

Regional Cerebral Blood Flow differences in early and severe Alzheimer Disease as assessed by SPECT and Principal Component Analysis

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Aim: In its development into severe Alzheimer's Disease (AD), early Alzheimer Disease (eAD) involves progressively larger regions of the brain. These regions share close anatomic-functional relationships. The aim of this study was to investigate the rCBF changes occurring in eAD and AD as compared to a group of normal individuals by means of SPECT and Principal Component Analysis.

Materials and Methods. Thirty eAD, 17 AD and 66 normal controls (CTR) were included in the study. 99mTc-HMPAO SPECT, using a three-headed gamma camera, was performed at rest and the uptake in 27 functional bilateral sub-volumes of the brain was assessed by a standardised digitalised brain atlas. Data were grouped into anatomic-functionally connected regions by means of PCA analysis performed on all 113 individuals. Analysis of variance (ANOVA) was used to test the significance of the differences in flow in such functional regions and data were covaried for age differences.

Results. In the global analysis, rCBF significantly differed between groups (0.001) with a progressive reduction of flow from CTR to AD. PCA reduced the 54 variables to 11 anatomic-functional regions that interacted with groups ($p < 0.001$) and gender ($p < 0.001$). In the overall analysis the three groups differed significantly in all functional regions except for bilateral occipital cortex, anterior cingulate cortex, thalamus and putamen. In both CTR/eAD and CTR/AD comparisons the largest rCBF reductions were found in functional regions including left ($p < 0.0001$) and right ($p < 0.0001$) temporo-parietal cortex and associative parietal cortex ($p < 0.0001$). When eAD was compared to AD, this latter showed the largest reductions in right temporo-parietal cortex ($p < 0.0001$) and in right prefrontal cortex ($p < 0.005$).

Conclusions. In this study the rCBF was investigated in early and severe Alzheimer's Disease taking into account the functional connectivity among brain regions. Our results confirm previous findings on the progression of the disease and validate the use of principal component analysis as a statistical tool able to highlight neural networks in

neurodegenerative disorders.

Regional cerebral blood flow changes as assessed by 99m-Tc-HMPAO SPECT in 70 Unipolar Depressed patients at rest

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Aim: Alterations in excitatory or inhibitory signals between cortical and sub-cortical regions in patients with unipolar depression (MDD) may be assessed by investigating changes in regional cerebral blood flow (rCBF). Regions with abnormal metabolic activity might participate in neural networks and affect the rCBF distribution in functionally connected structures. The aim of this study was to identify the brain regions showing rCBF changes in MDD by means of SPECT and Principal Component Analysis (PCA).

Materials and Methods: The rCBF distributions in 70 MDD and 66 control (CTR) subjects, at rest, were compared. 99mTc-HMPAO SPECT, using a three-headed gamma camera, was performed and the uptake in 27 functional bilateral sub-volumes of the brain was assessed by a standardised digitalised brain atlas. Data were grouped into functional regions by means of PCA analysis performed on all 136 individuals. Analysis of variance (ANOVA) was used to test the significance of the differences in flow in such functional regions.

Results: In the global analysis, rCBF significantly differed between groups (0.02). There were also significant hemisphere x groups interaction ($p < 0.003$) and gender difference ($p = 0.003$), with right hemisphere rCBF specifically increased in MDD and females showing a higher CBF. PCA identified 11 anatomic-functional regions that interacted with groups ($p < 0.001$) and gender ($p < 0.001$). As compared to CTR, MDD rCBF increased, bilaterally, in the right associative temporo-parietal cortex ($p < 0.007$), in right frontal cortex and prefrontal cortex ($p = 0.002$), in the temporal poles ($p < 0.03$) and in thalamus and basal ganglia ($p < 0.001$).

Conclusions: Higher rCBF in MDD at rest was found in 4 clusters of regions sharing close anatomical and functional relationships. These regions represented large parts of the right hemisphere and the downstream central structures. These findings confirm rCBF changes in unipolar depressive disorders, suggest mutual rCBF relationships

among different regions participating to critical networks and encourage the use of standardisation software and PCA for group evaluation.

