

Displacement detectability of [¹⁸F]MPPF from 5-HT_{1A} receptors by endogenous serotonin: a Monte Carlo simulation study

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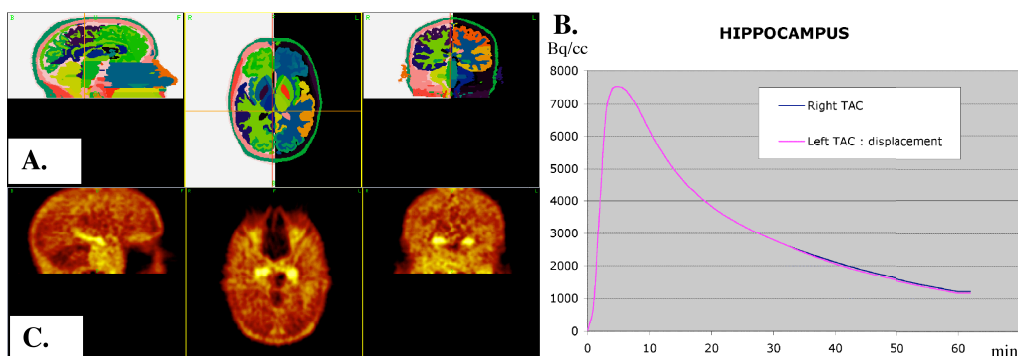
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Introduction: 5-HT_{1A} receptors are largely involved in psychiatric and neurological disorders such as depression, schizophrenia, dementia, or epilepsy. The MPPF fluorine 18 labeled tracer, competitor to endogenous serotonin binding on 5-HT_{1A} receptors [1], has been quantified and validated for clinical investigations [2]. Studies in rat [3] have shown that variations in serotonin concentration can be detected with MPPF, which would be of particular interest for human *in vivo* examination. Although theoretically, the discrimination of a displacement in non-noisy modeled kinetic is obvious, it may be undetectable in noisy real conditions of measure with PET.

Objective: The aim of this study was to evaluate the detectability of a displacement of MPPF binding consecutive to a serotonin release on a Monte-Carlo simulated PET data set.

Methods: Six MPPF PET dynamic data set were simulated with the SORTEO Monte-Carlo simulator [4] reproducing the physical disintegration process, the photon transport and the detection by CTI Exact HR+ camera. Emission volumes came from segmented MRI brain images classified in labeled cortical and subcortical brain structures (Fig A.). In regions rich in 5-HT_{1A} receptor, emission kinetics were analytically simulated from the compartmental model. Regions from the right hemisphere had a standard kinetics resulting from a single bolus injection of [¹⁸F]-MPPF tracer dose, whereas homologous regions of the left hemisphere resulted from a more complex model including an endogenous compartment from which a release of serotonin was simulated 20 minutes post-injection (Fig B). In regions poor in 5-HT_{1A} receptors and in background, kinetics were extracted from actual PET data obtained from a normative database acquired with our HR+ camera. After the simulation of PET acquisition processes (Fig C), regional time-activity curves were extracted from dynamic PET data to compute MPPF binding parameters with an adequate model. Parametric images were also computed. A statistical analysis of normal regions versus regions with displacement was performed to detect serotonin concentration modifications, both in ROI level and in a voxel based level with SPM. Simulated data were compared with actual data to evaluate realism of the simulations and detectability of displacement.

Results: Comparisons between left and right mean ROI values revealed a significant difference induced by the serotonin release. The individual SPM analysis did not reveal significant differences with normal subjects, whereas in the SPM group analysis, significant differences were found in some clusters located in regions with displacement. In conclusion, the sensitivity for detecting a displacement depended on the availability of 5-HT_{1A} receptor, the number of subjects, and the size of cortical structures.



[1] Zimmer L, et al., JNeurochem 2002; 80: 278-86

[2] Costes N, et al. JCBF 2002; 22: 753-763

[3] Rbah L, Synapse. 2003 ; 49(4):239-45

[4] Reilhac, et al. IEEE TNS 2004; 51: 46-52