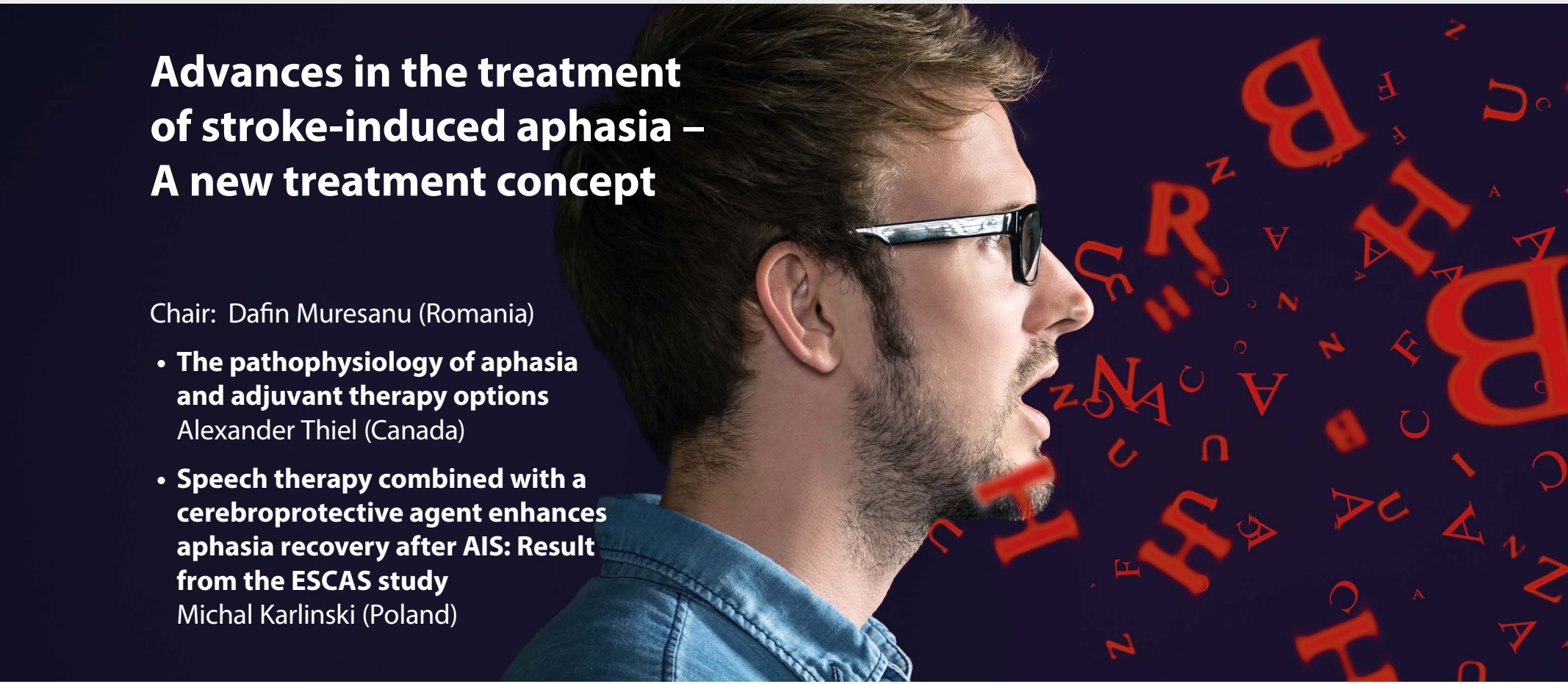
EVER PHARMA

ESOC 2024

ESOC Symposium Report | 15 May 2024 | Auditorium Montreal, Canada

Advances in the treatment of stroke-induced aphasia – A new treatment concept



Chair: Dafin Muresanu (Romania)

- **The pathophysiology of aphasia and adjuvant therapy options**
  Alexander Thiel (Canada)
- **Speech therapy combined with a cerebroprotective agent enhances aphasia recovery after AIS: Result from the ESCAS study**
  Michal Karlinski (Poland)

Advances in the treatment of stroke-induced aphasia – A new treatment concept

In mid-May, the European Stroke Organisation Congress (ESOC) 2024 in Basel provided a platform for intense discussions and the exchange of ideas with leading physicians and researchers in the field of stroke.

