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Several studies have been demonstrated that the motor improvement derived from high frequency deep brain stimulation (DBS) of the subthalamic nucleus (STN) in Parkinson's disease (PD) is maintained over time after surgery. Aim of the present prospective follow-up study was to assess regional cerebral blood flow (rCBF) changes related to such improvement in the long term. Methods: Ten PD patients with STN-DBS implantation underwent three rCBF SPECT at rest, once preoperatively in the off-drug condition, and the other two post-operatively in the off-drug/on-stimulation conditions at 5±2 and 42±7 months. Patients were administered with UPDRS, H&Y and S&E scales. SPM was used to investigate both the rCBF changes during long-term STN stimulation in comparison with pre-operative rCBF and the relationship between rCBF and UPDRS scores used as covariate of interest. Results: All patients showed a maximum clinical improvement during the first months after surgery and remained rather stable during further follow-up. The effect of STN-DBS from the pre- to the post-operative condition at 5 months was to produce rCBF increases in the pre-supplementary motor area (pre-SMA), premotor (PMC) and dorsolateral prefrontal cortices. From the post-operative condition at 5 months to that at 42 months the STN stimulation produced a further rCBF increases in these frontal areas, and also in the primary motor/sensory cortices, globus pallidi, ventral lateral thalamic nuclei, cerebellum, pons, and midbrain entailing the substantia nigra ($p < 0.0001$). A correlation was detected between the improvement in motor scores and the rCBF increase only in the right pre-SMA and in the left PMC ($p < 0.0001$). Conclusion: our follow-up study suggests that the long-term STN stimulation leads improvement in neural activity in frontal motor/associative areas. After an rCBF increase during the first months of stimulation, these cortical regions showed a further increment in the later phase which was accompanied by an increased activity in several subcortical structures. The correlation between motor improvement and rCBF increase in higher order motor cortical areas suggests that even in the long-term, as well as in the short one, the STN-DBS achieves its therapeutic benefit by restoring the activity within these cortical regions.

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### Anterior Cingulate Hypoperfusion Can Differentiate Progressive Supranuclear Palsy From Parkinson's Disease; Voxel-Based Analysis And CBA-Based PCA Analysis Of 99mTc-ECD SPECT Data

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Progressive supranuclear palsy (PSP) is an akinetic-rigid syndrome that could be difficult to differentiate from Parkinson's disease (PD) based only on clinical criteria, particularly at an early stage. Various neuroimaging techniques and methods (structural-MRI/DWI-MR/VBM/PET/SPECT), including $^{99m}$Tc-ECD SPECT, have been proposed as tools for aid the differential diagnosis. **Aim:** We used voxel-based analysis (SPM2) and Computerised Brain Atlas (CBA)/Principal Component Analysis (PCA) of $^{99m}$Tc-ECD SPECT data to test whether: 1) specific patterns of rCBF abnormalities could differentiate PSP from controls and PD; 2) functional connection between distinct brain regions can be found in PSP and PD. **Materials & Methods:** Nine PD (6M/3F, 65±6yrs, disease duration:2±2yrs), 16 PSP patients (9M/7F, 67±6yrs, disease duration:3±1yrs) and 10 controls (4M/6F, 59±16yrs) were studied with $^{99m}$Tc-ECD SPECT (Ceraspect/matrix:128x128/voxel size:1.67x1.67x1.67mm/Butterworth-cut-off:1-order:10/Chang-$\mu$=0.12 cm$^{-1}$). SPM2: images were spatially normalised in the MNI space (voxel size:2x2x2mm), smoothed (12mm), and normalised to the global brain activity (proportional scaling). A single-subject condition and covariate model (sex/age:nuisance variables; disease groups:different conditions) was used (voxel-level:uncorrected $p<0.001$; cluster-level:corrected $p<0.05$). PCA: images were spatially normalised in the CBA space and activity normalised to a global preset value (50 uptake units). Normalised rCBF brain counts obtained with a set of VOIs were analysed with ANOVA/Tukey's post-hoc test. PCA was applied to the VOI data to identify sequential principal components accounting in decreasing order for the global variability between the data. Statistical significance was set at $p<0.05$. Results are reported relative to the clinically more affected side. **Results:** SPM2 analysis revealed relative hypoperfusion in: anterior cingulate (AC, BA32) and ipsilateral medial frontal cortex (BA8) in PSP<Controls ($p=0.001$); contralateral AC (BA32) and medial frontal gyrus (BA9) in PSP<Controls&PD ($p=0.001$); contralateral AC (BA32) and medial frontal gyrus (BA9) ($p=0.048$) plus a trend ($p=0.074$) in contralateral prefrontal cortex (BA10/46/47) in PSP<PD. Discriminant analysis of contralateral AC (x,y,z:-4,25,30) peaks correctly classified 13/16 (81%) PSP patients.CBA analysis revealed relative hypoperfusion in: bilateral BA24/32 (PSP<Controls&PD, $p<0.005$); bilateral BA23 (PSP<Controls, $p<0.05$); ipsilateral BA39/40 (PD<PSP, $p<0.05$). PCA identified 3 factors including: bilateral BA23/24/caudate (PSPvs.Controls&PD, $p=0.000$); bilateral BA39/40 (PSPvs.PD, $p=0.019$); bilateral BA7/32 and ipsilateral thalamus (PSPvs.Controls, $p=0.009$). **Conclusions:** 1) AC hypoperfusion seems to be a distinct sign differentiating PSP from Controls and PD; 2) PSP patients show a relatively more preserved rCBF in parietal associative cortex and precuneus compared with PD; 3) clusters of cortical and subcortical brain regions with decreased (BA23/32/caudate) or preserved (BA39/40/7) rCBF are distinct functional components of brain abnormalities in PSP.

