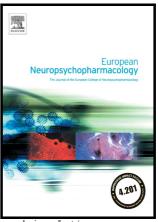
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ACCEPTED MANUSCRIPT

Verbal memory and 5-HT1A receptors in healthy volunteers – a PET study with [carbonyl-11C]WAY-100635

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Abstract

The serotonin 5-HT1A receptor is a putative drug development target in disorders with cognitive and in particular memory deficits. However, previous human positron emission tomography (PET) studies on 5-HT1A receptor binding and memory functions have yielded discrepant results. We explored the association between verbal memory and 5-HT1A receptor binding in 24 healthy subjects (14 male, 10 female, aged 18-41 years). The cognitive tests included the Wechsler Memory Scale-Revised (WMS-R), Wechsler Adult Intelligence Scale-Revised (WAIS-R) and Wisconsin Card Sorting Test (WCST). 5-HT1A receptor binding was measured with PET and the radioligand [carbonyl-11C]WAY-100635, which was quantified with the gold standard method based on kinetic modeling using arterial blood samples. We found that global 5-HT1A receptor binding was positively correlated with measures of verbal memory, such that subjects who had higher receptor binding tended to have better verbal memory than subjects who had lower receptor binding. Regional analyses suggested significant correlations in multiple neocortical brain regions and the raphe nuclei. We did not find significant correlations between 5-HT1A receptor binding and executive functions as measured with WCST.

We conclude that neocortical as well as raphe 5-HT-1A receptors are involved in verbal memory function in man.

Introduction

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