

# 痴呆の客観的核医学画像診断法確立のための神経伝達物質マッピングの基礎的研究

著者	久田 欣一
著者別表示	Hisada Kinichi
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# 1989 Fiscal Year Final Research Report Summary

## Basic research on neurotransmitter mapping for establishing objective nuclear medicine imaging of dementia

Research Project

### Project/Area Number

63440040

### Research Category

Grant-in-Aid for General Scientific Research (A)

### Allocation Type

Single-year Grants

### Research Field

Radiation science

### Research Institution

Kanazawa University

### Principal Investigator

**HISADA Kinichi** Kanazawa University, School of medicine, Professor, 医学部, 教授 (50019882)

### Co-Investigator(Kenkyū-buntansha)

MATSUDA Hiroshi Kanazawa University, School of Medicine, Assistant, 医学部, 助手 (90173848)

SHIBA Kazuhiro Kanazawa University, Radioisotope Center, Assistant, アイソトープ総合センター, 助手 (40143929)

AMANO Ryohei Kanazawa University, School of Allied Medical Professions, Associate professor, 医療技術短期大学部, 助教授 (30111769)

MORI Hirofumi Kanazawa University, Radioisotope Center, Associate Professor, アイソトープ総合センター, 助教授 (90019604)

### Project Period (FY)

1988 - 1989

### Keywords

dementia / neurotransmitter / autoradiography / neuroreceptor / acetylcholine / radioligand / nuclear medicine imaging / Alzheimers disease

### Research Abstract

A fundamental study was performed on the nuclear medicine imaging of cholinergic innervation in the brain. A cholinergic denervation model was experimentally prepared by producing an ibotenic acid lesion in unilateral basaltorebrain in the rat, which is reported to be one of animal models of Alzheimer's disease. To assess the passive avoidance performance in terms of acquisition of new responses and long term retention, a step-through apparatus with high precision was newly developed. Acquisition latencies showed no significant differences between models and sham-controls. However,

models revealed statistically significant shorter retention latencies than sham-controls. Histochemical investigation disclosed neuronal cell loss, gliosis, and diminished acetylcholine esterase (AChE) staining in a ventral region of globus pallidus, substantia innominata, and internal capsule in the basal forebrain lesion. Furthermore decreased AChE staining was observed in the frontal, parietal, and temporal projection cortices ipsilateral to the lesion in models. Quantitative determination of choline acetyltransferase (CAT) and AChE in parietal cortices showed statistically significant 46% and 40% decrease on an average, respectively, in the ipsilateral side compared to the contralateral side. These results suggest that this animal model is approved as an appropriate experimental model of Alzheimer's disease. Quantitative determination of acetylcholine in parietal cortices revealed statistically significant 31% decrease on an average in the ipsilateral side relative to the contralateral side to the lesion. In-vitro receptor autoradiography showed no significant differences in total, M<sub>1</sub>, and M<sub>2</sub> muscarinic acetylcholine receptors between the ipsilateral and contralateral cortices to the lesion. Simultaneous mapping of presynaptic cholinergic innervation using <sup>3</sup>H-2-(4-phenylpiperidino)cyclohexanol (AH5183) demonstrated significant 14% decrease of AH5183 binding on an average in the ipsilateral relative to the contralateral fronto-parieto-temporal cortices to the lesion. These results suggest that AH5183 is a promising ligand for tapping cholinergic innervation. The <sup>123</sup>I or <sup>99m</sup>Tc labelling of AH5183 is to be expected in view of application to a SPECT study.▲ Less

## Research Products (12 results)

All Other

All Publications (12 results)

- [Publications] Matsuda H, et al.: "Quantitative assessment of cerebral blood flow using Technetium-99m-hexamethyl-propylene amine oxime: part I design of a mathematical model." *Ann Nucl Med.* 2. 13-19 (1988) ▼
- [Publications] Matsuda H, et al.: "Determination of flow and rate constants in a kinetic model of [<sup>99m</sup>Tc]-Hexamethyl-propyleneamine oxime in the human brain." *J Cereb Blood Flow Metabol.* 8. 561-568 (1988) ▼
- [Publications] Matsuda H, et al.: "Direct autoradiographic comparison of <sup>99m</sup>Tc-HMPAO with <sup>125</sup>I-IMP in experimental brain ischemia." *Nucl Med Commun.* 9. 891-897 (1988) ▼
- [Publications] Matsuda H, et al.: "Double tracer autoradiographic method for sequential evaluation of regional cerebral perfusion." *Am J Physiol Imaging.* 4. 131-135 (1989) ▼
- [Publications] Matsuda H, et al.: "Autoradiographic analysis of IMP redistribution in experimental brain ischemia." *J Nucl Med.* 31. (1990) ▼
- [Publications] 久田欣一, 松田博史: "脳代謝とその異常" 中山書店, 405 (1989) ▼
- [Publications] Matsuda H, Oba H, Terada H, Tsuji S, Sumiya H, Shiba K, Seki H, Imai K, Mori H, Hisada K: "Quantitative assessment of cerebral blood flow using Technetium-99m-hexamethyl-propyleneamine oxime: part I. design of a mathematical model." *Ann Nucl Med.* 2. 13-19 (1988) ▼
- [Publications] Matsuda H, Oba H, Seki H, Higashi S, Sumiya H, Tsuji S, Terada H, Imai K, Shiba K, Mori H, Hisada K: "Determination of flow and rate constants in a kinetic model of [<sup>99m</sup>Tc]-hexamethyl-propyleneamine oxime in the human brain." *J Cereb Blood Flow Metabol.* 8, 561-568, 1988. ▼
- [Publications] Matsuda H, Tsuji S, Oba H, Imai K, Shiba K, Terada H, Seki H, Sumiya H, Mori H, Hisada K: "Direct autoradiographic comparison of <sup>99m</sup>Tc-HMPAO with <sup>125</sup>I-IMP in experimental brain ischemia." *Nucl Med Commun.* 9, 891-897, 1988. ▼
- [Publications] Matsuda H, Tsuji S, Oba H, Kinuya K, Terada H, Sumiya H, Shiba K, Mori H, Hisada K, Maeda T: "Double tracer autoradiographic method for sequential evaluation of regional cerebral perfusion." *Am J Physiol Imaging.* 4, 131-135, 1989. ▼
- [Publications] Matsuda H, Tsuji S, Oba H, Shiba K, Terada H, Kinuya K, Mori H, Sumiya H, Hisada K: "Autoradiographic analysis of IMP redistribution in experimental brain ischemia." *J Nucl Med.* ▼
- [Publications] Hisada K, Matsuda H: "SPECT (Single Photon Emission Computed Tomography) -application to dementia-." *Metabolism and Disease* 26 383-389, 1989. ▼

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