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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 some of 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 sertraline on dopamin transporter activity in depression. **Materials and methods**: We performed overall 30 123I-FP-beta-CIT-SPECT examinations in 8 healthy controls (MINI) and in 11 depressed patients (DSM-IV), the inclusion criteria was a score of at least 19 on the Hamilton Depression Scale (HAM-D, 21 items). In age-matched healthy subjects and in patients baseline 123I-FP-beta-CIT-SPECT investigations were done, in the depressed patient group the DAT SPECT was repeated after 3 weeks sertraline treatment. On the transversal reconstructed SPECT slices at the level of the basal ganglia, regions of interest were fixed by self-developed semiautomatic technique. The binding potential was estimated by the ratio of the specific to non-specific activity ({mean striatal activity-mean occipital activity}/mean occipital activity.) **Results**: In the patients group, the median baseline binding potential was 3.16 (range: 2.67-3.6), in the control group, this value was 3.09 (range: 2.78-3.6). A Mann-Whitney U-test revealed that this difference was not statistically significant (Z=-0.32, p=0.96). In the patient group, the median binding potential after sertraline administration was 2.79 (range: 2.64-3.33), which indicates a decrease of 9 % of FP-CIT binding. HAM-D scores showed 48% decrease after sertraline 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 occupancy (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 D_2 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. Additionally, endogenous dopamine release, induced by psychostimulants, may differ in drug-addiction. We recently developed a high-resolution single-pinhole SPECT system to perform studies 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 [^{123}I]IBZM and our pinhole SPECT system. **Materials and Methods***:* Male c57BL/6J mice were scanned on our single-pinhole SPECT system [Habraken et al. JNM 2001]. In this system, the mouse is tightly fitted 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 ARC3000© scintillation camera. A 2-mm pinhole aperture was used. All experiments were acquired, step and shoot, with a 20% energy window around 159 keV in a 64 x 64 matrix, ROR of 25 mm, field of view 28.8 mm. Reconstruction was performed using the Feldkamp algoritm. Images were analyzed with fixed ROIs for the striatum and cerebellum. In a first study, mice were injected intravenously with 20 up to 70 MBq [^{123}I]IBZM and scanned continuously up to 2 h p.i. (10 frames of 12 min.) to study the pharmacokinetics of the radiotracer (7 studies in 4 mice). In a second experiment, the feasibility to assess dopamine release was evaluated. Nine mice were injected 5 min. before IBZM injection (40 MBq) with saline i.p., and acquisition was started 90 min. (1 timeframe of 30 min.) after bolus injection of IBZM. Approximately 1 week later, the same group of mice was rescanned, but now the mice received 2.5 mg per kg body weight amphetamine i.p. 5 min. prior to the injection of IBZM. **Results**: Injection of [^{123}I]IBZM resulted in clear specific binding in the striatum, with highest specific to non-specific binding ratios 90 min. after injection. In the second experiment, amphetamine induced a significant decrease in striatal IBZM binding ratios. **Conclusion**: This study shows the unique possibility to image striatal D2R and to assess endogenous dopamine release in the mouse brain.

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

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Aim: Quantitative assessment of functional PET data is attractive since it can lower variability across institutions and may enhance the consistency of image interpretation independent of reader experience. Various quantitative indices have been suggested for functional brain 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 common 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. **Materials and Method:** 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 9 ^{18}F-DOPA studies of patients potentially suffering from Parkinson's disease. For the latter, the external brain contour was drawn manually using the patient's coregistered MRI to exclude the bony 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:** Phantom studies 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 (8.0). The SUSI estimate is nearly constant in the striatum for ROIs greater than 57 cm^3. Below this volume, the SUSI estimates are not reliable. The clinical studies seem to report 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 using phantom and clinical data that the SUSI is approximately independent of the ROI size allowing to guarantee good reproducibility of quantitative parameters estimates.

