2003 Fiscal Year Final Research Report Summary

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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Project Period (FY)

2001 – 2003

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 horn die neck and stereotaxically transplanted as nerve fragments into the ipsilateral striatum 2 weeks after nerotoxin 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). D_2 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 D_1 receptor showed no significant changes. Our results suggest that vagal autotransplantation induces upregulation of D_2 receptor in the ipsilateral striatum. Autotransplantation showed no significant effect on DAT, although DAT imaging is a sensitive test for dopaminergic damage. We need hurther study on dopaminergic system imaging after neural transplantation.
We evaluated the potencies of radioiodimted(-)-o-iodovesamicol [(-)-oIV] as a selective vesicular acetylcholine tmnsporter(VAChT) mapping agen. (-)-[^<125>1] oIV exhibited significant accumulationin rat brain. The regional brain distribution of radioactivity was similar for both (-)-[^<125>1] oIV and [^3H]vesamicol. The accumulation of (-)-[^<125>1] oIV in the brain was significant reduced by post-administration of unlabeled vesamicol(0.5μmol/kg^<-1>) and(-)-[^<125>1] oIV μmol/kg-1] in the other hand, the post-administration of sigma ligands hardy affected the accumulation of (-)-[^<125>1] oIV in die brain. These studies showed that (-)-[^<125>1] oIV, as well as [^3H]vesamicol, bound to VAChT with high affinity in die rat brain. Funhemore, (-)-[^<125>1] 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 radioiodimted(-)-[^<125>1] 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.: "Chracterization of (-)radioisodinated (-)-ortho-iodovesamicol binding in rat braid 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.: "Chracterization of (-)radioisodinated (-)-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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Published: 2005-04-18