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### Brain Glucose Consumption Deficits in Wilson's Disease as Imaged by [$^{18}$F]FDG-PET

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In Wilson's disease (WD), copper accumulation in the brain may result in Parkinson-like symptoms. This is in keeping with our recent findings of neurological WD being accompanied by a concordant pre- and postsynaptic deficit of dopaminergic neurotransmission [*Am J Neuroradiol* 2003]. It is unknown to a large extent, however, how the cerebral glucose consumption is altered in this disorder. To answer this question, the present study was initiated. For that, 50 patients with verified WD (gene diagnostics, [$^{64}$Cu]copper test) underwent high-resolution brain PET (ECAT EXACT HR+ camera, Siemens/CTI) after i.v. administration of 370 MBq [$^{18}$F]FDG. According to the course of the disease, the patients were sub-grouped as non-neurological WD (n=16), pseudoparkinsonian WD (n=9), pseudosclerotic WD (n=20) and mixed neurological WD (n=5). The severity of neurological symptoms was evaluated using an established linear scoring system (0=no to 4=severe symptoms). The PET data of the WD patients were analysed by comparing them voxelwise/on ROI basis with a normal template constructed of an age-matched control group (n=15) and applying the software BRASS (Hermes Medical Solutions). By employing the described technique, we found no significant (mean z-score in ROI < -2.0) [$^{18}$F]FDG uptake deficits in non-neurological WD patients. In contrast, in neurological WD patients, a significant decrease in [$^{18}$F]FDG uptake was detected bilaterally in caudate heads and putamina (mean z-scores = -2.0 to -3.8; $p < 0.001$). Most severe striatal deficits were found for the pseudosclerotic (mean z-score = -4.5), followed by the mixed neurological (-3.6) and pseudoparkinsonian (-2.4) course of the disease ($p(ANOVA) < 0.001$). The total volume of voxels with a z-score < -2.0 was significantly larger for the neurological vs. non-neurological WD patients (35 ± 29 vs. 18 ± 16 ml; $p = 0.018$). For all WD patients, the striatal [$^{18}$F]FDG uptake was negatively correlated with the severity of neurological symptoms and positively correlated with the duration of anti-copper drug treatment ($r = -0.61$ and $0.64$ ($p < 0.001$) for right putamen). From these results we conclude that patients with neurological WD (mainly) have a striatal deficit in brain glucose consumption. The degree of this deficit depends on the course and severity of the disease. Furthermore, there is initial evidence that [$^{18}$F]FDG brain PET might be suitable to monitor the effect of anti-copper therapy. Verification of this presumption, however, will require further analysis of the follow-up examinations in our WD patients which are currently underway.

