normally observed during the acute influx phase before the maximal venous blood alcohol concentration is reached (elimination phase). Despite the psychiatric and forensic relevance of the different ethanol effects, the underlying neuronal mechanisms are still unclear. It was the purpose of this study to investigate changes in neuronal activity by means of FDG-PET, EEG and psychophysiological testing during the acute cerebral ethanol uptake. **Methods:** We investigated so far 15 male healthy volunteers each with three different experimental conditions in a randomized order. 1. influx phase: FDG bolus simultaneously with an intravenous ethanol infusion; 2. elimination phase: FDG bolus 15 min after the end of the ethanol infusion (both conditions 40 g in 500 ml 0. 9% NaCl saline for 15 min); 3. placebo condition: FDG bolus simultaneously with an intravenous infusion of 0. 9% NaCl saline. During and after the ethanol (or placebo) infusion EEG and psycho-physiological testing were performed with subsequent PET acquisition. The PET data were analysed using SPM99. **Results:** The categorical comparisons of influx phase vs. placebo and elimination phase vs. placebo, respectively, revealed focal metabolic increases in the bilateral striatum ($p<0.001$) and decreases in occipital cortical areas (in particular in the primary visual cortex) ($p<0.001$). The comparison of influx phase vs. elimination phase showed a focal metabolic increase in the anterior cingulate cortex and in the right inferior frontal cortex ($p<0.001$). The correlation analysis of the PET data with the EEG spectra as well as with the psychophysiological data is currently under examination. **Conclusion:** The present data indicate a close inverse relationship between striatal and visual cortical activity under the acute influence of ethanol. Acute ethanol administration in healthy volunteers stimulates those striatal regions, which are considered to have particular relevance for alcohol craving ("reward system"). The reduced visual cortex metabolism might be the neuronal equivalent of the alcohol induced pathophysiological phenomena of visual field narrowing and perception threshold elevation.

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Effect of Gender on Cerebral Hemispheres and Lobes Uptake in 183 Subjects Examined at Rest by 99m-Tc-HMPAO SPET

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Aim: Recent magnetic resonance studies have demonstrated a higher decline with age in grey matter volume in man as compared to woman. On the other hand gender differences in regional cerebral blood flow studies have seldom been extensively taken into account. The aim of this study was to investigate by means of 99m-Tc-HMPAO and SPET the gender-related differences in rCBF in a large population of patients and normal controls. **Material and Methods:** Forty-seven patients with Alzheimer Disease, 70 with Major Depression and 66 Controls were studied by 99m-Tc-HMPAO SPET. Radiopharmaceutical uptake was analysed by a standardisation software (CBA) automatically defining hemispheric (n=2) and cerebral lobes (n=10) outlits and calculating rCBF values. Group, gender and regional differences were assessed, after covariation for age, by analysis of co-variance (ANCOVA). **Results:** There was no interaction between group and gender at any level and so we could consider the sex differences in all 183 subjects to be independent from groups. Gender accounted for significant differences at hemispheric ($p<0.005$) and cerebral lobes (0. 001) level. At cerebral lobes level there was an overall interaction between gender and lobes ($p<0.001$) and more specifically gender differences were found in occipital ($p<0.001$), parietal ($p<0.005$) and temporal lobes ($p<0.001$). Significant interactions between sex and hemispheres were shown in frontal ($p<0.05$) and parietal ($p<0.05$) lobes. Overall right hemisphere and females had higher CBF than left hemisphere and males respectively. **Conclusions:** Significant differences related to gender were found at hemispheric and cerebral lobes level. Females had a higher rCBF and there was a trend towards a least laterality. These findings suggest to perform an accurate gender matching when investigating group differences. Since gender influenced rCBF in frontal, parietal and temporal lobes particular attention should be paid in Alzheimer Disease, Depression and Frontal Lobe Dementia studies.

