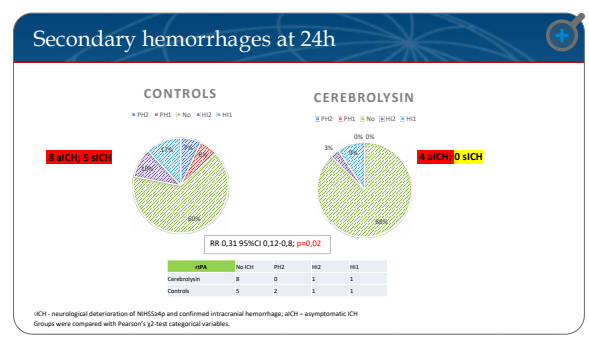

Figure 4

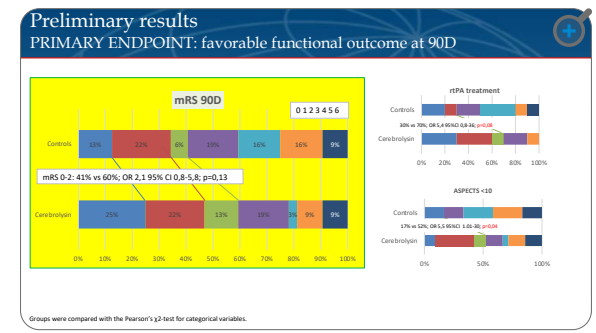

Figure 5

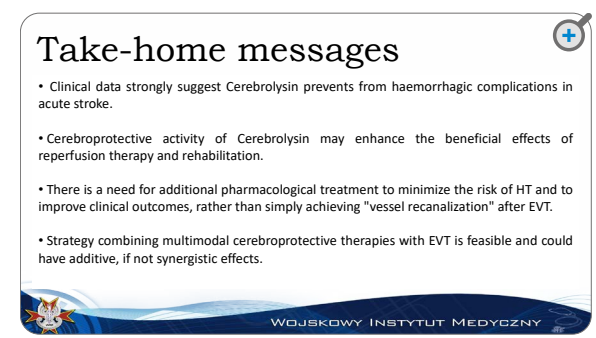

Figure 6

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Won-Seok Kim

Seoul National University College of Medicine,
Seoul National University
Bundang Hospital, Korea

Updated clinical practice guidelines for rehabilitation for motor recovery after stroke in Korea

ABSTRACT

The Korean Society for Neurorehabilitation (KSNR) has been publishing stroke rehabilitation guidelines since 2009, with updates in 2012 and 2016. The previous guidelines were established using SIGN methods; however, KSNR has recently adopted new evidence and GRADE methods for updating the guidelines.

The initial phase focused on revising the guidelines pertaining to motor recovery, a process that concluded in 2022. This comprehensive update addresses 24 questions related to rehabilitation for motor recovery after stroke.

Key areas covered include early mobilization, rehabilitation dosage, functional electrical stimulation, robotic gait training, repetitive transcranial magnetic stimulation, transcranial direct current stimulation, botulinum toxin injection, Cerebrolysin, and more.

For evidence synthesis, the studies were searched up until February 28th, 2022, using three databases (PubMed, EMBASE, Cochrane library) and meta-analyses were conducted using the selected studies.

During my presentation, I will provide a concise overview of the methodology employed in developing the revised Korean Stroke Rehabilitation Guidelines. Furthermore, I will present the evidence levels and recommendations for selected pivotal questions within the motor rehabilitation domain.

LECTURE SUMMARY

Panellist Professor Dr. Won-Seok Kim from Bundang Hospital, Korea, one of the co-authors of the Korean guideline for post-stroke rehabilitation for recovery of motor function, presented study data that led to the inclusion of Cerebrolysin in the current guideline. Based on the GRADE methodology, "Cerebrolysin is recommended for improving motor function in stroke patients, depending on the patient's condition and the risk of side effects", Grade B recommendation *(figure 7)*. Professor Kim also pointed out that this is the first time in Korea that a pharmacological agent is recommended for motor impairment, which will benefit the growing number of patients who need rehabilitation *(figure 8)*.