At the EVER symposium during the European Stroke Organisation Congress (ESOC) 2024, groundbreaking new data in the field of aphasia were presented by Prof. Alexander Thiel and Dr. Michal Karlinski, moderated by Prof. Dafin Muresanu.

Aphasia, a language disorder caused by stroke, affects millions of people worldwide. Presenting positive research results at the ESOC Congress offered an opportunity to share the latest insights and advances in aphasia treatment and to gain valuable perspectives into future developments.

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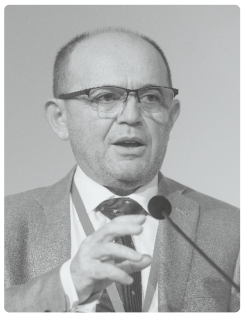


Dafin Muresanu

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

President of the European Federation of
NeuroRehabilitation Societies (EFNR)

Introduction

Prof. Muresanu began his introduction by commenting that ESOC focuses increasingly on new concepts in stroke treatment and particularly on rehabilitation after a stroke. Neurological disorders are the leading cause of disability worldwide and the second leading cause of death. Rehabilitation is a multimodal intervention encompassing the body, mind, and emotional health. There are different phases of recovery after a stroke: hyperacute, acute, early and late subacute, and chronic phases. *(figure 1)*

Combined therapies, involving both physical and pharmacological approaches, are the most promising, in particular Cerebrolysin as it has been recommended in various international guidelines already. *(figure 2)*

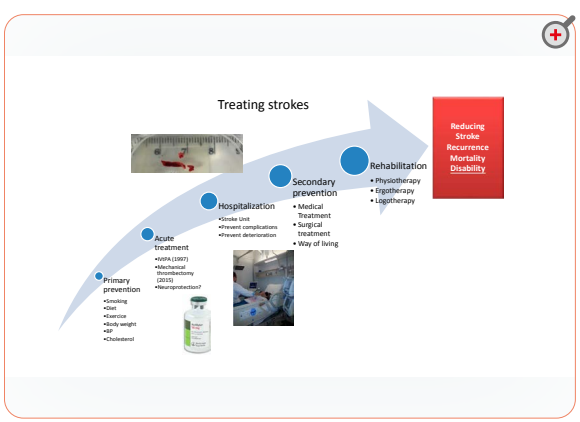
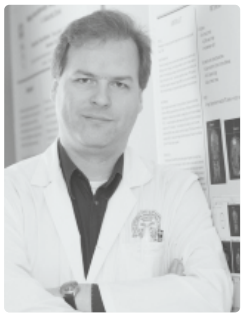


Figure 1

Figure 2



Alexander Thiel

Prof. Dr. med.
McGill University Jewish General Hospital,
Montréal, QC, Canada

The pathophysiology of post-stroke aphasia and adjuvant therapy options

ABSTRACT

Aphasia affects 15% to 40% of patients with acute stroke and independently predicts prolonged hospitalization and poor outcome. Speech therapy (ST) is the mainstay of aphasia treatment and therefore constitutes the recommended rehabilitation approach to aphasia after stroke. However, the intensity of ST provided in usual care settings is likely insufficient to achieve significant treatment effects on the language deficit beyond spontaneous recovery. In this talk we will review the physiological rationale for pharmacological and non-pharmacological (i.e. non-invasive brain stimulation) adjuvant treatments to augment the effects of ST on the recovery of language function after stroke.

SUMMARY OF THE PRESENTATION

Alexander Thiel began his talk by acknowledging the devastating impact aphasia can have on stroke survivors. He emphasized the importance of addressing this issue and gave an overview about different treatment options. *(figure 3)*

The primary treatment for aphasia remains traditional speech and language therapy (SLT), which aims to reactivate language networks in the brain that have been compromised by a stroke. Thiel explained that SLT targets these disrupted speech networks during therapy sessions. The success of SLT depends on the sensory-motor learning and retention achieved during these sessions, as it is crucial that the benefits of one session carry over to the next one in order to achieve a positive outcome long-term.