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### Role of coupled brain perfusion and dopamine transporter imaging in the diagnostic of cortico-basal degeneration (CBD): a double isotope study

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**Objectives:** CBD is a progressive movement disorder characterized by frontoparietal cortical degeneration and asymmetric parkinsonism. Because the clinical manifestations of CBD are diverse, they may overlap with those of other neurodegenerative diseases, making its diagnostic difficult. We sought to explore the interest of simultaneous perfusion and dopamine transporter imaging in the diagnostic of CBD. **Patients and methods:** Simultaneous dual isotope 99mTc-ECD and 123I-FP-CIT studies were performed in 9 consecutive patients clinically suspected of CBD and 9 normal subjects, using a triple-head camera with low energy, high resolution collimators. Projections were acquired in 8 asymmetric energy windows, corrected for scatter, cross-talk and high-energy penetration using an Artificial Neural Network previously developed (1), and reconstructed while modeling patient-specific attenuation and variable collimator response in the projector/backprojector of an OSEM algorithm (6 subsets, 12 iterations). FP-CIT and ECD studies were spatially normalized to respectively a FP-CIT and perfusion MNI template using SPM2 software. Z-scores of mean cortico-cerebellar ECD activity were then calculated in volumes of interest obtained from parcellation of the MNI MRI single subject brain (2). Z-scores of FP-CIT binding potential were also calculated in the caudate and putamen, as well as indexes of striatal asymmetry. The significance threshold was set to 1.5. **Results:** Striatal FP-CIT binding potential was significantly decreased in 5 patients, associated to a parietal hypoperfusion, thus consistent with the diagnostic of CBD. Uptake was asymmetric for both tracers in 4 of them. Hypoperfusion also involved asymmetrically frontal and temporal cortices, as well as subcortical structures. Diagnostic remained uncertain in one patient, showing asymmetric (20 %) but normal dopamine transporter uptake, and a unilateral parietal hypoperfusion (z-score = 3). FP-CIT uptake was normal in the 3 remaining patients. Two of them presented a severe bilateral although asymmetrical posterior cortical hypoperfusion, consistent with the pattern of anomalies observed in posterior cortical atrophy. The last one showed a bilateral frontal hypoperfusion, suggestive of frontotemporal dementia (3). **Conclusion:** Histopathological studies have demonstrated that « CBD syndrome » is not specific for CBD, but may correspond to other disorders such as Alzheimer's disease, progressive supranuclear palsy, and frontotemporal dementia. Our results suggest that quantitative double isotope studies are useful in the diagnostic of CBD patients.1) El Fakhri G et al. IEEE Trans Nucl Sci 2000 ; vol 47, 4:1573-1580. 2) Tzourio-Mazoyer N et al. NeuroImage (2002) ; 15, 273-289. 3) Wakabayashi K et al. Neuropathology 2004; 24 , 79-86.

## P310

### SPM Analysis of Brainperfusion SPECT and Cognitive Dysfunctions in Patients with Transient Global Anmesia

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**Objectives:** Transient global amnesia (TGA) is known as a disease of benign nature characterized with clinically transient global amnesia and a variable degree of global retrograde memory impairment, but it usually resolved within 24 hours. The aims of this study are to assess the alterations in regional cerebral blood flow (rCBF) by Tc-99m HMPAO imaging with statistical parametric mapping (SPM) analysis and to verify the cognitive deficits by neuropsychological test in TGA patients. **Methods:** Eleven patients (M/F :3/8, 55.1±8.2 years) with TGA and age-matched normal control subjects participated in this study. Education period of patients was 8.1±3.5 years. Tc-99m HMPAO brain perfusion SPECT was performed within 1 to 14 days (mean duration: 7.3±5.2 days) after the events to measure rCBF. SPM images were analyzed using SPM (SPM99) with Matlab 5.3 and Talairach daemon program. Korean-Mini Mental State Examination (K-MMSE) and Seoul Neuropsychological Screening Battery (SNSB) test was also done within 2 to 8 days (mean duration: 3.75±2.19 days) for cognitive functions in 8 of 11 patients with TGA. **Results:** The score of K-MMSE and SNSB were 3.8±2.2 and 27.5±2.9, respectively. The SPM analysis of SPECT images showed significantly decreased rCBF in the left inferior frontal gyrus (Brodmann area 9), the left supramarginal gyrus (Brodmann area 40), the left postcentral gyrus (Brodmann area 40) and the left precentral gyrus (Brodmann area 4) in patients with TGA ($p<0.01$, uncorrected). Neuropsychological test findings represented that several cognitive functions, such as verbal memory, visual memory, phonemic fluency and confrontational naming, were impaired in patients with TGA compared with normal control. Additionally, on SPM analysis, we found lesion of hyperperfusion in contralateral cerebral hemisphere. **Conclusions:** Our study shows perfusion deficits in the left cerebral hemisphere in TGA patients with several cognitive dysfunctions. And we found after clinical symptoms were resolved, the lesions of hypoperfusion were still remained in some case. We found that functional quantitative neuroimaging study and neuropsychological test are useful to understand underlying pathomachanism of TGA.