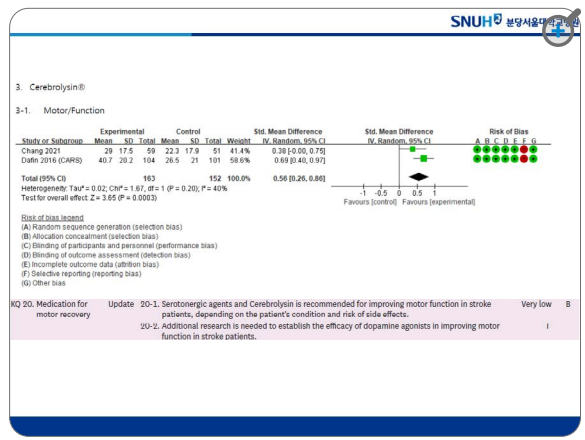

Figure 7

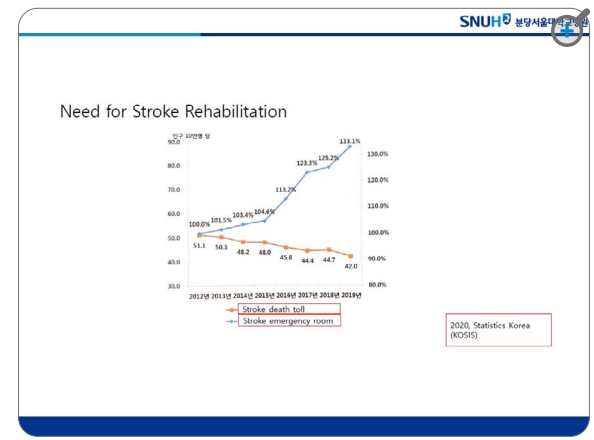

Figure 8

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webinar.everpharma.com/kim/

Ales Tomek

Neurologist at Motol University Hospital at Prague
Prague, Czech Republic

The importance of treatment algorithms in post-stroke rehabilitation

ABSTRACT

The global epidemiological burden of stroke leads to very high levels of disability adjusted life years (DALY) in low- and middle-income countries that contribute to a further increase of the socio-economic burden. In order to reduce these burdens, internationally recognised algorithms have been developed in almost all areas of stroke, leading to improvements in the standard of care – with one noteworthy exception – post-stroke rehabilitation. In this field of stroke care such algorithms have either not yet been developed or been implemented or are still too heterogenous.

Even if quality indicators have been identified they have not been standardized in the same way as in acute stroke care. The following requirements still need to be widely implemented:

- Rehabilitation needs to be organized more centrally and equally across different centers
- Rehabilitation needs indicators to monitor the quality of care with regular benchmarking
- Stroke rehabilitation needs detailed and practical guidelines for each type of treatment, including pharmacological support

In this context the EAN & EFNR Guideline on Pharmacological Support in Early Motor Rehabilitation of 2021 and other new guidelines on motor recovery will be briefly discussed.

At the end of this presentation a short excursion will be made into the orphan drug indication CADASIL (Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy) for which Cerebrolysin received an FDA orphan drug designation several years ago. At our centre in Prague we started the clinical development in this indication and will introduce briefly the trial protocol and the hypothesis why Cerebrolysin may be beneficial for CADASIL patients.

LECTURE SUMMARY

Professor Dr. Ales Tomek from the Motol Hospital in Prague, Czech Republic, pointed out that standardisation of care in post-stroke rehabilitation lags far behind acute care. While there are generally accepted algorithms for acute stroke treatment, these are still lacking for neurorehabilitation and for life after stroke *(figure 9)*.

Quality measures of clinical success are also urgently needed for stroke rehabilitation, such as a shorter "door to needle" time in acute care *(figure 10)*.

He also recalled the EAN/EFNR guideline recommendations for post-stroke rehabilitation and the rigorous evaluation process that led to the recommendation of Cerebrolysin in stroke rehabilitation *(figure 11)*.

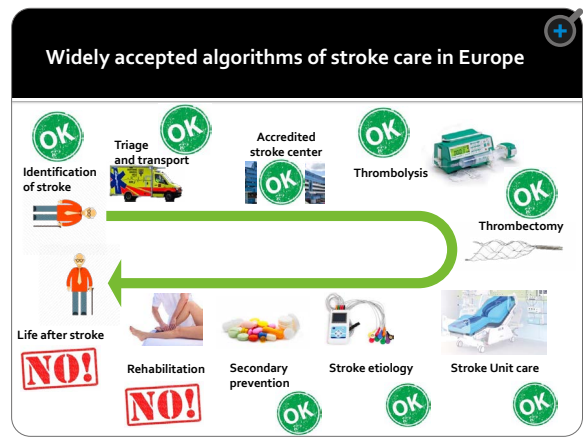

Figure 9

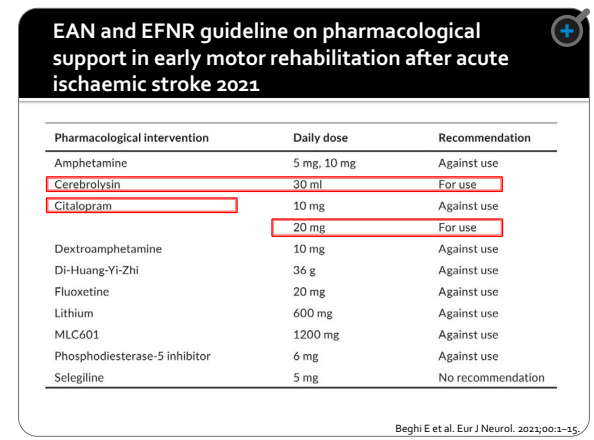

Figure 11

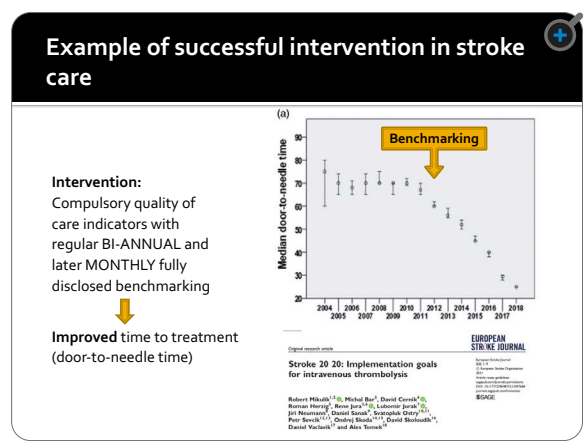

Figure 10

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Moderator:
Maciej Niewada (PL)

Experts:
Ales Tomek (CZ), Won-Seok Kim (KO), Jacek Staszewski (PL), Valeria Caso (IT), Rich Leigh (USA)

Expert Panel Discussion – Stroke Guidelines

LECTURE SUMMARY

The ensuing panel discussion, moderated by Dr Maciej Niewada from Warsaw, Poland, was lively and included many questions from the audience. It set the scene for the next three sessions.

