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The induction of TGF-βs in relation to immediate early genes following middle cerebral artery occlusion in rats

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Transforming growth factor βs (TGF-β1-3) form a small group of related proteins involved in the regulation of proliferation, differentiation, and survival of various cell types. TGF-β was suggested to be is neuroprotective because injection of TGF-β decrease, while injection of antagonist increased the infarct size. Previously, we described the expression of TGF-βs in the intact rat brain. In the present study, we induced focal ischemia using middle cerebral artery occlusion (MCAO) and examined the changes in the expression of TGF-β1, 2, and 3 using in situ hybridization histochemistry. All three types of TGF-βs were induced in neurons outside the infarct area. TGF-β1 showed elevated expression level in the penumbra around the lesion. The expression of TGF-β2 and 3 was increased in layers II, III, and V of the ipsilateral cerebral cortex. Subsequently, combinations of in situ hybridization histochemistry and immunolabeling was used to compare the distribution of TGF-βs with that of immediate-early genes Fos and activating transcription factor-3 (ATF-3). We demonstrated that TGF-β1 is co-localized with ATF-3 while TGF-β2 appears in Fos-expressing cells. In turn, these neurons did not contain Fluoro Jade C, a marker of neurodegenration. These observations suggest that endogenous TGF-β1 and TGF-β2 and 3 all participate in neuroprotection, although they are induced by different mechanisms following an ischemic attack.

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