Pharmacotherapy is an important adjuvant treatment option to enhance neuroplasticity and brain perfusion. Thiel details several drugs that have been studied in this context.

- Piracetam, , has shown some promise in improving language networks when combined with SLT, though large-scale evidence is still inconclusive.
- Memantine, an NMDA receptor antagonist, demonstrated short-term benefits in some trials but requires further extensive trials for validation.
- Donepezil, used for Alzheimer's treatment, could potentially aid in aphasia therapy due to its effects on learning and memory retention, but robust trial evidence is lacking.
- Dopamine agonists such as Bromocriptine and Levodopa have produced mixed results in trials and have not consistently shown effectiveness.
- Amphetamines, intended to improve attention during SLT sessions, have not demonstrated sustained therapeutic effects and face concerns over potential side effects.

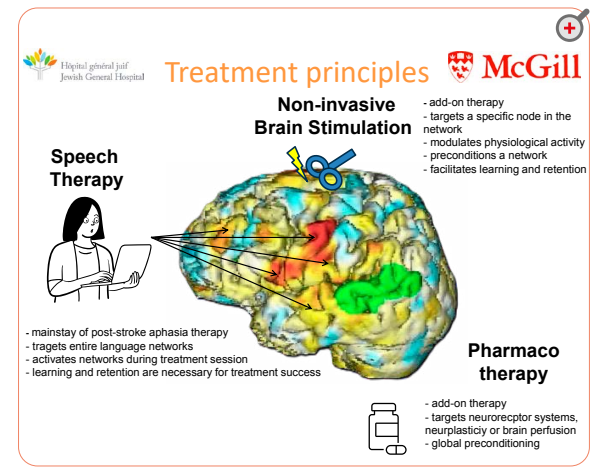


Figure 3

In summarizing pharmacotherapy, Thiel notes that no drugs currently have regulatory approval specifically for post-stroke aphasia, and their use remains off-label. *(figure 4)*

Thiel also provided an overview of non-pharmacological approaches, primarily focusing on non-invasive brain stimulation. He explains that rTMS and tDCS can be effective when applied in the early subacute phase. Contralesional inhibitory stimulation, which suppresses the right hemisphere, shows positive results during this phase but not in the chronic phase. Ipsilesional excitatory stimulation, targeting the left hemisphere, has shown potential in some trials but requires further investigation. *(figure 5)*

In his overall takeaway message, Thiel asserts that speech and language therapy is essential and proven effective for aphasia treatment. Non-invasive brain stimulation holds promise but needs further regulatory trials to establish its efficacy. Pharmacotherapy currently lacks strong evidence, though ongoing research may bring future breakthroughs.

Thiel concluded on a cautiously optimistic note, expressing hope that future studies, will provide more definitive answers and improvements in the field of aphasia treatment.

