



1. Neuropharmacology. 2010 Dec;59(7-8):640-9. Epub 2010 Aug 4.

Glial growth factor 2 promotes functional recovery with treatment initiated up to 7 days after permanent focal ischemic stroke.

Iaci JF, Ganguly A, Finklestein SP, Parry TJ, Ren J, Saha S, Sietsma DK, Srinivas M, Vecchione AM, Caggiano AO.

Acorda Therapeutics Inc., 15 Skyline Drive, Hawthorne, NY 10532, USA.
jjiaci@acorda.com

Comment in
Neuropharmacology. 2010 Dec;59(7-8):650-3.

Neuregulins are a family of growth factors essential for normal cardiac and nervous system development. The EGF-like domain of neuregulins contains the active site which binds and activates signaling cascades through ErbB receptors. A neuregulin-1 gene EGF-like fragment demonstrated neuroprotection in the transient middle cerebral artery occlusion (MCAO) stroke model and drastically reduced infarct volume (Xu et al., 2004). Here we use a permanent MCAO rat model to initially compare two products of the neuregulin-1 gene and also assess levels of recovery with acute versus delayed time to treatment. In the initial study full-length glial growth factor 2 (GGF2) and an EGF-like domain fragment were compared with acute intravenous delivery. In a second study GGF2 only was delivered starting at 24h, 3 days or 7 days after permanent ischemia was induced. In both studies daily intravenous administration continued for 10 days. Recovery of neurological function was assessed using limb placing and body swing tests. GGF2 had similar functional improvements compared to the EGF-like domain fragment at equimolar doses, and a higher dose of GGF2 demonstrated more robust functional improvements compared to a lower dose. GGF2 improved sensorimotor recovery with all treatment paradigms, even enhancing recovery of function with a delay of 7 days to treatment. Histological assessments did not show any associated reduction in infarct volume at either 48 h or 21 days post-ischemic event. Neurorestorative effects of this kind are of great potential clinical importance, given the difficulty of delivering neuroprotective therapies within a short time after an ischemic event in human patients. If confirmed by additional work including additional data on mechanism(s) of improved outcome with verification in other stroke models, one can make a compelling case to bring GGF2 to clinical trials as a neurorestorative approach to improving outcome following stroke injury.

PMID: 20691195 [PubMed - indexed for MEDLINE]