

分子イメージングによる痴呆疾患の客観的診断・治療効果判定に関する基礎的研究

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Fundamental Study on objective diagnosis and therapy effect decision of the dementia by the molecular imaging.

Research Project

Project/Area Number

13670925

Research Category

Grant-in-Aid for Scientific Research (C)

Allocation Type

Single-year Grants

Section

一般

Research Field

Radiation science

Research Institution

Kanazawa University

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Keywords

Dementia / Receptor / Transporter / Neurotransplantation / Radiopharmaceutical

Research Abstract

Parkinsonian rats were stereotaxically infused 6-OHDA into the unilateral mesostriatal dopamine pathway and measured apomorphine-induced rotational behavior. Controls were infused saline instead of neurotoxin. Animals were divided into transplantation (TP) and sham-operated (S) groups. Ipsilateral vagal nodosal ganglion was surgically removed from the neck and stereotaxically transplanted as nerve fragments into the ipsilateral striatum 2 weeks after neurotoxin infusion. Sequential brain sections underwent autoradiography of dopaminergic system 2 weeks after operation. Densities of dopamine D1, D2 receptors and dopamine transporter (DAT) were assessed by in-vitro autoradiography using [³H]SCH23390, [³H]YM-09151-2 and [³H]GBR12935. Significant DAT decrease in striatum was shown in the model animals compared with controls ($P < 0.0001$). D₂ receptor in the ipsilateral striatum increased significantly in transplanted animals compared with sham-operated animals (S/R-, 0.97 ± 0.08 ; TP/R-, 1.08 ± 0.08 ; $p = 0.039$ and S/R+, 1.06 ± 0.06 ; TP/R+, 1.19 ± 0.16 ; $p = 0.023$), whereas DAT and D₁ receptor showed no significant changes. Our results suggest that vagal autotransplantation induces upregulation of D₂ receptor in the ipsilateral striatum. Autotransplantation showed no significant effect on DAT, although DAT imaging is a sensitive test for dopaminergic damage. We need further study on dopaminergic system imaging after neural transplantation. We evaluated the potencies of radioiodinated (-)-o-iodovesamicol [(-)-oIV] as a selective vesicular acetylcholine transporter (VACHT) mapping agent. (-)-[¹²⁵I] oIV exhibited significant accumulation in rat brain. The regional brain distribution of radioactivity was similar for both (-)-[¹²⁵I] oIV and [³H]vesamicol. The accumulation of (-)-[¹²⁵I] oIV in the brain was significantly reduced by post-administration of unlabeled vesamicol ($0.5 \mu\text{mol/kg}$) and (-)-[¹²⁵I] oIV ($\mu\text{mol/kg}$) in the other hand, the post-administration of sigma ligands hardly affected the accumulation of (-)-[¹²⁵I] oIV in the brain. These studies showed that (-)-[¹²⁵I] oIV, as well as [³H]vesamicol, bound to VACHT with high affinity in the rat brain. Furthermore, (-)-[¹²⁵I] oIV binding in the ipsilateral cortex to the lesion was significantly reduced by 17.0%, compared with that in the contralateral cortex in a unilateral NBM-lesioned rat. These results suggested that radioiodinated (-)-[¹²⁵I] oIV may potentially be useful for the diagnosis of cholinergic neurodegenerative disorders. ▲ Less

Research Products (4 results)

All Other

All Publications (4 results)

[Publications] Shiba, K, Mori, H., et al.: "Characterization of (-)-radioiodinated (-)-ortho-iodovesamicol binding in rat brain preparations" *Life Sciences*. 71. 1591-1598 (2002) ▼

[Publications] Shiba, K, Mori, H., et al.: "Evaluation of radioiodinated (-)-o-iodovesamicol as a radiotracer for mapping the vesicular acetylcholine transporter" *Annals of Nuclear Medicine*. 17 · 6. 451-456 (2003) ▼

[Publications] Shiba K.: "Characterization of (-)-radioiodinated (-)-ortho-iodovesamicol binding in rat brain preparations" *Life Sciences*. 71. 1591-1598 (2002) ▼

[Publications] Shiba K.: "Evaluation of radioiodinated (-)-o-iodovesamicol as a radiotracer for mapping the vesicular acetylcholine transporter" *Annals of Nuclear Medicine*. 17(6). 451-456 (2003) ▼

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