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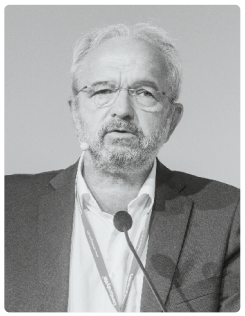


Helmut Trimmel

General Hospital of Wiener Neustadt,
ÖAMTC Air Rescue, Vienna
Danube Private University, Krems
Austria

Acute care of patients with severe traumatic brain injury

ABSTRACT

Severe traumatic brain injury (sTBI) represents an individual as well as a socioeconomic catastrophe and results in a diminished quality of life through impaired motor, cognitive, and emotional functioning.

In addition to the primary injury, secondary brain damage plays an important role: release of excitotoxic amino acids, neuroinflammation, oxidative stress with subsequent lipid peroxidation, disruption of the blood-brain barrier, brain swelling, disturbed cell metabolism and apoptosis are main factors. Both pre-hospital and early-hospital care are crucial for prognosis.

Avoidance of hypoxia, hypercapnia and hypotension is of paramount importance. Maintaining a systolic blood pressure of ^{3} 120 mm Hg, comprehensive airway management and adequate ventilation are essential components of EMS care. Transport to a Level I trauma center should be by helicopter. Treatment must follow algorithms defined here; Initial diagnostic imaging, ideally using a sliding gantry, must include angiographic imaging of the cerebral and cervical vessels.

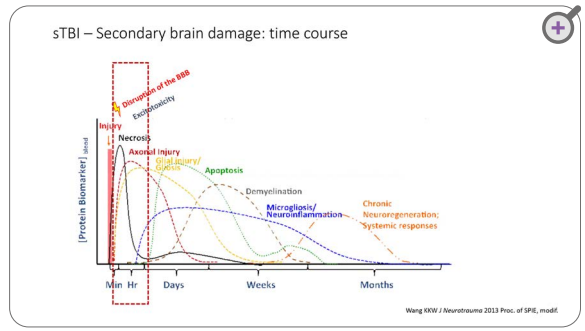
Surgical care must be performed immediately whenever needed. Treatment in the ICU must strictly follow guidelines (BTF, SIBICC recommendations) to maintain cerebral perfusion pressure > 65 mmHg, minimize brain oxygen demand, and maintain whole-body metabolic homeostasis.

Neuroprotective drugs can already support in the early stages: Recent data show their neuroprotective and neurotrophic properties as well as improved neurocognitive outcomes. Of particular note here are Cerebrolysin, citicoline, but also amantadine, ketamine, magnesium and statins. However, these drugs can only be part of a comprehensive treatment plan for sTBI patients, which also includes rehabilitation measures as early as possible.

LECTURE SUMMARY

Professor Dr. Helmut Trimmel, Head of Anaesthesiology at Wiener Neustadt Regional Hospital, presented the main treatment options in the pre-hospital phase following traumatic brain injury. He described the development of secondary damage *(figure 12)* and the experience of treating such damage with Cerebrolysin *(figure 13)*. In the last part of his lecture, Professor Dr. Trimmel presented his clinic's standard TBI treatment concept, which was developed by him and his team and includes Cerebrolysin. Remarkable cases of neurorecovery after TBI using this treatment concept have recently been published (https://doi.org/10.1002/ccr3.6626) and were presented in this lecture.

His "take home" messages were very clear and to the point and can be read on the last slide *(figure 14)*.



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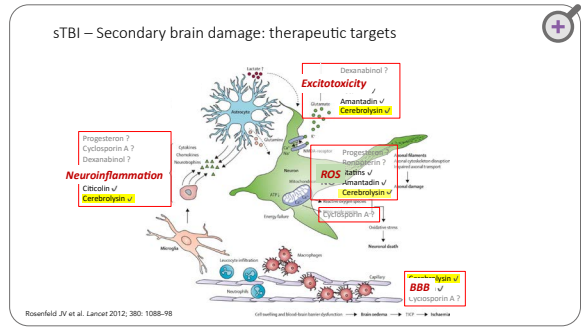


Figure 13

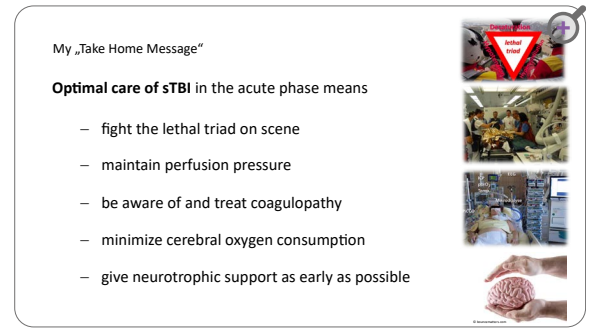
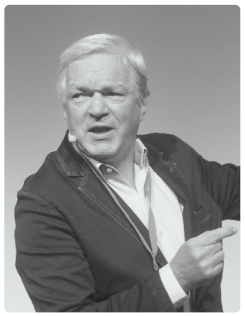


Figure 14



Christian Matula

Neurosurgical Department,
Medical University of Vienna
Vienna, Austria

The CAPTAIN's Tale – The story of an unbelievable TBI Trial

ABSTRACT

Traumatic Brain Injury (TBI) is an undisputed and fundamental problem worldwide.