## P311

### Tc-99m HSA Brain SPECT - a Nuclear Medicine Procedure for Evidence of Plasma Protein Extravasation in Patients with Cluster Headache ?

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**Aim:** Cluster headache is characterized by episodical unilateral periorbital headache attacks. A remission for several months occurs for several weeks in 90%. The hypothesis is that the cluster headache is mediated by inflammation in the area of the sinus cavernosus. The plasma protein extravasation is a parameter for the evidence of inflammation. This pilot study was performed with Tc-99m HSA (human serum albumin) brain SPECT and had the following aims: 1) Can a transudation of Tc-99m HSA in the sinus cavernosus ipsilateral to the pain location be assessed during the acute cluster headache attack (CHA) ? 2) Can different activity ratio´s (AR) be found during the cluster headache episode (CHE) and the remission episode (RE) in the ipsilateral sinus cavernosus as evidence for an inflammation ? **Methods:** Five patients (5 m, aged 25-50 yr) were investigated. 650 MBq Tc-99m HSA were injected intravenously. The first brain SPECT was performed 10 minutes after injection. After that the patients received 1.2 mg nitroglycerin i.v. to trigger a CHA. The patients were not treated in the first 20 minutes after triggering of the CHA in order to achieve a transudation of Tc-99m HSA but were treated after 20 minutes and a second brain SPECT was performed in the painless condition. The separate determination of AR of the Tc-99m HSA uptake in the sinus cavernosus for each side yielded the effect variable. Reference region was the cerebellum. The AR were determined in region of interest technique after fusion of SPECT with MRI data (software: MPI tool, firm Advanced Tomo Vision). The first comparison of the AR were performed within the CHE. AR was received before and after the CHA. The second comparison of the AR was done between the CHE and the RE. **Results:** No significant differences were found between the AR of the ipsilateral and contralateral sinus cavernosus in the CHE: AR before CHA 1:1.02 ± 0.08 (mean ± SD), AR after CHA 1:1.20 ± 0.46. AR in ipsilateral sinus cavernosus in CHE (4.3 ± 1.5) and in remission episode (4.0 ± 0.9) showed no significant differences. **Conclusions:** The results of this pilot study show that the Tc-99m HSA brain SPECT is not suitable for the assessment of a plasma protein extravasation as correlate for inflammation in the CHE.

## P312

### Evaluation of Cerebral Blood Flow during Hyperthermia using $^{99m}$Tc-HMPAO

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**Introduction:** Hyperthermia is a condition with significant impact on organ function. Clinical studies indicate that hyperthermia can cause heat-stroke with cerebral ischemia and brain damage. It is also known that there are casualties related to high environmental temperature. This study is the first to examine the direct effects of heating carotid arterial smooth muscle which is the main arterial blood supply to the brain, and tested the hypothesis that hyperthermia induces arterial vasoconstriction and thereby decreases cerebral blood flow. **Methods:** Adult male New Zealand White rabbits (n=20) were used in this study. Carotid arterial segments were prepared and set up for isometric tension recording in organ baths containing Krebs solution. Cerebral blood flow was assessed using $^{99m}$Tc-HMPAO (IV). Scintigraphic images were acquired using gamma camera and the average count was determined. Differences between mean values were tested for significance using Student t-test. They were considered significant if $P<0.05$. **Results:** Heating produced reproducible temperature-dependent contractions of the carotid artery segments, which was proportional to the temperature. Hyperthermia to 43° C inhibited norepinephrine concentration-dependent contractions ($ED_{50}$=1μM, 6μM for 37 & 43°C respectively, n=5, $P<0.05$). Heating also inhibited sympathetic electrical field stimulation (EFS) (70v, 2.5-50 Hz) evoked frequency-dependent contractions (at 43°C, 25 Hz response was reduced by 40.2±3%, n=5, $P<0.05$). The uptake of $^{99m}$Tc-HMPAO was significantly reduced by 80.1±5% (n=4, $P<0.01$), indicating a decrease in cerebral blood flow. **Conclusion:** Our data indicate that hyperthermia-induced vasoconstriction of the carotid artery is a crucial factor of cerebral ischemia as illustrated by significant decrease of $^{99m}$Tc-HMPAO uptake, and consequent brain damage of heatstroke. Based on these results and our previous finding of cooling-induced vasodilatation, cooling of the neck (cold neck collar) should be considered in the treatment of heatstroke.

