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学位論文名	Effect of linearization correction on statistical parametric mapping (SPM) : A $^{99m}\text{Tc}$ -HMPAO brain perfusion SPECT study in mild Alzheimer's disease (統計学的画像解析における直線化補正の効果—軽症アルツハイマー病の $^{99m}\text{Tc}$ -HMPAO 脳血流 SPECT 研究)
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## 論文内容の要旨

**Background :**  $^{99m}\text{Tc}$ -HMPAO SPECT with statistical parametric mapping (SPM) has been widely employed to detect the pattern of brain perfusion changes in Alzheimer's disease (AD). However, kinetic studies of  $^{99m}\text{Tc}$ -HMPAO showed that the retention of  $^{99m}\text{Tc}$ -HMPAO in brain is not instantaneous. Certain amount of back diffusion and wash out of this tracer occurs that lead to a saturation effect, as a result of which the radioactivity-count does not increase proportionally with the increase in the regional cerebral blood flow (rCBF). Linearization correction (LC) is an image processing method that applies Lassen's algorithm on each SPECT-voxel to enhance the image contrast in a post-processing manner to obtain a more direct proportionality between the corrected-count and blood flow without influencing spatial resolution on the tomographic images. This technique has been widely accepted for cerebral perfusion studies in stroke and related diseases. To detect the pattern of rCBF changes in the early stage of AD, LC method was adopted by some study groups, however, not by others. Since, it was reported that image reconstruction method might influence the sensitivity of interpretations of SPM therefore, it would be important to know whether linearization correction affects SPM analysis or, that to be used for detecting the earliest perfusion changes occurring in mild AD. The current study addressed this issue. We performed  $^{99m}\text{Tc}$ -HMPAO SPECT in mild AD patients and analyzed the effect of linearization correction for washout of the tracer on the detectability of abnormal perfusion. **Methods :** Eleven mild AD (NINCDS-ADRDA, male/female, 5/6 ; mean  $\pm$  SD age, 70.6  $\pm$  6.2 years ; mean  $\pm$  SD mini-mental state examination score, 23.9  $\pm$  3.41 ; clinical dementia rating score, 1) and eleven normal control subjects (male/female, 4/7 ; mean  $\pm$  SD age, 66.8  $\pm$  8.4 years) were enrolled in this study. SPECT was initiated within 10 minutes after injection of approximately 740 MBq (20 mCi)  $^{99m}\text{Tc}$ -HMPAO. The final data set consisted of 64  $\times$  64 matrix (4  $\times$  4 mm per pixel, 4 mm thickness) from the sum total of data acquired by the four cameras. Butterworth filter and Chang's attenuation correction were applied as routine. Thus, LU images were reconstructed. After

completing the identical procedures for LU images, we applied Lassen's algorithm for linearization correction (LC) to develop LC images (64×64 matrix, 4 mm slice thickness, transaxial oblique in-plane parallel to orbitomeatal line.). Lassen's algorithm is represented by the equation  $F_i/F_r = \alpha (C_i/C_r) / [1 + \alpha - (C_i/C_r)]$ , where  $F_i/F_r$  is a ratio of CBF in each region to that in a reference region and  $C_i/C_r$  is the ratio of count activity in each region to that in a reference region. Alpha ( $\alpha$ ) is the ratio between the rate of the back diffusion of the diffusible lipophilic  $^{99m}\text{Tc}$ -HMPAO from the brain to the blood and the rate of conversion of the lipophilic compound to the hydrophilic form. We used 1.5 as the value for  $\alpha$ , and cerebellum as reference regions for LC images that were previously validated in other studies. The pattern of hypoperfusion in mild AD on LU and LC images was detected by SPM99 applying the same image standardization and analytical parameters. A statistical inter image-group analysis (LU vs. LC) was also performed. **Results** : Clear differences were observed between the interpretation of SPM with LU and LC images. Significant hypoperfusion in mild AD was found on the LU images in the left posterior cingulate gyrus, right precuneus, left hippocampus, left uncus, and left superior temporal gyrus (cluster level, corrected  $P < 0.005$ ). With the LC images, significant hypoperfusion in AD was found only in the bilateral posterior cingulate gyrus and left precuneus (cluster level, corrected  $P < 0.005$ ). A pattern of greater rCBF distribution at the high flow cortices and low flow cortices was observed on LC and LU images, respectively, in the case of both controls and mild AD patients. **Conclusion** : Hippocampal hypoperfusion could be detected by means of SPM in the LU images but not in the LC images. The results of SPM may vary in  $^{99m}\text{Tc}$ -HMPAO SPECT with or without linearization correction, which should be carefully evaluated when interpreting the pattern of rCBF changes in mild Alzheimer's disease.

#### 論文審査の結果の要旨

アルツハイマー病の早期診断を目的として  $^{99m}\text{Tc}$ -HMPAO による脳血流検査 (SPECT) を施行し、SPM 解析によるアルツハイマー病の早期診断のための有用性を評価するために、線型補正法の妥当性を検討した。その結果、早期アルツハイマー病患者の  $^{99m}\text{Tc}$ -HMPAO SPECT 画像の解析において、線型補正を行なった場合 (LC 画像) と線型補正を行わない場合 (LU 画像) とでは大きな差異が認められることを見出した。早期アルツハイマー病患者脳では対照健常者脳と比較して、LU 画像では左後部帯状回、右前楔部、左海馬、左鉤回、左上側頭回において有意な脳血流量低下が認められたのに対して、LC 画像では両側後部帯状回、左鉤回においてのみ有意な脳血流量低下を認めた。この結果は、SPM 解析を用いて早期アルツハイマー病脳の局所脳血流量の低下を検出するためには LU 画像のほうが優れていることを示している。本研究は、早期アルツハイマー病の診断に、SPM 解析による脳血流量評価が有用であることを示し、解析法を工夫することによってアルツハイマー病の早期診断が可能になることを示唆した点において大きな意義を有する。よって本研究は学位の授与に値するものと判断する。