The majority of TBI trials failed and ended up mostly as a nightmare. Cerebrolysin as a pharmacological agent has created over the time a light at the horizon. This presentation tells the story of the Captain-Trial with all its ups and downs from its beginnings to newly designed clinical research we have achieved until today. The story of an unbelievable TBI trial, trying to make the impossible possible, opening the door widely to new styled TBI trials.

As all good tales, it starts with a "Once upon a time". In the 50/60ies TBI was seen as a pure surgical disease. Craniotomy for evacuation of hematomas was the only modality available for the reduction of intracranial pressure (ICP). Nowadays, after an explosion of new insights in TBI research has driven this paradigm shift on the physiology of healthy and injured brains. Today it is clearly seen as a cyto-pathological disease! Neurotrophic factors are the most important endogenous molecules involved in brain protection and recovery and they can switch DNA programs. Cerebrolysin is the only drug available on the market for clinical use containing active fragments of some important neurotrophic factors.

The Captain trial (Cerebrolysin Asian Pacific Trial in Acute Brain Injury and Neurorecovery) is a randomized, double-blind, placebo-controlled trial to investigate safety and efficacy of Cerebrolysin in patients with traumatic brain injury. The trial was designed to investigate the clinical effects of Cerebrolysin in the acute phase (neuroprotective strategy) as well as during the phases of early, long-term and overall recovery (neurorestorative strategy).

The CAPTAIN trial has been the first TBI trial with a ''true'' multidimensional approach based on full outcome scales while avoiding previous weaknesses, such as loss of information through 'dichotomization', unrealistic assumptions such as ''normal distribution,'' or bias by insensitivity to outcome clusters. Within the global outcome analysis, the cognitive assessments demonstrated highly significant results and may be a door opener for future guideline inclusions. Global Outcome in particular, Captain Cognition Scales could be proven to be particularly highly significant and the results served as a „door opener" for all future guideline inclusions!

We are currently living in a very depressive time and age; post-treatment depression is a previously neglected problem, even in various cerebrovascular emergencies! For most of the specialists in Neurosurgery, but also Neurology not so much in the foreground, but a real problem for the patient himself.

Today we can say, that the results from the Captain study significantly helped to optimize treatment concepts in any kind of cerebrovascular emergency based on a multidisciplinary team approach.

LECTURE SUMMARY

Professor Dr. Christian Matula from Neurosurgica Department, Medical University of Vienna highlighted the role of EVER Pharma as one of the few companies in the world conducting research in this indication and the only one doing so successfully. He presented the clinical development of Cerebrolysin in neurotrauma, in particular the design and statistically significant results of the CAPTAIN study *(figure 15)*.

He also spoke powerfully about his own experience as a neurosurgeon and how his involvement in the CAPTAIN study made him realise the importance of diagnosing and treating the cognitive and psychiatric sequelae of neurotrauma *(figure 16)*. The CAPTAIN study showed a highly significant reduction in depression in the group of patients treated with Cerebrolysin.

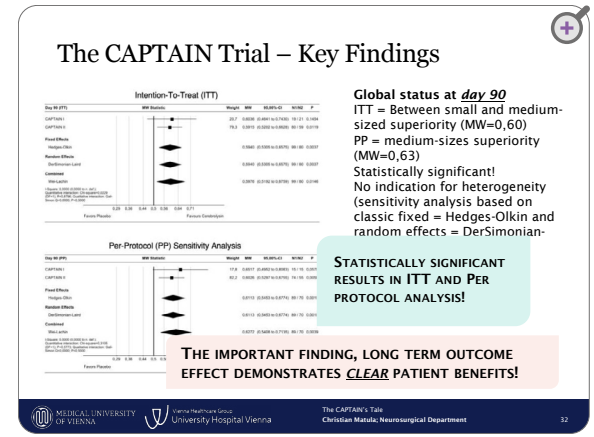


Figure 15

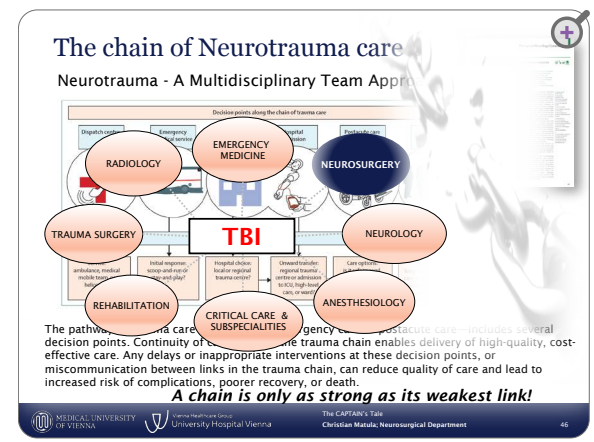


Figure 16

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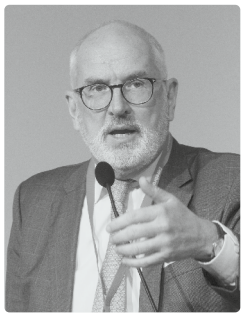

