**[18F]UCB-H RADIOTRACER AS A TOOL TO UNDERSTAND THE ROLE OF THE SV2A PROTEIN**

**ME. Serrano**, G. Becker, MA. Bahri, C. Warnier, Aerts J., F. Mievis, F. Giacomelli, Ch. Lemaire, E. Salmon, A. Luxen, A. Plenevaux

**Background:** SV2A is the most studied isoform of the Synaptic Vesicle 2 proteins, which are involved in the synaptic vesicle trafficking, being important both in normal as in pathological process (1, 2). Until now, only one study *in vivo* has been reported, showing a reduction of SV2A levels in the epilepsy (3). [18F]UCB-H was developed like a current tool to study the role of SV2A with *in vivo* techniques (4, 5), and as a tool in clinical investigations. The objective of this research was to evaluate the radiotracer specificity to this isoform comparing with the others, through a competition assay in rats with ex-vivo autoradiography and mPET imaging.

**Methods:** Forty male Sprague-Dawley were used in ex-vivo autoradiography experiments (N=20) and in microPET imaging (N=20). Animals were pre-treated 30 minutes before the injection of [18F]UCB-H with a dose IP either of vehicle, Keppra (SV2A ligand), UCB068 (SV2B ligand) or UCB054 (SV2C ligand). Ex-vivo autoradiography was carried out 5 minutes after radiotracer injection while mPET images were acquiring with a dynamic scanner of 1 hour. Standard Uptake Value (SUV) and Distribution Volume (VT) were calculated and the correlation between both parameters was determined.

**Results:** In ex-vivo autoradiography, ANOVA of two-ways showed statistical significant differences in brain uptake of [18F]UCB-H among the groups pretreated with Keppra or the ligand for SV2B and the control group. Regarding mPET data, statistical significant differences were found between the group injected with keppra and the rest of groups. Pearson Correlation between SUV and VT was strong, with a value of 0.955.

**Conclusion**: Even if a considerable affinity between the ligands UCB068 and UCB054, and the receptor for the isoform SV2A exists, it is only detected during the first 5 minutes (ex-vivo technique), being certainly due to a nonspecific binding. This binding is not strong enough to show a direct competition with the radiotracer during a mPET acquisition. These results allow us to conclude that [18F]UCB-H is a suitable radiotracer for the imaging of the isoform SV2A in vivo, allowing us the clinical study about the molecular base of a disease with a high population impact, like the epilepsy.

**Keywords:** SV2, [18F]UCB-H , competition assay, autoradiography, microPET.

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