Basic research on neurotransmitter mapping for establishing objective nuclear medicine imaging of schizophrenic disorder

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1987 Fiscal Year Final Research Report Summary

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Research Project

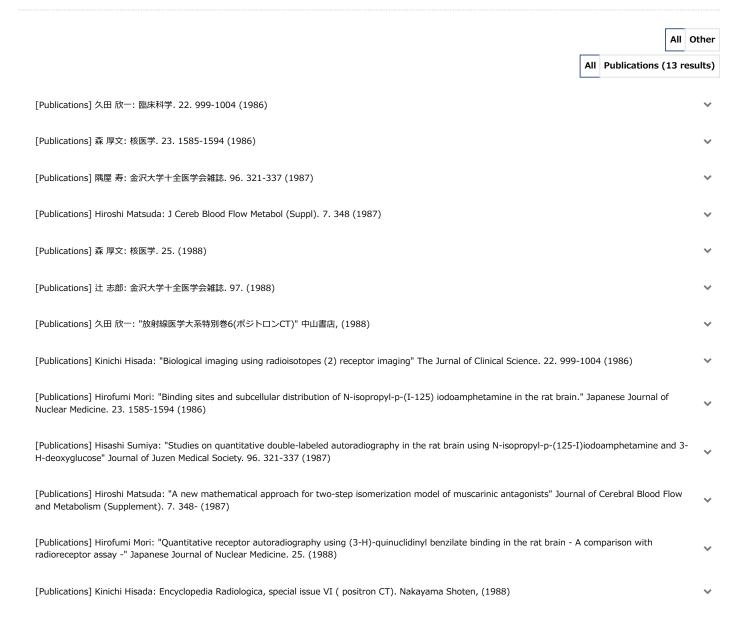
Research Abstract

Project/Area Number
61440045
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 School of Medicine, Kanazawa Univeristy Professor, 医学部, 教授 (50019882)
Co-Investigator(Kenkyū-buntansha)
KURACHI Masayoshi Toyama Medical and Pharmaceutical University Professor, 医学部, 教授 (80019603) KOJIMA Kazuhiko School of Allied Medical Professions, Kanazawa University Professor, 医療技術短期大学部, 教授 (60019916) MATSUDA Hiroshi School of Medicine, Kanazawa University Assistant, 医学部, 助手 (90173848) SHIBA Kazuhiro Radioisotope Center, Kanazawa University Assistant, アイソトープ総合センター, 助手 (40143929) MORI Hirofumi Radioisotope Center, Kanazawa University Assistant Professor, アイソトープ総合センター, 助教授 (90019604)
Project Period (FY)
1986 – 1987
Keywords
Schizophrenic disorder / neurotransmitter / autoradiography / image processing / mathematical model / 99mTc-labeled agent / ^<99m>Tc標識薬剤 / 向精神薬

A fundamental study was performed on a quantitative measurement of brain receptor using an autoradiographic technique in rats. Highly qualified autoradiograms were obtained using six different ligands labeled with tritium after the investigation of appropriate incubation time and washing time, and of

presence or absence of saturation. In a comparative study in quantitation and manipulation among the following three systems for anlayzing autoradiograms:1)scanning densitometer, 2) drum scanner, 3)video digitizer system (VDS), the VDS system showed by far the most convenient manipulation without any significant differences in quantitation. Appropriate setting of conditions in the ligandreceptor interaction revealed the similarity of the hitherto discordant values for the maximum number of binding sites of the muscarinic acetylcholine receptor and equilibrium dissociation conastant of its antagonist, H-quinuclidinyl bezylate, between in -vitro receptor assay and receptor autoradiography in the conventional Scatchard analysis. It is said that ligand-muscarinic receptor complex shows a conformational change from low to high affinity from (isomerization). In this isomerization model four rate constants were estimated with the use of a mewly developed mathematical equation. The validity of this new analysis was confirmed from the observation that the apparent equilibrium dissociation rate constant from these rate constants was in a good agreement with that from non-isomerization model. Schizophrenic model rats were developed eutger by administrating methamphetamine or by injection of 6-OHDA to prefrontal cortex, of which cerebral blood flow and glucose metablolsm were not significantly different from controls. Further investigations are being carried out on receptor changes in these models. Twenty to thirty percent derease in the maximum number of binding sites of 5-HT2 receptor was demonstrated in a part of frontal cortex after administrating clomipramine in the receptor autoradiography. For single photon emission computed tomography, 99mTc-labeled chelating agent was developed which crosses the blood-brain barrier. A multi-tracer autoradiographic technique was also established for simulataneous evaluation of cererbral blood flow and its metabolism.

Research Products (13 results)



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