Eugen Trinka

Neurology Department,
Universitätsklinik für Neurologie
Salzburg, Austria

Post-TBI seizures and epilepsy

ABSTRACT

At least 2 to 15% of patients with moderate to severe traumatic brain injury (TBI), will suffer from acute symptomatic seizures. Most studies report figures between 2 and 5%. Half of these acute symptomatic seizures occur in the first 24 hours and rates of Status Epilepticus vary between 0.2 and 5%. Acute symptomatic seizures in TBI are associated with an increased mortality, with an increased risk for the development of posttraumatic epilepsy, and with a poor functional outcome.

There is more than 50 years of clinical research in preventing acute symptomatic seizures and its sequelae, especially posttraumatic epilepsy. With our currently available antiseizure medicines, we can significantly lower the risk of early posttraumatic seizures occurring in the first seven days after injury, but these treatments have no significant effect on the risk of late posttraumatic seizures.

Unfortunately, antiseizure medicines are not without any harm, especially on neurocognitive and rehabilitation outcome, independent of the onset of epilepsy.

There is significant clinical variability in the current practices of pharmacological management of acute posttraumatic seizures in adults across the globe.

Despite major advances in epidemiology and pathophysiology, some questions still remain unanswered: What is the significance of small posttraumatic MRI-abnormalities? What is the significance of ictal EEG-abnormalities and non-convulsive seizures and Status Epilepticus? Are mild TBI's at all associated with epilepsy? What is the influence of antiseizure medicines on recovery and long-term outcome? Only sound clinical trials can answer these questions and there is enough evidence to design such.

LECTURE SUMMARY

Professor Dr. Eugen Trinka from the Department of Neurology, Christian Doppler Medical Centre, Salzburg, Austria, presented the latest findings on the management of epilepsy and seizures, very common complications following TBI. This was followed by the current definitions of early and acute or late and remote post-traumatic seizures (PTS) *(figure 17)* and the risks of early seizure onset *(figure 18)*. In patients with moderate to severe TBI, essentially the population of the CAPTAIN study, about 3-5% of patients experience seizures, 50% of them within the first 24 hours.

Prof Dr Trinka presented the performance of various drugs in preventing PTS *(figure 19)* and pointed out that existing guidelines for the prevention and treatment of seizures are poorly followed.

He concluded that, overall, the evidence on the prevention and possible sequelae of early PTS in TBI is still too limited *(figure 20)*.

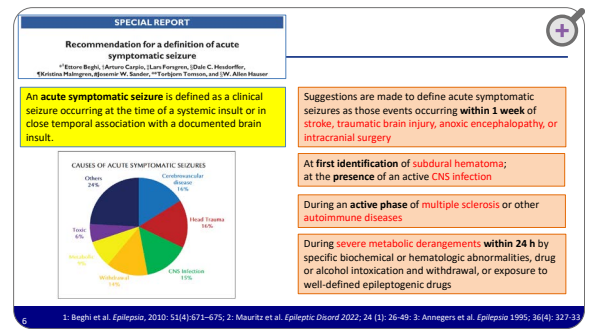

Figure 17

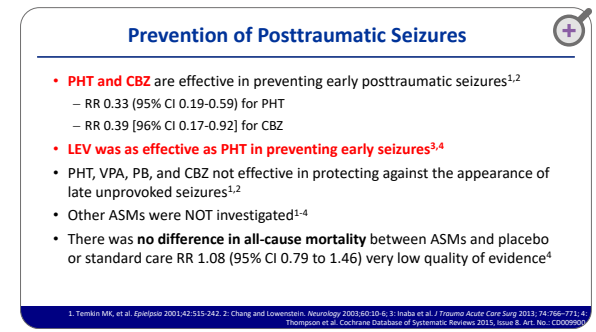

Figure 19

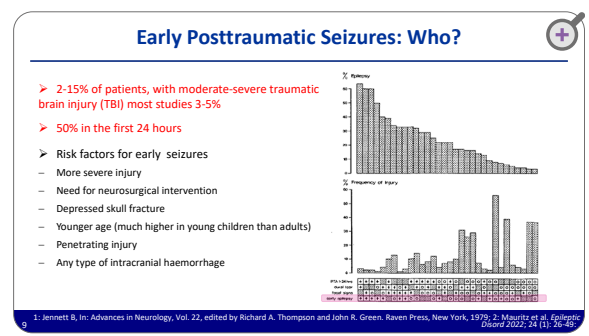

Figure 18

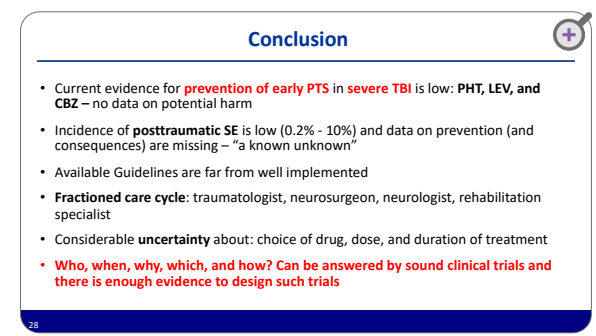

Figure 20

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Andreas Winkler

Institut Neuromed
Korneuburg, Austria

The Role of Non-Invasive Brain Stimulation in Neurorehabilitation

ABSTRACT

The field of neuromodulation encompasses a wide spectrum of distinct and innovative technologies that modify neuronal and neuronal-network activity within the brain and nervous system.