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Assessment of Regional GABA-A Receptor Binding Using ^{18}F-fluoroflumazenil Positron Emission Tomography in Spastic Type Cerebral Palsy without Periventricular leukomalacia on MRI

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Objective: Periventricular leukomalacia (PVL) due to hypoxic ischemic insult to the immature brain, chorioamnionitis and maternal infection are the major etiological factors of spastic type cereral palsy (CP). In this study, cerebral gamma-aminobutyric acid (GABA)-A receptor PET imaging using [^{18}F]-fluoroflumazenil (FMZ) was performed in 5 patients(mean age 10.6±4.09 years old, 3 males and 2 females) with spastic diplegia type CP without obvious PVL on conventional MRI, and compared with those of normal control (n=10, 8 males and 2 females, mean age 21±2.2 years) to investigate the role of the GABAergic inhibitory neurotransmission in the pathogenesis of abnormal motor function in CP. **Methods**: The Gross Motor Function Classification System (GMFCS) scales were measured in the patients. Diffusion tensor imaging with tractography was performed to evaluate the connectivity of the pyramidal tract. The PET data were acquired for 20 minutes 20 minutes after injection of approximately 5.5 MBq (0.15 mCi)/Kg of [^{18}F]-FFMZ in 3-D mode to avoid non-specific $GABA_A$ receptor binding. [^{18}F]-FFMZ-PET images obtained from the patients and controls were compared using Statistical Parametric Mapping (SPM) software. Significant increases and decreases of regional uptake were obtained using t-statistics at every voxel from patients and normal control groups. Clusters consisting of a minimum of 50 contiguous voxels with an uncorrected P<0.01 were considered to be significantly different. **Results:** The GMFCS scales of the spastic diplegia type CP patients were Level 1 in 2 patients, Level 2 in two and Level 4 in one patient.The pyramidal tracts in the patients were grossly normal in terms of connectivity and white matter volume. [^{18}F]-FFMZ binding was increased in the motor and premotor areas and bilateral visual cortices. **Conclusion;** Altered $GABA_A$ receptor binding in the motor cortices might play a important role in the pathogenesis of motor dysfunction in spastic type CP as The GABAergic signaling in the motor and visual cortices plays an important role in the development of peri-lesional or use-dependent plasticity after brain damage.

P306

The role of neuroimaging in the diagnosis of multiple systemic atrophy (MSA)

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MSA is a neurodegenerative disease that manifests itself with clinical symptoms of parkinsonism combined with cerebellar ataxia, autonomic failure and pyramidal signs. The form with predominant parkinsonism (MSA-P) accounts for 80% cases and its differentiation from Parkinson's disease (PD) is often difficult. **The aim** was to examine potential role of scintigraphy in differerential diagnosis of MSA-P and PD using binding potential of the striatum for 123I-FP-CIT (DaTSCAN) and 123I-IBZM to reveal complex dysregulations in dopaminergic transporter/receptor system. **Methods:** The study has been performed in patients suspected for diagnosis of MSA-P based on clinical criteria including MRI and poor response to dopaminergic therapy (n = 13), patients with verified PD (n = 25), and age-matched healthy controls in order to obtain normal values of diagnostic indices with FP-CIT (n = 20) and IBZM (n = 9). Inclusion of individuals and their informed consent has been approved by ethical committee of the hospital. In patients, both FP-CIT and IBZM examinations have been performed with the same administered activity (185 MBq). Control subjects underwent only one study, either FP-CIT or IBZM. SPECT data have been recorded by triple-head gamma camera Picker Prism 3000 and dual-head gamma camera GE Infinia-Hawkeye. Striatal binding capacity has been assessed visually and semi-quantitatively as binding ratios striatal/occipital (SOR) for FP-CIT and striatal/frontal (SFR) for IBZM. **Results:** In comparison with healthy controls, significantly reduced SOR has been found in both MSA-P and PD patients (p=0.01) in nucleus caudatus and in putamen. However, no difference has been found between the two groups of patients. In patients with MSA-P, there was no difference in density of presynaptic D-transporters between nucleus caudatus and putamen. In contrast, SFR has been significantly reduced in nucleus caudatus and in putamen in patients with MSA-P with respect to healthy controls (p=0.01) while no such difference was found in patients with PD. In 5 of 13 patients suspected for MSA-P, diagnosis has been changed to PD due to normal density of D2 receptors in the striatum. In patients with MSA-P, binding capacity for postsynaptic D2 receptors was reduced more in putamen than in nucleus caudatus (p=0.05). **Conclusion:** Assessment of dopaminergic transporter density in striatum using only FP-CIT is not sufficient to differentiate MSA-P from PD. Instead, complex information is required on the dysfunction of dopaminergic transporter/receptor system in the striatum that can be obtained by comparison of FP-CIT and IBZM scans.