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Effects of auditory recall experience on regional cerebral blood flow as assessed by 99m-Tc-HMPAO SPECT in 13 Post Traumatic Stress Disorder patients

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Aim: Post Traumatic Stress Disorder (PTSD) is a severe condition affecting about 8% of population and increasing the risk of depression. PTSD patients, among other symptoms, suffer from intrusive distressing recollections of the traumatic event and avoidance of stimuli related to trauma. The aim of this study was to investigate the differences in regional cerebral blood flow (rCBF) between two groups of subjects exposed to the same type of traumatic stressor either developing PTSD or not.

Materials and Methods: Thirteen subway drivers developing PTSD (PTSD) and 19 not developing PTSD (CTR) after being exposed to earlier person-under-the-train accident were included in the study. The rCBF distribution was compared between the two groups during a situation involving an auditory evoked re-experiencing of their traumatic event. 99mTc-HMPAO SPECT, using a three-headed gamma camera, was performed and the radiopharmaceutical uptake in 7 bilateral regions of the brain was assessed using a standardised digitalised brain atlas. The chosen regions were those supposed to be involved in fear and emotional response and were located in the thalamus, limbic cortex and prefrontal, temporal and parietal lobes. Analysis of variance (ANOVA) was used to test the significance of the differences in flow in such functional regions.

Results: In the global analysis, rCBF significantly differed between groups (0.04), hemispheres ($p < 0.02$) and regions ($p < 0.0001$). There was also a significant region x hemisphere interaction ($p < 0.0001$). As compared to CTR, PTSD rCBF increased in the primary and associative auditory cortex ($p < 0.03$) and in the temporal poles ($p < 0.02$). Significant hemispheric differences were found in these latter regions ($p < 0.001$ and $p < 0.0001$, respectively), anterior cingulate cortex ($p < 0.0001$) and multi-medial parietal association cortex ($p < 0.0001$).

Conclusions: Higher rCBF values in PTSD patients under

recall of their traumatic experience were found as compared to CTR. The regions with increased flow were part of the temporal limbic system and the primary and secondary auditory pathways. No significant changes were found in prefrontal and orbito-frontal cortex between the two groups. A higher rCBF response in some regions of the brain involved in emotional processes during re-experiencing the traumatic stressor was found in symptomatic subjects as compared to the symptoms-free ones. This study encourages the use of SPECT and standardisation software for group comparison investigations in psychiatry.

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Brain SPECT in Psychiatry : Delusion or Reality ?

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Aim: The need for functional information is becoming increasingly evident for proper therapeutic approaches to the treatment and follow up of psychiatric diseases. While data on this subject already exists, there is a general lack of consensus about the use of brain SPECT in this domain and also a considerable negative prejudice due to a number of factors including poor quality imaging and unrealistic expectations. Based on a large group of brain SPECT-s performed over the past 3 years we attempted to sort and refine the indications for SPECT in psychiatry. **Materials and Methods:** High resolution brain SPECT was performed with triple head gamma camera, super-high resolution fan beam collimator and Tc-HMPAO. A comprehensive semiquantitative color, 3D surface as well as multi-thresholded volume display was routinely used and supplemented by automatic realignment in case of longitudinal follow-up.

Results: 470 brain SPECT-s done on 432 patients were all referred by psychiatrists or neuro-psychiatrists for a wide spectrum of psychiatric diseases and ranged in age from 7 to 88 years. The most common primary reasons for referral were : attention deficit hyperactive disorder (ADHD); anxiety; obsessive-compulsive disease, depression (refractory, chronic, bipolar), impulse control problems; oppositional defiance, post traumatic brain injury; seizures, learning difficulties, pervasive development disorders, memory loss and differential of dementia. Among common denominators were long duration of the disease, unresponsiveness to treatment, worsening of clinical status, and presence of multiple conditions at the same time. The multiparametric display used enabled a comprehensive evaluation of the brain volume which included the hemispheric surfaces; the basal ganglia (striatum) and the thalamus, several components of the limbic and paralimbic systems: anterior and posterior cingulate and their respective subdivisions, insula-s and their subdivisions, apical and mesial temporals. The cataloging of the various shape and magnitude increases and / or decreases in any of these

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