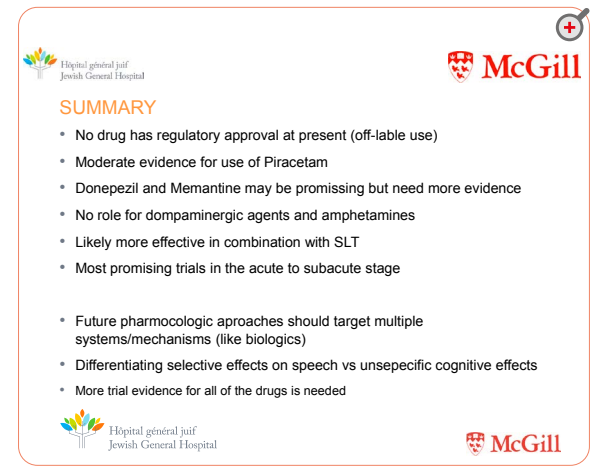


Figure 4

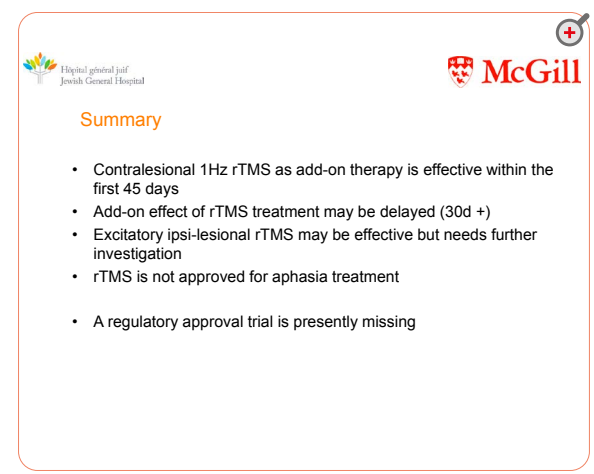


Figure 5

Michal Karlinski

MD, PhD
Institute of Psychiatry and Neurology,
Warsaw, Poland

Speech therapy combined with Cerebrolysin enhances aphasia recovery after acute ischemic stroke

ABSTRACT

Background: Despite increasing access to standard speech and language therapy (SLT), post-stroke aphasia significantly affects the quality of life of each patient and remains a major cause of long-term disability. Cerebrolysin, a neuroprotective and neurotrophic agent, has shown benefit as an addition to intensive rehabilitation in patients after moderate-to-severe strokes manifesting as right upper limb paresis combined with aphasia. The aim of this study was to evaluate the efficacy of Cerebrolysin as an addition to SLT in treating post-stroke aphasia.

Methods: The ESCAS trial was a randomized, controlled, double-blind phase 4 study conducted in two Romanian stroke centers. It included right-handed patients with the first-ever left middle cerebral artery territory ischemic stroke resulting in Broca or mixed non-fluent aphasia. Beginning 3 to 5 days after the onset, patients were treated with Cerebrolysin 30 or placebo in addition to intensive SLT delivered in three 10-day cycles in two-week intervals. The primary outcome measure was improvement at day 90 in the Western Aphasia Battery (WAB).

Results: Of 132 enrolled patients, 123 were included in the Intention-To-Treat analysis. Patients from the Cerebrolysin group had a significantly larger improvement of aphasia (+36 vs +17 WAB points, $p<.05$) and more frequently achieved excellent functional outcome (44.8% vs 29.1% of patients with modified Rankin Scale score 0 to 1 point, $p<.05$). Safety analysis raised no concerns.

Conclusions: The addition of Cerebrolysin to SLT shows a promising potential for enhancing recovery in post-stroke aphasia. However, further studies are needed to confirm the efficacy of this combination therapy.

SUMMARY OF THE PRESENTATION

In his lecture, Karlinski discussed the results of the ESCAS (**E**fficacy and **S**afety of **C**erebrolysin in **A**phasia after AI**S**) study, emphasizing the need for effective treatments that can improve rehabilitation outcomes for stroke patients, especially those suffering from aphasia. He acknowledged the complexity of aphasia manifestations and their profound impact on patients' lives, leading to communication difficulties, social isolation, frustration, and depression.

The ESCAS study is a prospective, randomized, controlled, double-blind trial that assesses the efficacy and safety of combining Cerebrolysin with speech and language therapy, compared to a placebo combined with the same therapy, in treating non-fluent aphasia following an acute ischemic stroke. *(figure 6)*

The study includes right-handed patients with ischemic stroke in the left-middle cerebral artery territory, and who had no previous stroke or severe comprehension deficits. They were enrolled three to five days after the onset of symptoms. *(figure 7)*

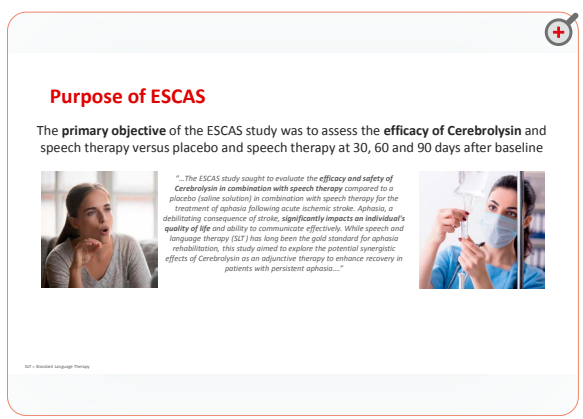


Figure 6

The intervention involves administering Cerebrolysin combined with one hour of speech and language therapy daily for 10 days, in three cycles, interspersed with breaks, and comparing it to a placebo with the same therapy regimen.

