



Title: Pharmacological support with multimodal and monomodal drugs in brain neurorestoration and neurorehabilitation

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Abstract:

Over the last decades, therapeutic approaches for stroke have significantly evolved and improved as a consequence of the implementation of modern stroke units, improvement of general medical care and more structured and early administered rehabilitation schemes. Thrombolytic therapy with rt-PA (recombinant tissue plasminogen activator) has been developed and a number of clinical trials have recently confirmed the effectiveness of thrombectomy to be better than rtPA alone. Except thrombolytic therapy and thrombectomy there is still no widely accepted therapy for acute ischemic stroke.

Current data shows that even if advanced procedures can be used, 60% of stroke patients die or remain with a certain level of deficit. As it is widely accepted that immobilization-related complications cause over 50% of stroke patients' deaths, rehabilitation plays an important role in stroke care.

It is getting clearer that multimodal drugs may play an important role in pharmacological support of neurorehabilitation after stroke. The results of recently published large and well-controlled clinical studies show a positive effect of Neurotrophic factors on neurological recovery after acute ischemic stroke.

The CARS study assessed the efficacy and safety of Neurotrophic factors in combination with a standardized rehabilitation program. The primary study endpoint was the Action Research Arm Test (ARAT) at day 90, assessing upperlimb motor functions. Neurotrophic factors was administered for 21 days, starting within 48-72 hours after ischemic stroke. The study showed a statistically significant group difference in the upper-limb motor function (ARAT) at day 90 – primary end point. Neurotrophic factors was also superior over placebo in most of the secondary endpoints like the NIHSS, Barthel Index and mRS. Also, at day 90, patients treated with Neurotrophic factors showed less depressive symptoms and better quality of life. In addition, the most important measure for early benefit, the NIHSS at day 21, showed statistically significant superiority of Neurotrophic factors. Analysis of the safety parameters did not show any clinically statistical significant differences between the treatment groups. The trial indicates that early combination of rehabilitation with a multimodal medication of neuroprotective and recovery properties is a valid therapeutic approach.

Furthermore, CARS 1 and CARS 2 meta-analysis provides evidence that Neurotrophic factors has a beneficial effect on motor function recovery in early rehabilitation patients after stroke. All pre-planned primary meta-analytic results were statistically significant.