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Effects of amyloid-β peptides on the serotoninergic 5-HT_{1A} receptors in the rat hippocampus

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Abstract

A recent [^{18}F]MPPF-positron emission tomography study has highlighted an overexpression of 5-HT_{1A} receptors in the hippocampus of patients with mild cognitive impairment compared to a decrease in those with Alzheimer's disease (AD) [Truchot, L., Costes, S.N., Zimmer, L., Laurent, B., Le Bars, D., Thomas-Antérion, C., Croisile, B., Mercier, B., Hermier, M., Vighetto, A., Krolak-Salmon, P., 2007. Up-regulation of hippocampal serotonin metabolism in mild cognitive impairment. Neurology 69 (10), 1012–1017]. We used *in vivo* and *in vitro* neuroimaging to evaluate the longitudinal effects of injecting amyloid-β (Aβ) peptides (1–40) into the dorsal hippocampus of rats. *In vivo* microPET imaging showed no significant change in [^{18}F]MPPF binding in the dorsal hippocampus over time, perhaps due to spatial resolution. However, *in vitro* autoradiography with [^{18}F]MPPF (which is antagonist) displayed a transient increase in 5-HT_{1A} receptor density 7 days after Aβ injection, whereas [^{18}F]F15599 (a radiolabelled 5-HT_{1A} agonist) binding was unchanged suggesting that the overexpressed 5-HT_{1A} receptors were in a non-functional state. Complementary histology revealed a loss of glutamatergic neurons and an intense astroglial reaction at the injection site. Although a neurogenesis process cannot be excluded, we propose that Aβ injection leads to a transient astroglial overexpression of 5-HT_{1A} receptors in compensation for the local neuronal loss. Exploration of the functional consequences of these serotoninergic modifications during the neurodegenerative process may have an impact on therapeutics targeting 5-HT_{1A} receptors in AD.

Keywords: Alzheimer's disease; Amyloid peptides; Rat; MicroPET; [^{18}F]MPPF; 5-HT_{1A}; Astrocytes