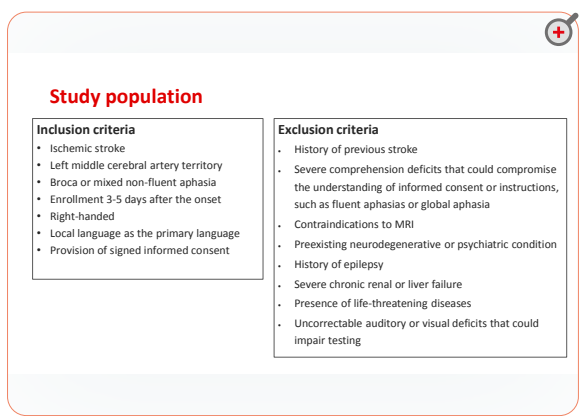


Figure 7

The primary outcome measure is the Western Aphasia Battery (WAB), with secondary measures including the NIH Stroke Scale (NIHSS), Barthel Index, and modified Rankin Scale (MRS).

The results show that both the treatment and control groups improve over time, but the Cerebrolysin group consistently shows significantly greater improvement in WAB scores at days 30, 60, and 90. Patients in the Cerebrolysin group improved from severe to mild aphasia, while the placebo group showed less pronounced improvement. *(figure 8)*

Similar trends were observed in NIHSS and Barthel Index scores, with the Cerebrolysin group demonstrating greater benefits. Importantly, a significantly higher percentage of patients in the Cerebrolysin group achieved an MRS score of 0-1 at day 90, indicating a significantly better overall recovery. *(figure 9)*

Karlinski concluded that the combination of Cerebrolysin with intensive speech and language therapy appears to be a safe and effective treatment for improving both neurological and functional outcomes in stroke patients with non-fluent aphasia. He emphasized the importance of combining the drug with intensive rehabilitation and suggested that further studies are needed to confirm these findings in other populations.

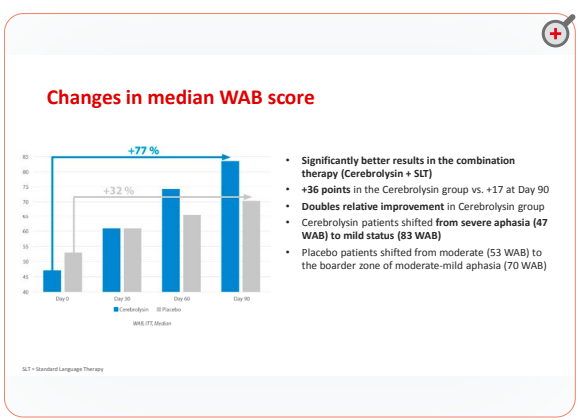


Figure 8

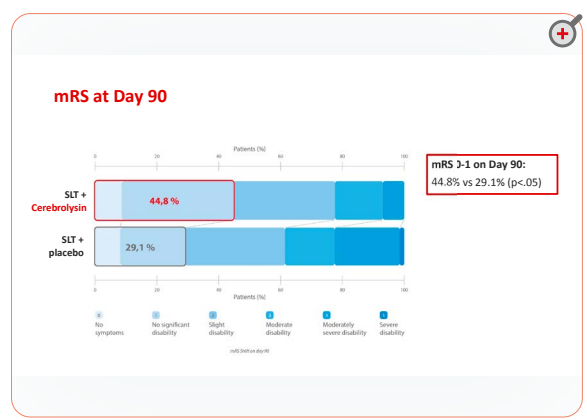


Figure 9

Summary

Combination treatments including **Cerebrolysin** improve post-stroke complications!

The ESCAS results indicate that **Cerebrolysin** could be a valuable addition to rehabilitation strategies for stroke patients whose aphasia does not resolve within the first few days post-stroke.

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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