Significant effect of sertraline on dopamine transporter (DAT) in major depression measured by β-CIT SPECT

Szabó Z\textsuperscript{1}, Besenyi Zs\textsuperscript{2}, Árgyelán M \textsuperscript{1,2}, Eőrdegh G\textsuperscript{1}, Godó Gy\textsuperscript{1}, Szkaliczki A\textsuperscript{1}, Pávics L\textsuperscript{2}, Janka Z\textsuperscript{1}

1 Department of Psychiatry, 2 Department of Nuclear Medicine
University of Szeged, Szeged, Hungary

INTRODUCTION

The antidepressant drug bupropion, which thought to be a primary dopamine transporter (DAT) inhibitor, shows about 20% contribution on DAT occupancy (1,2). Sertraline is considered to block primarily the serotonin transporter and we think that this 5-HT inhibitory effect is the most important factor in its efficiency. However, in vitro examinations found a high DAT blocking activity of sertraline, but in vivo measurements haven’t confirmed this result yet. Nevertheless, there are equivocal results in the functional imaging field of DAT activity in major depressive patients. In this study we investigated the baseline DAT activity of depressed patients and compared that to the values found in healthy controls. Further, we examined the improvement of depression due to sertraline treatment (Zoloft in this study). We also investigated the occupancy on DAT of healthy controls and major depressed patients treated with sertraline.

METHODS I

Image Acquisition, Processing, Analysis

Image analysis was performed on a PC workstation using MATLAB (Mathworks Inc., Natiek, MA, USA) and SPM2 software (Wellcome Department of Cognitive Neurology, London, U.K.). On the reconstructed images, 3D regions of interests (ROI) were fixed semi-automatically. First, the images were spatially normalised into the Talairach space with SPM2 using brain blood flow SPECT template, then the accuracy of this non-linear registration was checked visually. 3D masks were generated by WFU Pickatlas software. These masks (also in Talairach space) were used as ROI, and a MATLAB script calculated average photon impact. Two anatomic regions were marked out with masks, a specific binding region: striatum (size: 2815 voxel), and a non-specific binding region: occipital lobe (size: 21322 voxel) (Figures 1 and 2). The ratio of specific and non-specific activity estimates the binding potential (BP), that correlates with the dopamine transporter (DAT) density of the specific binding compartment. Thus, we calculated the [(striatum mean activity - occipital mean activity)/occipital mean activity] ratio (SOR). Occupancy ratio equals 100% x (DAT BP scan1 - DAT BP scan2)/ DAT BP scan1. Results are reported as mean ± SD.

METHODS II

Study Course

β-CIT SPECT was employed to explore the baseline DAT activity of depressed patients and healthy controls. Every participant went through a SPECT examination, and in the depressed group we repeated the SPECT inspection after 3 weeks of sertraline treatment (the daily dose of sertraline was between 50-100 mg). Nine depressed patients (diagnosed by the instructions of DSM-IV) and 14 healthy controls (checked by M.I.N.I.) participated in the study. An other inclusion criterion was to have more than 19 points on the Hamilton Depression Scale (21-item version). Exclusion criteria were the presence of serious internal or neurological diseases (checked by internal, laboratory and CT examinations). For statistical analysis we used STATISTICA 7.1 software. Kolmogorov-Smirnov-test, Student’s t-test, Chi square test and Product moment and Partial correlation analysis were applied.

RESULTS

The baseline DAT score of patients didn’t differ significantly from healthy controls (p= 0.8451). In the patients group we found significant difference after 3 weeks sertraline treatment (p=0.0261). The DAT occupancy ratio was 12.13% (SD: ±12.72%). The change during the treatment of Hamilton Depression Scale (HAM-D) values was also significant in the patient group (p=0.00079). The mean change of HAM-D scores was 51.24%. However, we didn’t find significant relationship between the baseline HAM-D value and the change of DAT activity.

DISCUSSION

Our in vivo imaging measurements demonstrate that the therapeutic dose of sertraline significantly influences the DAT activity (beside the known serotonin transporter blocking property) in subjects under antidepressant therapy. This finding can be useful in several clinical conditions, and it may play an important role in the understanding of mechanism of sertraline action. According to our results we may conclude that sertraline, which earlier was thought to be a selective serotonergic compound, may be considered as a dual-action antidepressant. Nevertheless, there was no significant difference between the baseline DAT activity of depressed patients and control subjects, similarly to the results found in our previous (bupropion) SPECT study (1,2).

The authors declare no conflict of interest related to the study.

Figure 1 represent the baseline DAT activity of a depressed patient on SPECT images in three different sections.

Figure 2 shows the SPECT images of the same subject after three weeks sertraline treatment. Black colour demonstrates the specific marks (ROIs) on the dopamine binding region (striatum area). The yellow colour in the black field shows the DAT activity after 3 weeks sertraline treatment. The difference between the extent of the two different coloured regions suits to the occupancy on DAT. The other yellow area in the occipital cortex is the reference region in the current threshold level.

Figure 1

Figure 2

References