Several data suggest the role of the dopaminergic system in depression, but the results with functional imaging are contradictory. The selective serotonin reuptake inhibitor (SSRI) antidepressants are believed to mainly act by selectively binding to the serotonin, but the SSRIs also exhibit other neuropharmacologic effects. The aim of this study was to evaluate the DAT activity of untreated patients with unipolar depression and compared to healthy volunteers. We also studied the effect of striatal dopamine transporter activity in depression. Materials and Methods: We performed overall 30 123I-FP-beta-CIT-SPECT examinations in 8 healthy controls (MINI) and 12 patients. We performed positron emission tomography (PET) 3 weeks after the last scintigraphic study. The transversal reconstructed SPECT slices at the level of the basal ganglia, regions of interest were fixed by self-developed semautomatique technique. The binding potential was calculated by the ratio of uptake in a region with specific receptor binding to a reference region of interest (ROI) and the spatial resolution of the imaging system. Results: In the patient group, the median binding potential to striatal administration was 2.79 (range: 2.45-3.36), which indicates a decrease of 7% of FP-CIT binding. HAM-D scores showed 48% decrease after scintigraphic treatment. Spearman’s correlation indicated no significant relationship among binding potentials, HAM-D scores, age, and education (p>0.5). Conclusion: We didn’t find any significant difference in the baseline values of DAT activity between control and untreated depressed subjects. The HAM-D score showed decrease after treatment, which prove effectiveness of therapy. Sertraline treatment decreased the DAT activity (9%) but further investigations are needed to support this finding.

P39 – Monday, Oct. 15, 2007; 2:30 pm – 4:00 pm, Poster Area Neurology/Psychiatry - Receptors / Transporters

P303 Pinhole SPECT of dopamine D2 receptors and endogenous dopamine release in mice

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Aim: Dopamine D2 receptor (D2R) availability appears to be important in addictive behavior. For example, low striatal D2R binding predicts high rates of intravenous cocaine self-administration in animals. The study of striatal D2R availability in mouse models of cocaine addiction may therefore be important to unravel the role of the D2R in addiction. In addition, endogenous dopamine release, induced by psychostimulants, may differ in drug-addiction. We recently developed a high-resolution small animal pinhole SPECT system in small laboratory animals. In this study, we evaluated the feasibility to image D2R and to assess dopamine release in mice using the D2R antagonist [3H]IBZM and our pinhole SPECT system.

Methods and Materials: Male C57BL/6J mice were scanned on our single-pinhole SPECT system (Habakern et al. JNM 2001). The system is in a cylinder which is positioned directly and horizontally above the pinhole aperture, and rotates during data acquisition. The pinhole collimator is connected to an ADAC ARCO3002® scintillation camera. A 2-mm pinhole aperture was used. All experiments were performed with regulated ROIs for the striatum and cerebellum. In a first study, mice were injected intraperitoneally with 20 μg to 70 μg [3]HIBZM and scanned continuously up to 2 h. In a second experiment, mice were injected intraperitoneally with 20 μg to 70 μg [3]HIBZM and scanned continuously up to 1 h. Injection and scanning times were 60 min. After injection, mice were injected intraperitoneally with 2.5 mg/kg body weight amphetamine i.p. in 10 frames of 12 min. After injection of the dopamine transporter ligand [123I]IBZM and scanning, approximately 2 h after the last injection of amphetamine, mice were injected intraperitoneally with 2.5 mg/kg body weight adenosine i.p. in 10 frames of 12 min. After injection of [123I]IBZM and scanning, approximately 1 h after adenosine injection, mice were injected intraperitoneally with 2.5 mg/kg body weight amphetamine i.p. in 10 frames of 12 min. After injection of [123I]IBZM and scanning, approximately 1 h after amphetamine injection, mice were injected intraperitoneally with 2.5 mg/kg body weight adenosine i.p. in 10 frames of 12 min.

Results: In the [3H]IBZM scans, with higher concentration of the imaging agent in the striatum, we observed a decrease in activity in the striatum of mice that were pre-treated with amphetamine or adenosine. This decrease was more pronounced in the case of amphetamine pre-treatment. In the [123I]IBZM scans, with lower concentration of the imaging agent in the striatum, we observed an increase in activity in the striatum of mice that were pre-treated with amphetamine or adenosine. This increase was more pronounced in the case of amphetamine pre-treatment. Therefore, we conclude that our pinhole SPECT system is able to image the D2R and to assess dopamine release in mice using the D2R antagonist [3H]IBZM and our pinhole SPECT system.

P304 Validity of the Specific Uptake Size Index (SUSI) in quantitative analysis of clinical 18F-DOPA brain PET studies

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Aim: Quantitative assessment of functional PET data is attractive since it can lower variability among centers and may enhance the consistency of image interpretation independent of reader experience. Various quantitative indices have been suggested for the functional imaging of the dopaminergic system including advanced kinetic models and simplified semi-quantitative measures such as the Specific Binding Index (SBI) computed as the ratio of uptake in a region with specific receptor binding to a reference region. A receptor problem with these indices is their dependence on the reference region of interest (ROI) and the spatial resolution of the imaging system. Therefore, partial volume effect results in underestimates of this index compared to the true value. Material and Methods: A new index named the Specific Uptake Size Index (SUSI), which considers total uptake in the object not just activity concentration, was recently proposed and claimed to be independent of ROI size and system resolution. The validity of this index is assessed in this work using PET images acquired from an anthropomorphic striatal phantom study and a 18F-DOPA studies of patients potentially suffering from Parkinson’s disease. For the latter, the external beam contour was drawn manually requiring an expert neurologist to outline the lateral orbito-zygomatic skull and cerebral border thus avoiding partial volume effect. The influence of ROI size was assessed by drawing non-overlapping ROIs of different size around the striatum not necessarily covering the whole striatum. Results: The SBI showed that SBI measures based on maximum counts were 2.94 and 3.12 for right and left striatum, respectively, and proved to deviate considerably from the true value (4.35). The SUSI estimate is nearly constant in the striatum for ROIs greater than 57 cm². Below this volume, the SUSI estimates are not reliable. The clinical studies seem to support that the SBI derived from SUSI is always greater than the SBI derived from maximum counts in the ROIs. The SBI derived from SUSI that uses total uptake instead of maximum uptake is likely to be more accurate for small objects.

Conclusion: We have demonstrated phantom and clinical data that the SUSI is approximately independent of the ROI size allowing to guarantee good reproducibility of quantitative parameters estimates.