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Separating functional and structural damage in Long-Term Postanoxic Vegetative State using 18-FDG PET coregistered to 3D-MRI and voxel based morphometry

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Aim: Positron emission tomography (PET), has proven to contribute new aspects to the understanding of persistant vegetative state (PVS). Most PET studies measured resting brain metabolism and demonstrated a global reduction in cerebral metabolic rate for glucose (1). Analysis of functional data, however, has not yet directly been compared to structural damage implicit in PVS. While Laureys et al. demonstrated altered cortico-cortical connectivity with the metabolically most impaired areas in frontal and parietal associative cortices (2), a direct correlation to morphologic data was not performed. The present study was intended to separate functional and structural damage in PVS using 18-FDG PET coregistered to 3D-MRI using statistical parametric mapping (SPM2b) and voxel based morphometry (VBM). **Material and Methods:** Seven patients in late stages of postanoxic PVS (3 m-4 yrs, mean 1. 6 yrs) were investigated by 18-FDG-PET and 3D-MRI. Analysis of functional and structural data was performed using SPM2b and an age matched normal database for the respective modalities. FDG-PET were coregistered to the individual 3D-MRI prior to normalization using a study-specific template created from the 7 individual MRI data sets. Results of metabolic analysis and of VBM were compared to separate regions with combined functional and structural damage from regions with functional impairment exceeding structural loss. **Results:** 18-FDG-PET showed a widespread hypometabolism at $p<0.001$ (corrected) in the parietal and frontotemporal cortices, the cuneus and precuneus, the cingulum, the frontal medial gyrus, the precentral gyrus, and the transverse temporal gyrus. In addition, there were significant hypometabolic areas within the bilateral thalamus, with the maximum localized in the right dorsomedial subnucleus (coordinates x y z: 10 -17 -10). VBM revealed extensive structural loss at $p<0.001$ (corrected) in the named cortical areas, but to a lesser extent in the thalamus. **Conclusion:** 18-FDG-PET is very sensitive for detecting metabolic impairment in PVS. Due to severe changes in morphology, however, a combined analysis of metabolic and structural data is mandatory to differentiate functional and structural damage. {1} Rudolf J. Fortschr Neurol Psychiatr 2000;68(8): 344-51. {2} Laureys S et al. , J Neurol Neurosurg Psychiatry 1999;67(1): 121.

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The Influence of Anaesthetic Concentrations of Xenon on the Regional Cerebral Glucose Metabolism Rate (rMRGlu) in Humans: A Positron Emission Tomography (PET) Study.

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Aim: In many ways, the inert gas xenon is a nearly ideal anaesthetic. Patients go under and emerge faster than with any other anaesthetic, and xenon also shows a high cardiovascular and neurohumoural stability. In contrast to isofluran or propofol, it is not yet known how xenon acts on the rMRGlu in humans when applied in anaesthetic concentrations up to cerebral saturation. This PET study, conducted on volunteers, was done to determine this mechanism (general ethics committee AC, BIS). **Methods:** So far, we examined five healthy subjects with PET, both awake and under xenon anaesthesia. About 250 MBq F-18-FDG were administered in the anaesthetic steady state (about 45 minutes after administering xenon) and the waking state and several blood samples were taken after injection (Sokoloff-Phelps kinetic model). Emission was measured 45 minutes after injection. A total of eight cerebral regions of interest (ROIs) of each subject were defined for the two superimposed reoriented scans and transferred to the corresponding PET slices, followed by absolute quantification. **Results:** Statistical analysis of rMRGlu values of paired samples for the 40 (5x8) ROIs in waking (MW+/-SD: 41. 40+/-7. 90) and anaesthetised state (MW+/-SD: 32. 60+/-5. 9) yielded a highly significant difference ($p<0.0005$) between both states. Xenon led to a significant decrease in rMRGlu of 21. 4%. A comparison of rMRGlu average values for the individual regions also yielded significant differences. **Conclusion:** Administered at deeper anaesthesia, xenon caused a significantly lower decrease in rMRGlu (-21. 4%) than did isofluran (-46%) or propofol (-55%) (Alkire et al. 1995). Therefore, the results show that Xenon does not impair glucose metabolism as strong as both other substances. But, the mechanisms are not fully understood yet. References: Alkire et al. rCMRGlu during propofol anesthesia in humans studied with PET. Anesthesiology 1995.

806 - August 25, 2003, 11:30 am - 1:00 pm, Hall E/F

Radiopharmacy / Radiochemistry: Therapeutics

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Co-injection Of Dtpa With [y90-dota-tyr-octreotide (y90-octreother) Reroutes Non-incorporated Ionic Yttrium. A Study In Rats.

