

The development of radiolabeled molecular imaging agents for diagnosing Alzheimer's disease.

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2004 Fiscal Year Final Research Report Summary

The development of radiolabeled molecular imaging agents for diagnosing Alzheimer's disease.

Research Project

Project/Area Number

14570845

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)

2002 - 2004

Keywords

sigma receptor / iodovesamicol / molecular imaging agent / Alzheimer's disease

Research Abstract

We evaluated the potential of the (+)-enantiomer of radioiodinated 2-[4-(4-iodophenyl)piperidino]cyclohexanol ((+)-[¹²⁵I]-p-iodovesamicol) [(+)-[¹²⁵I]pIV], radioiodinated at the para position of the 4-phenylpiperidine moiety, as a single photon emission computed tomography (SPECT) ligand for mapping sigma-1 receptor in the central nervous system.

In competitive inhibition studies, (+)-pIV (K_i=1.3nM) had more than 10 times higher affinity to the sigma-1 (σ-1) receptor than (+)-pentazocine (K_i=19.9nM) or haloperidol (K_i=13.5nM) known as sigma ligands. Also, the binding affinity of (+)-pIV to the σ-1 receptor (K_i=1.3nM), was about 16 times higher than the sigma-2 (σ-2)

receptor ($K_i=20.4\text{nM}$). (+)-pIV ($K_i=1262\text{nM}$) had a much lower affinity to VACht than (-)-vesamicol ($K_i=13.0\text{nM}$) or (-)-pIV. (+)-[^{125}I]pIV had low affinity to the dopamine, serotonin, adrenaline and acetylcholine receptors. Furthermore, in a saturation binding study, (+)-[^{125}I]pIV exhibited a K_d of 6.96 nM with a maximum number of binding sites B_{max} of 799.3 fmol/mg of protein.

In vivo studies, significant amounts (approximately 3% of the injected dose) of (+)-[^{125}I]pIV accumulated in rat brain and its retention was prolonged. The accumulation of (+)-[^{125}I]pIV in the rat brain was significantly reduced by the co-administration of sigma ligands such as pentazocine or haloperidol. Ex vivo autoradiography of the rat brain at 1 hr following i.v. injection of (+)-[^{125}I]pIV showed high localization in brain areas rich in sigma-1 receptor. Thus, the distribution of (+)-[^{125}I]pIV was thought to bind to sigma-1 receptor in vivo. These results suggest that radioiodinated (+)-pIV may have the potential to image sigma-1 (σ -1) receptor in vivo, at least in animals.

Research Products (6 results)

All	2005	2003	2002
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All	Journal Article
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[Journal Article] In vitro characterization of radioiodinated (+)-2-[4-(4-iodophenyl) piperidino]cyclohexanol [(+)-pIV] as a sigma-1 receptor ligand.

2005 ▾

[Journal Article] In vitro characterization of radioiodinated (+)-2-[4-(4-iodophenyl)piperidino]cyclohexanol [(+)-pIV] as a sigma-1 receptor ligand.

2005 ▾

[Journal Article] Evaluation of Radioiodinated (-)-o-iodovesamicol as a radiotracer for mapping the vesicular acetylcholine transporter

2003 ▾

[Journal Article] Evaluation of Radioiodinated (-)-o-iodovesamicol as a radiotracer for mapping the vesicular acetylcholine transporter

2003 ▾

[Journal Article] Characterization of radioiodinated (-)-ortho-iodovesamicol binding in rat brain preparations

2002 ▾

[Journal Article] Characterization of radioiodinated (-)-ortho-iodovesamicol binding in rat brain preparations

2002 ▾

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