

Age-related changes of the binding of [³H]SA4503 to sigma₁ receptors in the rat brain

Kiichi ISHIWATA,* Tadayuki KOBAYASHI,** Kazunori KAWAMURA**** and Kiyoshi MATSUNO****

*Positron Medical Center, Tokyo Metropolitan Institute of Gerontology

**M's Science Co.

***SHI Accelerator Service Co. Ltd.

****Nara Research and Development Center, Santen Pharmaceutical Co. Ltd.

We have recently developed 1-([3-*O*-methyl-¹¹C]3,4-dimethoxyphenethyl)-4-(3-phenylpropyl) piperazine ([¹¹C]SA4503) as a selective radioligand for mapping sigma₁ receptors in the brain by positron emission tomography (PET). In the present short communication we evaluated the age-related changes of the binding of this ligand to sigma₁ receptors in Fisher-344 rats (1.5-, 6-, 12-, and 24-month-old) by the *in vitro* binding assay. We also measured the binding of [³H](+)-pentazocine to sigma₁ receptors and the binding of [³H]1,3-di-*O*-tolylguanidine to sigma₂ receptors, which are current standard methods. The specific binding of the three radioligands increased age-dependently. Both K_d and B_{max} values of the 24-month-old rats for each radioligand were significantly higher than those of the young rats (1.5- and 6-month-old). The increased numbers of both sigma₁ and sigma₂ receptor subtypes in the aged rats compensate for the lowered affinity, and rather enhanced the radioligand-receptor binding. The results contrast strikingly with the age-dependent decrease in the dopaminergic, cholinergic and glutamatergic receptors that are reported to be correlated with the sigma receptors, and indicate that a PET study with [¹¹C]SA4503 to evaluate the aging process in humans would be of great interest.

Key words: [¹¹C]SA4503, sigma₁ receptor, aging, rat