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Peptide Receptor Radionuclide Therapy is being performed with radiolabelled DOTA-conjugated peptides, such as ^{90}Y-OctreoTher. The incorporation of ^{90}Y is typically ≥ 99. 5 %, however, since a total patient dose can be as high as 400 mCi the amount of free $^{90}Y^{3+}$ (=non-DOTA-incorporated) can be substantial. Free $^{90}Y^{3+}$ accumulates in bone with unwanted irradiation of bone marrow. Even if ^{90}Y-DTPA is unstable in serum *in vitro*, *in vivo* it has rapid renal excretion. Transforming free $^{90}Y^{3+}$ to ^{90}Y-DTPA might reroute this fraction from accumulation in bone to renal clearance, as therefore we have investigated: a. the biodistribution in rats of $^{90}YCl_3$, ^{90}Y-OctreoTher and ^{90}Y-DTPA; b. and the possibilities to complex the free $^{90}Y^{3+}$ in ^{90}Y-OctreoTher into ^{90}Y-DTPA prior to intravenous injection; c. the effects of free $^{90}Y^{3+}$ in ^{90}Y-OctreoTher, with/out DTPA, on the biodistribution of in rats. **Results:** 1. $^{90}YCl_3$ had high skeletal uptake (i. e. 3%ID per g femur, with main localization in the epiphyseal plates) and a 24h total body retention (TB) of 74 %ID. 2. ^{90}Y-OctreoTher had high and specific uptake in somatostatin receptor-positive tissues, and 24h TB of 20 %ID. 3. ^{90}Y-DTPA had rapid renal clearance, and 24h TB of <5 %ID. 4. Free $^{90}Y^{3+}$ in ^{90}Y-OctreoTher could be complexed to ^{90}Y-DTPA. 5. Accumulation of ^{90}Y in femur, blood, liver and spleen showed a dose-relation to the amount of free $^{90}Y^{3+}$, while these accumulations could be normalized by the addition of DTPA. **Conclusion:** if non-DOTA-incorporated $^{90}Y^{3+}$ is present in ^{90}Y-OctreoTher the addition of DTPA is strongly recommended. Corresponding author: Wouter AP BreemanErasmus MC,Dept of Nuclear Medicine3015 GDRotterdamThe Netherlandse-mail: w. a. p. breeman@erasmusmc. nlTel: #-31-10-4635317Fax: #-31-10-4635997

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Preclinical Evaluation of New and Highly Potent Analogs of Octreotide for Targeted Radiotherapy

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Aim: Earlier studies have shown that the modification of the octapeptide octreotide in position 3 and 8 may result in compounds with increased somatostatin receptor affinity and if radiolabeled, an improved uptake in somatostatin receptor positive tumors. The purpose of this study was to find radiopeptides with an improved somatostatin receptor binding profile in order to extend the spectrum of targeted tumors. **Methods:** Parallel solid phase peptide synthesis was used to

the haemo-dynamically significant ASD from non-significant. It has a valuable impact on the clinical management.

1104 - August 26, 2003, 8:00 am - 9:30 am, Hall L

Neurology / Psychiatry: Psychiatric Disorders

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Influence of the Type of Traumatic Event on rCBF Response to Auditory Experience Recall in Post Traumatic Stress Disorder. A SPET study.

M. M. E. Pagani[1], G. Högberg[2], D. Salmaso[1], J. Soares[3], A. Åberg-Wistedt[3], A. Sanchez-Crespo[4], H. Jacobsson[5], T. Hällström[2], S. A. Larsson[4], Ö. Sundin[3]; [1]Institute of Cognitive Sciences and Technology, CNR, Rome, ITALY, [2]NEUROTEC, Division of Psychiatry, Karolinska Institute, Huddinge University Hospital, Stockholm, SWEDEN, [3]Department of Clinical Neuroscience, Karolinska Institute, Karolinska Hospital, Stockholm, SWEDEN, [4]Section of Nuclear Medicine, Karolinska Hospital, Stockholm, SWEDEN, [5]Department of Radiology, Karolinska Hospital, Stockholm, SWEDEN.

