論　文　内　容　の　要　旨
Synopsis of Thesis

氏　名 Name	二宮　貢士
論文題名 Title	Intranasal delivery of bone marrow stromal cells to spinal cord lesions （急性期脊髄不全損傷ラットに対する骨髄間質細胞鼻腔内投与について）

論文内容の要旨

〔目　的(Purpose)〕

The intranasal delivery of bone marrow stromal cells (BMSCs) to the injured brains of rodents has been previously reported. We investigated whether BMSCs migrate to spinal cord lesions through an intranasal route and whether the administration affected functional recovery.

〔方法ならびに成績(Methods/Results)〕

Methods: Forty Sprague-Dawley rats that were subjected to spinal cord injuries at the T7-8 level were divided into 5 groups (injured + intranasal BMSC-treated group, injured + intrathecal BMSC-treated group, injured-only group, injured + intranasal vehicle-treated group, and injured + intrathecal vehicle-treated group). The Basso, Beattie, and Bresnahan (BBB) scale was used to assess hind limb motor functional recovery for 2 or 4 weeks. Intralesionally migrated BMSCs were examined histologically and counted at 2 and 4 weeks. To evaluate the neuroprotective and trophic effects of BMSCs, the relative volume of the lesion cavity was measured at 4 weeks. In addition, nerve growth factor (NGF) and brain-derived neurotrophic factor (BDNF) levels in the cerebrospinal fluid (CSF) were evaluated at 2 weeks.

Results: Intranasally administered BMSCs were confirmed within spinal cord sections at both 2 and 4 weeks. The highest number, which was detected in the intrathecal BMSC-treated group at 2 weeks, was significantly higher than that in all the other groups. The BBB scale score of the intranasal BMSC-treated group showed good improvements by one week compared to the control group. However, in the final BBB scale scores, there was a statistically significant difference only between the intrathecal BMSC-treated group and the control group. The cavity ratios in the BMSC-treated groups were smaller than those of the control groups, but we did not find any significant differences in the NGF and BDNF levels in the CSF among the treatment and control groups.

〔総　括(Conclusion)〕

BMSCs reached the injured spinal cord through the intranasal route and contributed to the recovery of hind limb motor function and lesion cavity reduction. However, the effects were not as significant as those seen in the intrathecal BMSC-treated group.

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論文審査の結果の要旨及び担当者

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論文審査の結果の要旨

申請者は、脊髄損傷に対する急性期治療として、骨髄間質細胞を用い、これまで報告のなかった鼻腔内投与という新しい手法を用いて、ラットの脊髄損傷部への移行と治療効果を検討した。組織学的検討の結果、鼻腔内投与した骨髄間質細胞は脊髄損傷部まで移行するという全く新しい知見が得られた。残念ながら治療効果としては髄注群に及ばなかったものの、コントロール群と比べるとよい後肢機能回復と組織の修復がみられた。治療効果の差を考える上で、バイオマーカーとなりうるか、損傷後2週目での髄液中の神経栄養因子（NGF, BDNF）濃度を測定したものの、各群で有意差はなく、今後の検討課題と考えられた。今後は鼻腔内への細胞投与量や投与回数における工夫の余地があり、脊髄損傷に対する新たな治療ルートとしての可能性が残されていると思われた。

以上より、申請者の研究は学位授与に値すると考えられる。