（博士課程医学領域）　　（別記様式第５号）
（課程・論文博士共通）

論　文　内　容　要　旨

※ 整理番号		（ふりがな） 氏名（自署）	印
論文題目	Neuroprotective effects of neurotropin in a mouse model of hypoxic–ischemic brain injury （低酸素脳虚血マウスモデルにおけるノイロトロピンの脳保護作用）		

論文内容要旨

（研究の目的）

Ischemic–hypoxic insult leads to detrimental effects on multiple organs. The brain is especially vulnerable, and it is hard to regenerate once damaged. Currently, therapeutic options are very limited. Previous studies have reported neuroprotective effects of neurotropin, a non-protein extract derived from the inflamed skin of rabbits inoculated with vaccinia virus, using a murine model of peripheral nerve injury and cultured cell lines.

However, whether neurotropin might have protective effects against brain injuries remains unclear. We, therefore, investigated the neuroprotective effect of neurotropin and possible underlying mechanisms, using a mouse model of hypoxic–ischemic brain injury.

(方法)

Hypoxic–ischemic brain injury was induced via a combination of the left common carotid artery occlusion and exposure to hypoxic environment (8% oxygen) in adult male C57BL/6 mice. Immediately following induction of hypoxia–ischemia, mice received either saline or 2.4 units of neurotropin.

After the hypoxic-ischemic insult, the survival rate over 7 days was assessed. Neurological functions were evaluated using the neurological deficit score (0: no deficit; 1: flexion of the torso; 2: circling to one side; 3: longitudinal circling; 4: no spontaneous activity; 5: death).

備　考

１　※印の欄には記入しないこと。
２　論文題目が外国語の場合は，カッコを付し和訳を付記すること。
３　論文題目が日本語の場合は，カッコを付し英訳を付記すること。
４　論文内容要旨は，（研究の目的），（方法），（結果），（考察），（結論）の順に日本語（２，０００字程度）もしくは英語（半角５，０００字程度）でまとめ，タイプ等で印字すること。　（文字数を記載してください。）

論文内容要旨（続紙）

（ふりがな）
氏名（自署）　　印

Another set of 20 mice was used and euthanized 24 hours after the hypoxic-ischemic insult. Infarct volume was analyzed using 2,3,5-Triphenyl tetrazolium chloride (TTC). Further, Real-time PCR was used to evaluate inflammatory cytokine expressions.

(結果)

Compared to the control group, the neurotropin group exhibited a significantly higher survival rate (100% vs. 62.5%, $p < 0.05$) and lower neurological deficit scores (1; 0–2 vs. 3; 0–5, median; range, $p < 0.05$) after the hypoxic–ischemic insult. The administration of neurotropin also reduced infarct volume (18.3 ± 5.1% vs. 38.3 ± 7.2%, $p < 0.05$) and mRNA expression of pro-inflammatory cytokines.

(考察)

In the present study, exposure to hypoxic–ischemic insult caused cerebral infarction and led to a 40% mortality rate in untreated mice. The administration of neurotropin after hypoxic–ischemic insult successfully attenuated the brain injury and improved survival rate and neurological function, demonstrating the neuroprotective effect of post-treatment with neurotropin.

Administration of neurotropin systemically did not affect the heart rate or blood pressure, suggesting cerebral blood flow was not affected by neurotropin. Thus, the neuroprotective effects of neurotropin observed in this study were unlikely to be a result of changes in hemodynamics.

The neurological function of neurotropin-treated mice at 7 days after hypoxic–ischemic insult was found to be almost fully recovered, possibly indicating that neurotropin attenuates hypoxic–ischemic brain injury by suppressing not only the initial local inflammation but also the expansion of the inflammation. Inhibition of pro-inflammatory cytokine production is a likely mechanism underlying the neuroprotective effect of neurotropin.　(3015文字)