Aim: Post traumatic stress disorder (PTSD) is a clinical condition that occurs in victims of major psychological trauma. Subjects reporting assaultive events (A) are more likely to be affected by PTSD as compared to those reporting not-assaultive events (NA). The aim of this study was to investigate the differences in regional cerebral blood flow (rCBF) between two groups of subjects exposed to either assaultive or not-assaultive traumas and developing or not PTSD. **Material and Methods:** Fourteen A and 33 NA subjects were included in the study. Among them 20 developed PTSD (S) and 27 did not (NS). The rCBF distribution was compared between groups during an auditory evoked re-experiencing of their traumatic event. 99mTc-HMPAO SPECT, using a three-headed gamma camera, was performed and the uptake in 29 bilateral regions of the brain was assessed using a standardised brain atlas. Analysis of variance (ANOVA) was used to test the significance of the differences in flow. **Results:** In the global analysis, rCBF significantly differed between groups ($p<0.001$), clinical status ($p<0.05$) and hemispheres ($p<0.001$). There was also a significant group x hemisphere interaction ($p<0.02$). The higher flow was found in the right hemisphere of the A group. The larger differences between A and NA were found in hippocampus, nc. caudatus, anterior cingulate, prefrontal and auditory cortex. When S and NS were compared the most striking differences where in nc. caudatus, anterior cingulate, prefrontal and anterior temporal cortex. **Conclusion:** Higher rCBF values under recall of their traumatic experience were found in A as compared to NA. A higher rCBF response was also found in S as compared to NS. The regions that seem to be mostly involved in the emotional response to the auditory re-experiencing are nc. caudatus and some cortical regions considered to be part of the limbic system. These findings confirm the higher morbidity of assaultive traumas and the functional substrate of PTSD symptoms.

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Cerebral blood flow alterations induced by Vagus Nerve Stimulation in patients with treament-resistant depression

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Aim: Vagus nerve stimulation (VNS) is suggested to have clinically significant antidepressant effect in patients with treatment-resistant depression (TRD). The purpose of the study was to investigate the effect of vagus nerve stimulation (VNS) on cerebral blood flow in patients with TRD, focusing on depression-relevant regions (left prefrontal cortex, anterior gyrus cinguli, caudate nuclei) and VNS-relevant regions (mesial temporal regions [hippocampus/amygdala], medulla/brain stem, thalamus, hypothalamus, cingulate, right postcentral gyrus) according to recent literature. **Material and Methods:** 99mTc-hexamethyl propylene amine oxime (HMPAO) SPECT brain scans were acquired for 12 patients with TRD before and after 4 weeks of VNS treatment using a annular brain-dedicated SPECT system (Ceraspect, D. S. I). Voxel-by-voxel analysis was performed using SPM99 to investigate cerebral blood flow alterations by VNS. SPECT scans were spatially normalized and paired t-test was used on a significance threshold of $P<.01$ for hypothesized regions to identify significant changes in cerebral blood flow. Patients were also rated by Hamilton Rating Scale for Depression (HRDS) before and 10 weeks after VNS treatment to assess clinical response. **Results:** 5 of 12 patients showed significant reduction of psychopathological symptoms measured by HRDS (> 50% reduction); however all patients showed a decrease in HRDS scores. On significance threshold of $P<.01$ a significant increase of cerebral blood flow was found in the left prefrontal cortex; a significant reduction of blood flow was found bilaterally in the hippocampus, the left nucleus caudatus and in the brain stem. **Conclusion:** As other antidepressant treatments (e. g. antidepressant medication, psychotherapy) VNS also shows typical regional blood flow alterations in the left prefrontal cortex with reduction of psychopathology, which reinforces the suggestion that VNS is effective antidepressant treatment modality. The similar findings in the limbic system and the brain stem as in VNS-treated epileptic patients underline the key function of these areas in the therapeutical mechanisms of VNS.

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Serotonin Transporter Availability in Patients with Symptomatic Bulimia Using a Novel SPET Ligand I-123-ADAM

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Aim: The serotonin system is believed to be affected in bulimia nervosa. Serotonin transporter (SERT) availability is believed to reflect presynaptic serotonergic function. There are no published data on SERT availability in midbrain area in patients with bulimia. In a previous SPET study in healthy subjects using ^{123}I-ADAM, a novel highly spesific radioligand for SERT, we found highest SERT concentration in midbrain. Pons, thalamus and striatum also showed significant activities. Our aim was to evaluate the SERT availability in the midbrain area of symptomatic bulimic patients versus a healthy control group using ^{123}I-ADAM. **Subjects and Methods:** The group of bulimic patients included eight women (mean age 24 ± 2 years) and the control group nine women (mean age 36 ± 13 years). SPET studies were performed 10 minutes, 5 hours and 7 hours after injection of ^{123}I-ADAM. For quantification of brain SERT availability, the ratio of spesific to non-spesific ^{123}I-ADAM brain binding at 5 hours was used (V_3" = (target region-cerebellum)/cerebellum). **Results:** The spesific SERT binding in the midbrain area was similar in both groups. The V_3" for the bulimic group was 1.80 ± 0.26 and for the control group 1.70 ± 0.34 ($p>0.5$). The SERT availability in the midbrain did not correlate with age in either of the groups ($p>0.5$ for both). **Conclusions:** In this preliminary analysis, we found no difference in the midbrain SERT availability between patients with bulimia and control subjects. The age difference between the two groups may have influenced the results. However, we do not believe this to affect our results significantly as there was no correlation between age and midbrain SERT availability in either of the groups. Further analyses on bulimic patients are needed to determine the SERT status in other brain areas such as thalamus, which is known to be involved in regulation of eating.