## P313

### 18f-fdg pet in the evaluation of brain function after extra-corporeal circulation.

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Antegrade selective cerebral perfusion ASCP is a method of cerebral protection introduced recent years. Aim of our study was to evaluate the efficacy of brain protection to prevent neurocognitive deficits and ischemic brain injury following aortic arch operations.We prospectively studied 12 patients treated with aortic arch operation with ASCP according to the Kazui technique and 8 patients aged and sex matched treated with elective on-pump CABG.All patients underwent 3 PET scans: the first before surgery, the second within the first week after surgery and the third delayed 6 months after surgery.PET scans (15' em, 2' trans) were acquired 30' after the injection of 370 MBq of 18F-FDG with GE ADVANCE Nxi scanner.Images were reconstructed with a standard OSEM 2D iterative algorithm and the segmented attenuation correction was applied.All images were visually inspected by an expert nuclear medicine physicians and no areas of significant abnormalities, in terms of 18F-FDG uptake, were detected.All 20 patients acquired before surgery, 12 from the aortic group and 8 from the coronary group, were used as control group. The two groups after surgery and the two groups delayed were separately analysed and compared with the control group using SPM2 software in a voxel-wise manner.A 2-sample t-test ($p<0.005$, uncorrected) was used for statistical analysis and significant voxels were projected onto the 3D render brain for visualization of the t-score statistics.The coronary group didn't show any significant statistical differences from the control group for both the post surgery and the delayed scans.The post surgery aortic group showed an area, located in the occipital lobe, of statistically significant reduction of glucose uptake compared to the control group. The same area got normal in delayed images.Neuropsychological assessments showed no significant difference in pre-surgical, early and delayed post surgical tests.Our preliminary results show that FDG PET could be an useful tool to monitor brain damages after extra-corporeal circulation. Glucose hypo metabolism in early scan in aortic group needs to be confirmed and further investigated.

P29 — Monday, October 17, 2005, 2:30 pm — 4:00 pm

## Dementia

## P314

### Improved Diagnosis of Moderate Alzheimer's Disease by Optimising Counts Normalisation. A CBA-based Principal Component Analysis of Perfusion SPECT

**M. M. E. Pagani**[1], F. Nobili[2], D. Salmaso[1], C. Jonsson[3], M. Finnbogason[3], C. Rickman[3], S. A. Larsson[3], G. Rodriguez[2]; [1]Institute of Cognitive Sciences and Technologies,CNR, Rome, ITALY, [2]Clinical Neurophysiology, Dept. of Endocrinological and Metabolic Sciences,University of Genoa, Genoa, ITALY, [3]Dept. of Nuclear Medicine,Karolinska Hospital, Stockholm, SWEDEN.