The primary goal is set to achieve a measurable therapeutic and clinical effect with the least possible side effects and within a reasonable range of costs. Available therapies including deep brain stimulation (DBS), vagal nerve stimulation (VNS), intracranial cortical stimulation (ICS), transcranial direct current stimulation (tDCS), and transcranial magnetic stimulation (TMS) have all shown promising results across a range of neurological and neuropsychological disorders.

In general, NIBS techniques use electrical and, or magnetic energy to induce changes in excitability of the underlying brain cortex in a non-invasive fashion and potentially induce long-lasting neuroplastic changes in the sense of long-term potentiation or long-term depression.

Especially rTMS and tDCS have been increasingly used in neurorehabilitation in recent years. TMS can be either used as diagnostic tool to learn about brain function and to reveal mechanisms of brain function, or rTMS and tDCS can alternatively be used as therapeutic tools to modulate brain function and to improve behavior (language, sensation, cognition, motor function etc.).

In my talk I will give a comprehensive overview of technical prerequisites, different protocols of NIBS and it´s clinical usefulness in rehabilitation-therapy.

LECTURE SUMMARY

Dr. Andreas Winkler from the Neuromed Institute in Korneuburg , Austria, presented the scientific basis of neuronal repair and the latest findings on non-invasive brain stimulation (NIBS) *(figure 21)*. Of particular importance is a sensitive post-ischemic time window that can be exploited for neuromodulation treatment *(figure 22)*.

In particular, his research focuses on transcranial direct current stimulation (tDCS) in chronic stroke patients, in which weak electrical currents stimulate synaptic plasticity in the relevant target regions of the brain to improve motor function.

Finally, he presented his concept of triple therapy consisting of physiotherapy, tDCS and Cerebrolysin. The results of a pilot study with 44 chronic stroke patients are already very promising *(figure 23)*.

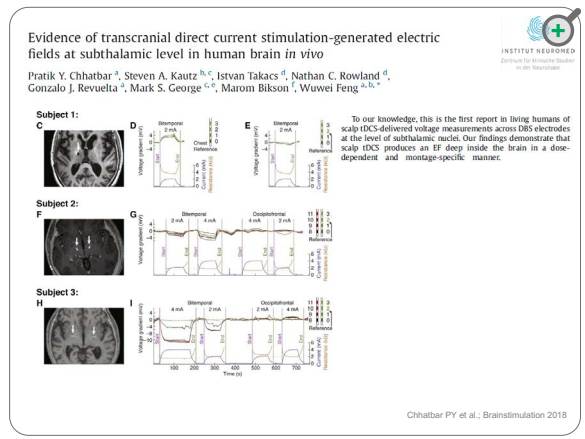

Figure 21

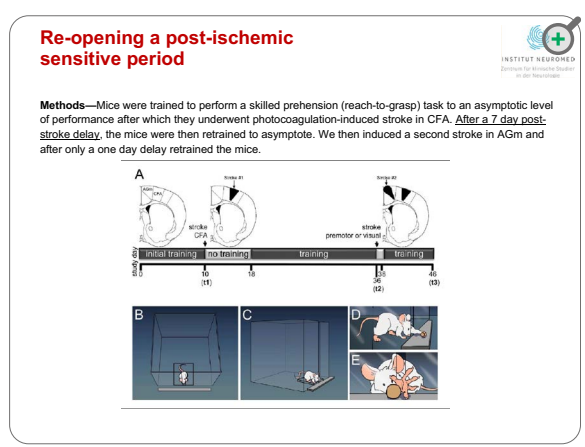

Figure 22

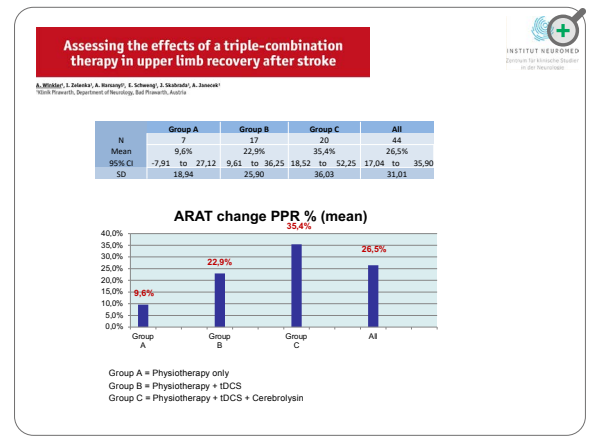

Figure 23

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Katrin Rauen

Neurological Rehabilitation Center Godeshöhe GmbH
Bonn, Germany

Head trauma & Depression

ABSTRACT

Traumatic brain injury (TBI) is a major global health burden and affects predominantly the frontal lobes with relevant neuropsychiatric sequels including cognitive, sleep, and affective dysfunctions. These symptoms tridirectionally influence each other, and hamper complete recovery with up to half of patients suffering from depressive disorder after TBI.

