アルツハイマー病の早期診断を目的とした放射性神経機能診断薬の開発

メタデータ	言語: Japanese
	出版者:
	公開日: 2021-11-08
	キーワード (Ja):
	キーワード (En):
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URL	https://doi.org/10.24517/00063205

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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

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Project Period (FY)

2002 – 2004

Keywords

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

Research Abstract

We evaluated the potential of the (+)-enantiomer of radioiodinated 2-[4-(4-iodophenyl)piperidino]cyclohexanol ((+)-[^<125>I]-p-iodovesamicol) [(+)-[^<125>I]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 (Ki=1.3nM) had more than 10 times higher affinity to the sigma-1 (σ-1) receptor than (+)-pentazocine (Ki=19.9nM) or haloperidol (Ki=13.5nM) known as sigma ligands. Also, the binding affinity of (+)-pIV to the σ-1 receptor (Ki=1.3nM), was about 16 times higher than the sigma-2 (σ-2)

receptor (Ki=20.4nM). (+)-pIV (Ki=1262nM) had a much lower affinity to VAChT than (-)-vesamicol (Ki=13.0nM) 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 Kd of 6.96 nM with a maximum number of binding sites Bmax 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

All | Journal Article

[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 brainpreparetions 2002

[Journal Article] Characterization of radioiodinated (-)-ortho-iodovesamicol binding in rat brainpreparetions 2002

URL: https://kaken.nii.ac.jp/report/KAKENHI-PROJECT-14570845/145708452004kenkyu_seika_hokoku_

Published: 2006-07-10