Total Mini-Mental State Examination score and regional cerebral blood flow using Z score imaging and automated ROI analysis software in subjects with memory impairment

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Abstract

Objective The Mini-Mental State Examination (MMSE) is considered a useful supplementary method to diagnose dementia and evaluate the severity of cognitive disturbance. However, the region of the cerebrum that correlates with the MMSE score is not clear. Recently, a new method was developed to analyze regional cerebral blood flow (rCBF) using a Z score imaging system (eZIS). This system shows changes of rCBF when compared with a normal database. In addition, a three-dimensional stereotaxic region of interest (ROI) template (3DSRT), fully automated ROI analysis software was developed. The objective of this study was to investigate the correlation between rCBF changes and total MMSE score using these new methods.

Methods The association between total MMSE score and rCBF changes was investigated in 24 patients (mean age ± SD 71.5 ± 9.2 years; 6 men and 18 women) with memory impairment using eZIS and 3DSRT. Step-wise multiple regression analysis was used for multivariate analysis, with the total MMSE score as the dependent variable and rCBF change in 24 areas as the independent variable.

Results Total MMSE score was significantly correlated only with the reduction of left hippocampal perfusion but not with right (P < 0.01).

Conclusions Total MMSE score is an important indicator of left hippocampal function.

Keywords MMSE · SPECT · eZIS · 3DSRT · Left hippocampus

Introduction

The Mini-Mental State Examination (MMSE) is considered a useful supplementary method to diagnose dementia and evaluate the severity of cognitive disturbance. An impaired total MMSE score indicates a cognitive deficit [1]. However, it remains unclear which part of the brain is associated with the function reflecting the total MMSE score. Measurement of regional cerebral blood flow (rCBF) using single-photon emission computed tomography (SPECT) enables regional cerebral function to be evaluated. The easy Z score imaging system (eZIS), a new method for evaluating rCBF that uses a Z score map and shares a normal database, has recently been developed [2, 3]. SPECT with eZIS can detect subtle CBF changes and avoid the influence of age- and sex-related physiological rCBF changes because Z values are determined by comparison with an age- and sex-matched normal database [2, 3]. In addition, a three-dimensional stereotaxic region of interest (ROI) template (3DSRT) has been developed for fully automated evaluation of rCBF values [4, 5].
In this study, we investigated the correlation between age- and sex-adjusted rCBF changes and total MMSE score using these new methods, to detect which brain areas influence the total MMSE score.

Materials and methods

All procedures followed the clinical study guidelines of our institute, which are approved by the Institutional review board. We retrospectively chose 24 patients (mean age ± SD 71.5 ± 9.2 years; 6 men and 18 women) from the Memory Disorder Clinic at the Department of Psychiatry, Yokohama City University. In clinical diagnosis, the subjects were 7 patients with dementia of Alzheimer’s type, 11 patients with dementia not otherwise specified, and 6 patients with mild cognitive impairment. All patients had no focal neurological deficit and no significant abnormal findings on head X-ray computed tomography. All of them underwent both brain perfusion SPECT and MMSE within a 2-month period. In all the cases, clinical examinations, including SPECT, were performed with informed consent of either the patients themselves or their closest relatives.

Patients were injected when lying in the supine position with eyes closed, in a dimly lit, quiet room. Each received a 600-MBq intravenous injection of 99mTc-ethyl cysteinate dimer (99mTc-ECD). Ten minutes after the injection of 99mTc-ECD, brain SPECT acquisition was performed using a single-head SPECT system (Starcam 3000, GE Medical Systems, Milwaukee, WI, USA) equipped with a low-energy general purpose collimator. The spatial resolution of the system (full width at half maximum) at a 100-mm distance from the camera is 10.2 mm. The SPECT acquisition was undertaken in 64 steps and each step collected counts for 20 s. A Butterworth filter with a matrix of 64 × 64 was used to reconstruct the SPECT images. Attenuation correction was carried out using Sorenson’s method. Each SPECT image was anatomically standardized by Statistical Parametric Mapping 99, compared with age- and sex-matched control images from a normal database supplied by the National Center Hospital for Mental, Nervous, and Muscular Disorders, and converted into a Z score image using eZIS. Data sets were normalized to the mean global activity. Z score = (normal mean – individual value)/(normal SD). Prior to using eZIS, Hoffman three-dimensional brain phantom data were used to correct for differences in equipment and reconstruction processes between our study and the normal database. A positive Z score represents a reduced rCBF in the patient relative to the control mean. To measure rCBF changes, the mean Z score for each patient was calculated by 3DSRT, with fully automated evaluation of the 12 ROIs (callosomarginal, precentral, central, parietal, angular, temporal, posterior cerebral, pericallosal, lenticular nucleus, thalamus, hippocampus, and cerebellum) in each hemisphere.

Statistical analysis was performed using SPSS software for Windows ver.11.5.1J (SPSS Japan, Tokyo, Japan). Step-wise multiple regression analysis was used to determine which areas influenced the total MMSE score, with the total MMSE score as the dependent variable and Z value in 24 areas as the independent variable. In addition, a similar analysis was done for each subordinate item, such as orientation, registration, calculation, recall, and language. A P value of <0.01 was considered to be statistically significant.

Results

Total MMSE scores ranged from 6 to 30 points (mean ± SD 20.5 ± 6.8). A typical image analyzed by eZIS is shown in Fig. 1. The step-wise multiple regression test showed that the total MMSE score was significantly correlated with rCBF changes only in the left hippocampus. But no regions related to any subordinate item were detected. Figure 2 shows the correlation between total MMSE score and segmental CBF changes in the left hippocampus.

Discussion

Mini-Mental State Examination is used for the screening of cognitive impairment, and can be applied to any kind of dementing disorder. In this study, we evaluated total MMSE scores without regard to the categories of dementia. Several studies have reported a relationship between MMSE score and rCBF in patients with dementia. Ushijima et al. [6] reported a correlation between mean CBF and MMSE score with low correlation coefficient in patients with Alzheimer’s disease (AD), but laterality was not investigated. They measured rCBF using N-isopropyl-p-[123I]iodoamphetamine SPECT and defined square ROIs (6 × 6 pixels) in the 16 locations. However, there may have been discrepancies between the ROIs and the actual shapes of target areas because of placement of square ROIs. Therefore, rCBF of the target areas may not have been clearly measured. Rodriguez et al. [7] reported a correlation between MMSE score and bilateral hippocampal perfusion. Although they used manual ROIs to reduce discrepancies between the ROIs and the actual shapes, errors owing to variability between operators might still have been recorded. In