However, TBI rehabilitation primarily targets physical outcome with unmet psychiatric treatment needs across Europe. Thus, it is time to improve psychiatric diagnostics and treatment in post-TBI care.

Here, we outline

- the clinical picture of post-TBI in comparison to post-stroke depression,
- the diagnostic relevance of screening the TBI patient's disease-specific and health-related quality of life (HRQoL) to identify the risk of a depressive disorder early,
- the frontal lobe dysfunction with challenges and pitfalls of psychiatric diagnostics in TBI patients,
- the non-pharmacological and pharmacological treatment of post-TBI depression, and
- future perspectives for TBI research and clinical practice to overcome the current lack of psychiatric diagnostics and treatment after TBI.

LECTURE SUMMARY

Dr Katrin Rauen Neurological Rehabilitation Center Godeshöhe GmbH, Bonn, Germany, spoke about post-traumatic depression and the importance of assessing quality of life after trauma. She presented the relationship between brain regions, neuronal circuits and associated responses in brain areas associated with anxiety or PTSD *(figure 24)*.

She pointed out that health services around the world do not diagnose or treat post-TBI problems such as cognitive deficits, depressive and other psychiatric disorders sufficiently. Research statistics show that there are ten times more clinical research projects on depression after stroke than on depression after TBI, resulting in a lack of long-term follow-up for TBI patients *(figure 25)*.

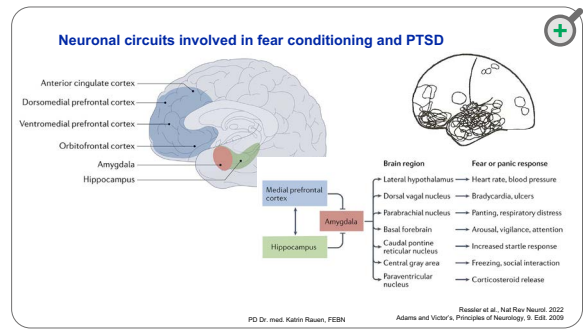

Figure 24

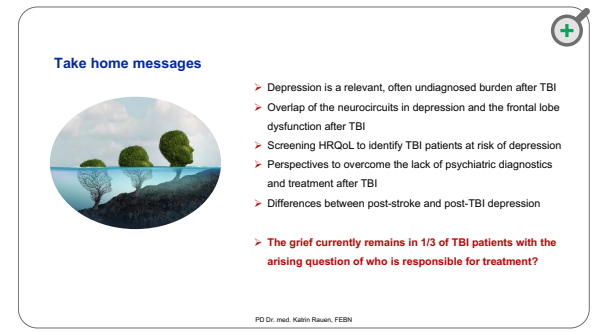

Figure 25

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Wojciech Dabrowski

First Department of Anaesthesiology and
Intensive Therapy Medical University of Lublin
Lublin, Poland

The devil called delirium is not so dangerous when treated with Cerebrolysin

ABSTRACT

Delirium is an acute alteration in mental status characterized by confusion, inattention and a fluctuating level of arousal. It is a serious clinical problem that is associated with prolonged hospital stay and an increased risk of mortality.

The pathomechanisms of delirium are not well recognized, however a disturbance in the cholinergic system, dopamine synthesis, neuronal plasticity, inflammation and oxidative stress following cerebral ischemia or hyperoxia appear to play a key role in this process.

Cerebrolysin improves neuronal plasticity, attenuates post-ischemia disorders, improves cholinergic activity and attenuates post-ischemic disorders reducing the severity of oxidative stress. Hence, it may be useful in prevention and treatment of delirium. A single-center study documented that Cerebrolysin significantly reduces the risk of postoperative delirium in cardiac surgery patients.

Additionally, use of Cerebrolysin significantly improves neuropsychological outcome in septic shock patients, reducing the risk of delirium and subsequently the length of stay in the intensive care unit.

Based on these results, Cerebrolysin can be suggested as an effective drug in prevention and treatment of delirium in critically ill patients.

LECTURE SUMMARY

Dr. Wojciech Dabrowski from the Medical University of Lublin, Poland, discussed the medical problem of delirium, its many risk factors and how it could be better managed through the use of Cerebrolysin. Approximately half of cardiac surgery patients and half of critically ill patients in intensive care units are affected by delirium. The strong correlation between the pathomechanisms of delirium and the mechanism of action of Cerebrolysin *(figure 26)* prompted Dr. Dabrowski to gain his own experience with Cerebrolysin. The results obtained showed a clear advantage over the current standard of care *(figure 27 and 28)*, but further studies are needed to confirm these initial results. This concluded the neurotrauma session.