**Aim:** In brain perfusion SPECT studies normalising voxel intensity to values chosen with different modalities might affect the results in group comparisons. Already in the moderate phase of Alzheimer's Disease (AD) decreased count density distribution involves a large amount of voxels not only in parietal and temporal cortex but more diffusely across the brain. Including their values to calculate the common denominator chosen for normalisation could result in lower analysis sensitivity. The aim of this study was to normalise the data sets of moderate AD and normal controls (CTR) to a variety of common denominators representing voxels with different intensities and to identify those yielding better groups discrimination. **Material and Methods:** Thirty-seven CTR and 27 patients with moderate AD (mean MMSE score: 14.6) were investigated with 99mTc-HMPAO and SPECT. Raw data were normalised to 8 common denominators ranging from the average of the 40% of voxel with the lowest intensity value to the average of the 80% of voxels with the highest intensity value. Principal Component Analysis (PCA) was implemented for each normalisation on 27 VOIs in each hemisphere, thus identifying the factors to be analysed. The statistical differences relative to each normalisation procedure were assessed by ANCOVA and step-wise discriminant analysis was performed to assess the concordance between SPECT data and clinical diagnosis. **Results:** PCA grouped VOIs into a number of factors ranging from 7 to 12, varying with the common denominator chosen. Four factors including regions from anterior cingulate cortex, frontal pole, left temporal pole and visual cortex, respectively, were highly reproducible across the 8 different normalisation procedures. Group difference between AD and CTR was significant after normalising the raw data for the average of the highest 20%, 40% and 60% of total counts. The corresponding accuracy values in discriminant analysis were 83%, 83% and 91%, respectively. **Conclusion:** Grouping of VOIs into factors varied across the different normalisation procedures. Normalising the raw SPECT data for the highest 60% of the total counts resulted in a better discrimination between AD and CTR reaching diagnostic sensitivity and specificity of 89% of 92%, respectively.

## P360

### [$^{123}$I]ADAM SPECT in Primate Brain with and without Fluoxetine Pre-treatment

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[$^{123}$I]ADAM is a new radioligand specific for serotonin transporters. In this study, we evaluated the specificity of [$^{123}$I]ADAM after pre-medication with fluoxetine in primates. **Methods:** Two healthy primates (*Macaca cyclopis*) were studied. Before bolus injection of [$^{123}$I]ADAM (180 MBq), the fluoxetine(5mg/kg)was administration intravenously over 25 min. Dynamic SPECT studies were performed after administration of [$^{123}$I]ADAM for 4 h using a dual-headed camera equipped with ultrahigh resolution fan-beam collimators (GE, Millennium VG Hawkeye). Simple [$^{123}$I]ADAM SPECT without pre-medication with fluoxetine was also performed. Except for visual inspection, specific uptake ratios (SUR) of midbrain (MB), thalamus (TH) and striatum (ST), using cerebellum as reference were measured. **Results:** The simple [$^{123}$I]ADAM SPECT without pre-medication with fluoxetine showed a prominent uptake of $^{123}$I-ADAM in the MB, TH, and ST whereas the cerebellum had little uptake. The SPECT of fluoxetine pre-treatment showed enhanced initial uptake of [$^{123}$I]ADAM in the whole brain. However, the brain [$^{123}$I]ADAM uptake was gradually diminished after 1 hour of SPECT imaging. The SUR of MB, TH, and ST in the fluoxetine pre-treatment studies were marked lower than those of single [$^{123}$I]ADAM injection studies. There was no major side effect found during and after imaging. **Conclusion:** The brain distribution of $^{123}$I-ADAM in primates appears correlated with the known distribution of SERT. The transient increase of [$^{123}$I]ADAM in the whole brain shortly after [$^{123}$I]ADAM injection may represent non-specific circulatory uptake due to fluoxetine blockade of serotonin transporters outside the brain. The decreased SUR of MB, TH, and ST in the fluoxetine pre-treatment studies suggest [$^{123}$I]ADAM was high specific for serotonin transporters.

