
To the Editor:

We read with great interest the study by Iwai et al,1 which reports increased oligodendrogenesis and recovery of neurological function by delayed and repeated administration of erythropoietin (EPO) after neonatal hypoxic–ischemic brain injury in rats. Since the first in vivo evidence of EPO-mediated neuroprotection against neonatal hypoxic–ischemic brain injury in 2003,2,3 many experimental studies have confirmed the efficacy of EPO in neonatal hypoxic–ischemic encephalopathy in rodents.4 Then, it was shown that EPO administration immediately after neonatal hypoxic–ischemic brain injury significantly improves long-term neurobehavioral outcomes and brain injury in rats when analyzed during the subsequent phase of brain maturation and even in adulthood.5 Finally, a recent clinical trial has shown that repeated administration of EPO reduces the risk of disability in newborns with moderate hypoxic–ischemic encephalopathy without apparent side effects.6 However, the mechanisms of the beneficial effect of EPO in hypoxic–ischemic encephalopathy are not fully elucidated.

Iwai et al,1 for the first time, report enhanced oligodendrogenesis and recovery of injured white matter (WM) as a novel mechanism by which EPO exerts its beneficial effect in hypoxic–ischemic encephalopathy. Although delayed administration of EPO does not decrease infarct volume, EPO-stimulated oligodendrogenesis and WM recovery are also correlated with the improvement of neurological functional outcomes. As the authors discuss, further studies are needed to clarify the exact mechanisms of oligodendrogenesis stimulated by EPO. Although oligodendrocytes and their progenitors and oligodendrocytes express EPO receptor,7,8 data are beginning to associate cell type-specific effects of EPO with the interactions between diverse receptors that lead to the activation of specific signaling pathways.9 Besides the classical EPO receptor, other receptors such as a heterodimer composed of EPO receptor with a common chain

Disclosures

None.

Acknowledgments

We thank Kemal Ugur Tufekci for critical reading of the manuscript for English.

Sermin Genc, Kursad Genc, Abdullah Kumral and Hasan Ozkan

Stroke. 2010;41:e595; originally published online September 30, 2010;
doi: 10.1161/STROKEAHA.110.590844

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/41/11/e595

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Stroke can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Stroke is online at:
http://stroke.ahajournals.org//subscriptions/