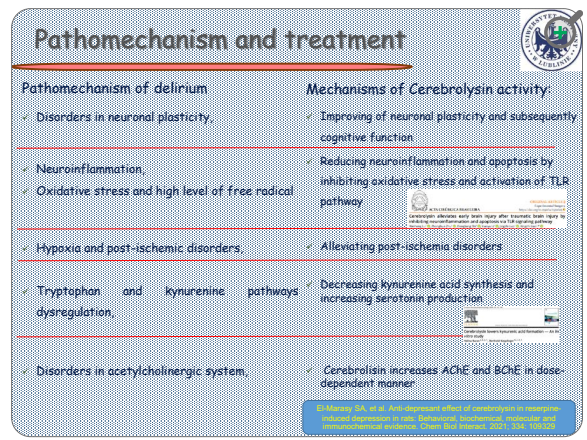

Figure 26

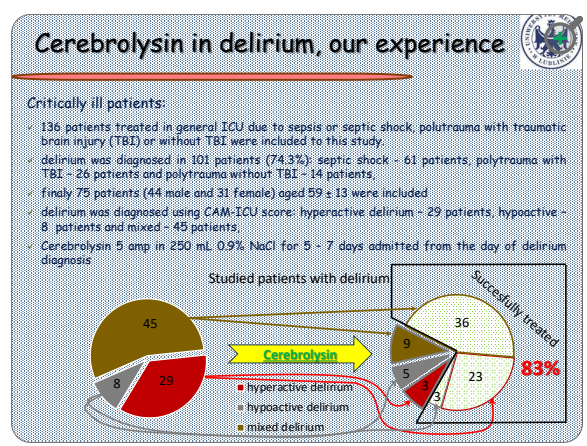

Figure 27

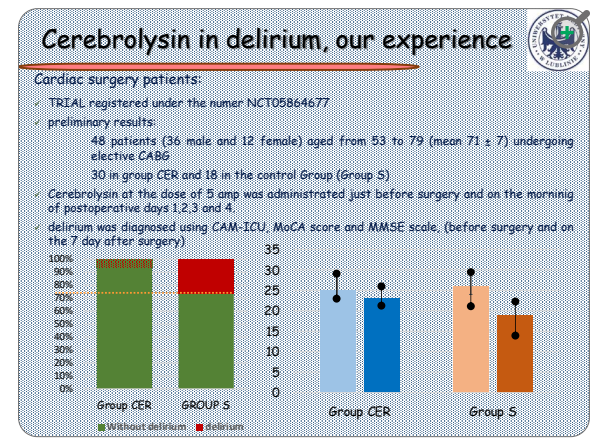

Figure 28

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Dafin Muresanu

Chairman Department of Neurosciences,
University of Medicine and Pharmacy 'Iuliu Hatieganu'
Cluj-Napoca, Romania

Closing & Perspectives for the future

To conclude the 27th IMMM, Professor Dr. Dafin Muresanu spoke about the concept of brain reserve *(figure 29)*, its quantification and improvement. He also presented the first results of a new clinical trial which showed that the combination of speech therapy and Cerebrolysin produced a statistically significant improvement in AIS patients *(figure 30)*. Publication is expected in the first half of 2024.

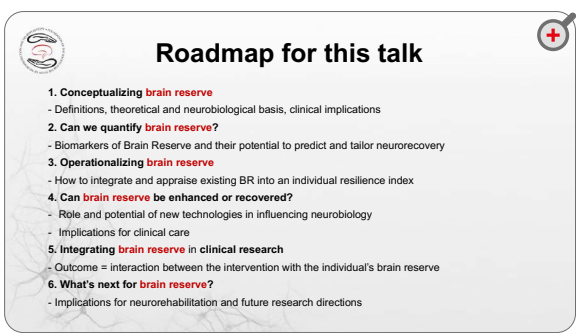

Figure 29

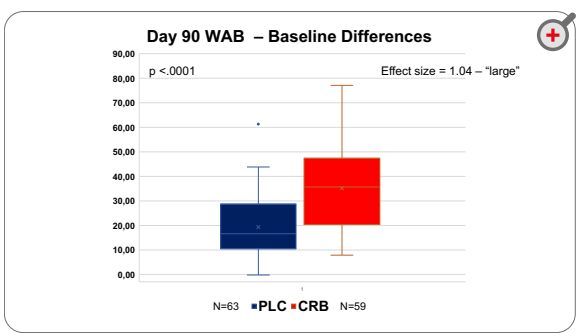

Figure 30

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ABBREVIATED PRESCRIBING INFORMATION. Name of the medicinal product: Cerebrolysin - Solution for injection. Qualitative and quantitative composition: One ml contains 215.2 mg of Cerebrolysin concentrate in aqueous solution. List of excipients: Sodium hydroxide and water for injection. Therapeutic indications: For treatment of cerebrovascular disorders. Especially in the following indications: Senile dementia of Alzheimer's type. Vascular dementia. Stroke. Craniocerebral trauma (commotio and contusio). Contraindications: Hypersensitivity to one of the components of the drug, epilepsy, severe renal impairment. Marketing Authorisation Holder: EVER Neuro Pharma GmbH, A-4866 Unterach. Only available on prescription and in pharmacies. More information about pharmaceutical form, posology and method of administration, special warnings and precautions for use, interaction with other medicinal products and other forms of interaction, fertility, pregnancy and lactation, effects on ability to drive and use machines, undesirable effects, overdose, pharmacodynamics properties, pharmacokinetic properties, preclinical safety data, incompatibilities, shelf life, special precautions for storage, nature and contents of the container and special precautions for disposal is available in the summary of product characteristics.

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