## P361

### Dopamine Transporter (DAT) imaging in the canine brain

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IntroductionSince patients with Parkinson's disease are reported to have comorbid depression in 50% of cases, SSRI are regularly used as antidepressive treatment. SSRIs selectively block the Serotonin Transporter (SERT) and hereby increase serotonine in cortical and subcortical regions.[123I]FP-CIT SPECT (DAT-scan, Amersham) is used to assess Dopamine transporter (DAT) binding index. This tracer is threefold more selective for the DAT compared to the SERT and in striatum, DAT is 30-fold more present compared to SERT.In this study we investigate the feasibility of [123I]FP-CIT receptor imaging in the dog and the feasibility to study the effect of SSRIs on the DAT in the dog brain.MethodsTwo healthy female german shepherd dogs (age 2y and 6y) were included in the study.[123I]FP-CIT (DATscan, Amersham) was used to calculate the DAT binding index. Dogs were injected [123I]FP-CIT (185 Mbq) and scanned after 3 h during 20 minutes.SPECT imaging was performed with a triple headed gamma camera (equipped with high resolution fan beam collimators (FWHM 7.8 mm). ROIs were placed on the activity distribution in the MRI neuroanatomical region of the striatum. The cerebellar cortex was used as a reference region since the cerebellum is void of DAT.Dogs were scanned in blank conditions and were scanned after administration of citalopram and sertralin (SSRIs) in physiological doses.ResultsThe blank scan experiment revealed the highest binding index in the striatum. Binding in others regions was negligible. After administration of citalopram (0.25 mg/kg) or sertralin (1.25 mg/kg) the binding index in the striatum increased with a mean of 180% .DiscussionThe SERT blocking study with citalopram and sertralin assessed with [123I]FP-CIT SPECT demonstrated that the striatal/cerebellar ratio is increased after administration of an SSRI. These results are compared with the existing literature in animals and humans and hypotheses explaining this finding are generated.ConclusionAt first, this study demonstrated the feasibility of [123I]FP-CIT SPECT in dogs. Since radiation burden is less an issue in animal studies, the effect of different SSRIs at different doses can be compared in a within-subject design.Secondly, since the administration of a single dose of SSRIs increased the striatal/reference region 123I]FP-CIT SPECT binding index, this finding must be further explored in human experiments, especially in Parkinson's Disease patients that have a reduced DAT/SERT ratio in the striatum.

## P362

### Atypical versus Conventional Antipsychotics: Clinical and Functional Follow-up of Schizophrenic Patients

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**Aim:** We evaluated regional cerebral blood flow (rCBF) changes in schizophrenic patients after substitution of haloperidol by risperidone, correlating differences in symptomatology and brain perfusion caused by different effects of these drugs, which is important because of the non-uniformity in follow-up of schizophrenic patients and incosistencies in rCBF findings according to different conventional and atypical antipsychotic treatments. **Materials & Methods:** 29 patients who met DSM-IV criteria for schizophrenia were included in the study, all treated with haloperidol. Patients symptoms were assessed using Positive and Negative Syndrome Scale on the day of their first single photon emission tomography (SPECT), which was performed 45 minutes after injection of 1110 MBq of $^{99m}$Tc-ethylcysteinate dimer. Both protocols were repeated three months after substitution of haloperidol by risperidone. We performed intrasubject analysis of the same regions between two SPECT studies and correlated symptom dimensions to brain perfusion. Descriptive statistisc, parametric (t-test) and nonparametric (Wilcoxon test) methods of determination of differences, as well as Pearson correlation between symptoms and rCBF, were applied in data processing and analysing. **Results:** We found significant decrease in symptom score dimensions, suggesting clinical improvement after substitution of haloperidol by risperidone, as well as the frequency and the intensity of extrapyramidal side effects. We found hypofrontality in both SPECT studies, but even we noticed slightly higher perfusion rates in the second study, the differences were not statistically significant, except for the lower perfusion in the right central region. Significantly increased perfusion was found in inferior temporal region bilaterally and decreased in thalami, both slightly greater on the right side of the brain. In both studies and in most of the regions, we found right-left hemisphere assimetry. There were numerous correlations between symptoms and locoregional perfusion which changed after risperidone treatment and clinical improvement. **Conclusion:** Comparing two SPECT studies in the same patient, we had the possibility to confirm functional impairments and follow up rCBF changes during different antipsychotic regimens, thus objectively evaluating therapy response. Symptoms correlated with dysfunction in various regions of the brain, following diverse lateralisation patterns. Accordingly, different types of antipsychotics with different affinities for many kinds of receptors in different ways modifies brain perfusion. Psychopathological improvement and the drug by its own mechanism alterate correlations between symptoms and cerebral blood flow in particular brain regions.

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### Clozapine effect on rCBF in patients with treatment-refractory schizophrenic patients.