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Principal Component Analysis and Volumes of Interest Analysis in Depressed Patients by 99m-Tc-HMPAO SPET - A Methodological Comparison

M. M. E. Pagani[1], A. Gardner[2], D. Salmaso[1], A. Sanchez-Crespo[3], C. Jonsson[3], H. Jacobsson[4], T. Hällström[2], S. A. Larsson[3]; [1]Institute of Cognitive Sciences and Technology, CNR, Rome, ITALY, [2]NEUROTEC, Division of Psychiatry, Karolinska Institutet, Huddinge University Hospital, Stockholm, SWEDEN, [3]Section of Nuclear Medicine, Karolinska Hospital, Stockholm, SWEDEN, [4]Department of Radiology, Karolinska Hospital, Stockholm, SWEDEN.

Aim: Several methods have been proposed to analyse radiopharmaceutical uptake in regional cerebral blood flow (rCBF) studies. Volume of Interest (VOI) analysis evaluates the 3D data in a predefined region. Principal Component Analysis (PCA), by reducing the number of VOIs to factors, takes also into account correlations between variables, reflecting presumably human brain anatomo-functional connectivity. The aim of this study was to assess rCBF differences in two groups of depressed patients and normal controls and to compare the results according to these two analysis methods. **Material and Methods:** 70 outpatients bearer of Major Depressive Disorder (MDD) along with audiological and physical symptoms and 66 normal controls (CTR) were studied by 99m-Tc-HMPAO SPET. rCBF was analysed in twenty-seven VOIs, bilaterally, automatically defined by a standardisation software (CBA). PCA was used to reduce the number of variables by grouping the VOIs in positively correlated factors. The differences between radiopharmaceutical uptake in MDD and CTR found at VOI level were then compared to those found at factor level. **Results:** PCA resulted in 11 factors that significantly interacted with groups ($p<0.001$). Increased rCBF was shown by both methods with several overlaps in frontal and temporal lobes and in central structures. All VOIs differing significantly between MDD and CTR were included in three out of the four significantly different factors. The last significant factor, that grouped VOIs belonging to temporal and parietal lobe, did not include any VOI reaching singularly the level of significance ($p<0.05$). **Conclusion:** Increased rCBF was found in a selected group of MDD outpatients. PCA grouped regions in factors according to their reciprocal rCBF positive relationships and highlighted significances in areas larger than those found at VOI level. One factor was significantly different between groups independently from significance in the single VOIs strengthening the value of investigating the correlation between variables. Factors represent cerebral areas with possible anatomo-functional connections and their analysis might help in shedding light on the interactions between different regions in MDD.

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High- vs. low dosis therapy with the atypical antipsychotic amisulpride: Effects on the striatal dopamine transporter and dopamine D2 receptors

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Aim: Amisulpride appears to be an effective agent for treating positive and negative symptoms of schizophrenia depending on dose. The aim of this study was to assess striatal dopamine D2 receptor availibility by means of [I-123]IBZM and to investigate the effects on the dopamine transporter on the basis of [Tc-99m]-TRODAT-1 SPECT in patients treated with high and low doses of this atypical antipsychotic drug. **Material and Methods:** A total of 28 patients (eighteen males, ten females, range 19-64 yrs) suffering from schizophrenia under treatment with high (sixteen patients, 400-1300 mg, mean dose 706 mg) or low doses (twelve patients, 200-300mg, mean 245 mg) of amisulpride were examined. Simultaneous brain SPECT scans were performed 3 h p. i. of 800 MBq [Tc-99m]TRODAT-1 and 2 h p. i. 185 MBq [I-123]IBZM. Images were acquired using a triple-head gamma camera (Picker Prism 3000 XP) equipped with fan-beam collimators. For semiquantitative evaluation transverse slices corrected for attenuation (Chang's first-order method) were used to calculate specific binding in the striatum with the

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