

学位論文抄録

A novel angiogenic method for chronic cerebral hypoperfusion in a rat model

(慢性脳低灌流ラットモデルにおける新たな血管新生法)

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## Abstract of the Thesis

**Background and Purpose:** Granulocyte-colony stimulating factor (G-CSF) mobilizes hematopoietic bone marrow cells into systemic circulation and has been used clinically to treat chemotherapy-induced neutropenia. Recently, G-CSF has been shown to have neuroprotective and angiogenic effects in acute cerebral infarction. We hypothesized that G-CSF could act as an enhancer of angiogenesis after indirect bypass surgery.

**Methods:** Chronic cerebral hypoperfusions were induced in male Wistar rats by permanent bilateral internal carotid artery occlusion (BICAO). After BICAO, unilateral indirect bypass and encephalo-galeo-synangiosis (EGS) were performed and human recombinant G-CSF (10 µg/kg) or saline was injected intramuscularly for 5 consecutive days. We measured regional cerebral blood flow (rCBF) by laser Doppler flowmetry and performed immunohistochemical analysis 21 days after BICAO.

**Results:** BICAO decreased rCBF to  $62.52\% \pm 5.8\%$  of control ( $P < 0.01$ ). The rCBF increased significantly 21 days after BICAO in all treatment groups ( $n = 10$ ;  $P < 0.05$ ) except in the G-E-group. The rCBF increase observed in the G+E+ group was significantly higher than that observed in other groups. Both G-CSF and EGS treatments significantly increased the number of small vessels ( $P < 0.01$ ), and G-CSF and EGS showed additive effect in increasing the number of small vessels.

**Conclusions:** Combined use of G-CSF and indirect bypass surgery induces an increase in rCBF and angiogenesis under cerebral chronic hypoperfusion conditions. This is the first report to demonstrate that G-CSF can enhance angiogenesis induced by indirect bypass surgery, and this combined therapy is safe and easy method of treatment.