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Aim:Clozapine is a second generation antipsychotic drug with superior therapeutic action, however its mechanism has not been fully understood. The aim of study was to investigate the clozapine effect on rCBF and to test the correlation between the perfusion changes and clinical/neurocognitive response in schizophrenia.Material and method:Fifteen schizophrenics (7 f, 8 m, 29.9 ± 8 yrs) who met DSM-IV criteria were studied. Patients were given clozapine after one week of drug free interval. Psychopathology and neurocognitive functioning were assessed at baseline and 8 weeks after initiation of treatment. Psychopathology was assessed by PANSS. Patients were divided into subgroups according to % PANSS change with therapy. Six patients were responders with more than %25 decrease in PANNS, while 9 were nonresponders.Radionuclide imaging was performed before and 8 weeks after clozapine therapy. SPECT study was performed after injection of 740 MBq 99mTc-HMPAO (dual-headed camera, matrix:128x128, pixel: 3.9 mm, 128 projections). Attenuation correction was applied. The calculated mean counts/pixel for cortical and subcortical ROI's according to the Talairach's atlas were divided by cerebellar (C) mean counts/pixel values to obtain perfusion ratios. In addition, ratios for frontal/basal ganglia and frontal/thalamus were calculated.Results:Cortical region/C perfusion ratios did not change significantly after treatment and they were not different significantly between groups at baseline and after treatment. However, subcortical/ C ratios were significantly lower in responders after treatment bilaterally (L Thalamus/C: 0.87 ± 0.10 vs 1.04 ± 0.08, p=0.005; L Basal ganglia/C: 0.86 ± 0.09 vs 1.08 ± 0.09, p=0.009; R Thalamus/C:0.86 ± 0.09 vs 1.04 ± 0.78, p=0.003; R Basal ganglia/C: 0.85 ± 0.11 vs 1.07 ± 0.09, p=0.001). Left and right Frontal/basal ganglia ratios were higher in responders compared to nonresponders, indicating relatively better perfusion of frontal cortex (L F/BG: 0.99 ± 0.13 vs 0.83 ± 0.09, p=0.01; R F/BG: 1.012 ± 0.03 vs 0.826 ± 0.12, p=0.02, respectively). Responders showed higher % change in frontal/subcortical perfusion ratios ( L F/tha.: %13.9 ± 9 vs -3.2 ± 15, p= 0.04; L F/basal gang.: %16.48 ± 6.5 vs -5.8 ± 15, p=0.005; R F/basal gang.: %14.7 ±11.8 vs -2.6 ± 14, p=0.03).Conclusion:It seems that clozapine causes relative increase in bilateral frontal cortex perfusion and relative decrease in bilateral subcortical perfusion in schizophrenic patients with clinical improvement in short-term. In contrast, unresponsive patients have relative higher perfusion in subcortical regions.

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### Increased rCBF in Atypical Depression as compared to Major Depressive Disorder and Normal Controls. A SPECT study.

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**Aim:** Atypical Depression (AtD) is a subtype of Major Depressive Disorder (MDD) and is considered to be neurotic in nature resulting in an increased psychopathological response to external stimuli. A previous study found that AtD as compared to normal controls (CTR) showed global brain hypoperfusion, especially in the right frontal lobe. The aim of the present study was to assess regional cerebral blood flow (rCBF) differences at hemispheric and Volume of Interest level between AtD and MDD patients and CTR. **Material and Methods:** Eleven AtD and 12 MDD outpatients and 23 CTR were studied. 99mTc-HMPAO SPECT, using a three-headed gamma camera, was performed and group analysis was carried out by a Computerised Brain Atlas able to standardise brain anatomy in 3D space. The uptake in 27 functional sub-volumes (VOIs) of the brain bilaterally, including the most of Brodmann areas (B), basal ganglia and thalamus, was analyzed by ANOVA. The significance level was set at p = 0.05. **Results:** No age difference was found between the groups. ANOVA showed a significant hemispheric difference ($p<0.001$) and a VOI*group interaction ($p<0.001$). In the CTR/AtD comparison, there were significant rCBF differences in nc.caudatus ($p<0.025$) and in right hemisphere ($p<0.005$). A significant rCBF difference was also found in MDD/AtD comparison in B5. In all these regions there was a rCBF increase in Atd as compared to the other groups. **Conclusion:** This study confirms previous findings of neurobiological abnormalities underlying Atypical Depression. Atypical Depression as compared to Major Depressive Disorder showed increased rCBF in parietal associative cortex, previously described as the core perfusion deficit in depressed patients. Furthermore, we found in Atypical Depression patients as compared to normal controls, raised rCBF in nc.caudatus, gathering all nervous fibres from associative cortices, and in the whole right hemisphere, known to be involved in processing emotions. These findings confirm rCBF changes in psychiatric disorders and support the concept of considering Atypical Depression reactive in origin.