Multimodality image quantification using Talairach grid

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ABSTRACT

We present an application of the widely accepted anatomical reference of the Talairach atlas as a system for semiautomatic segmentation and analysis of MRI and PET images. The proposed methodology can be seen as a multimodal application where the anatomical information of the MRI is used to build the Talairach grid and a co-registered PET image is superimposed on the same grid. By doing so, the Talairach-normalized tessellation of the brain is directly extended to PET images, allowing for a convenient regional analysis of volume and activity rates of brain structures, defined in the Talairach Atlas as sets of cells. This procedure requires minimal manipulation of brain geometry, thus fully preserving individual brain morphology. To illustrate the potential of the Talairach method for neurological research, we applied our technique in a comparative study of volume and activity rate patterns in MRI and PET images of a group of 51 schizophrenic patients and 24 healthy volunteers. With regard to previous applications of the Talairach grid as an automatic segmentation system, the procedure presented here features two main improvements: the enhanced possibility of measuring metabolic activity in a variety of brain structures including small ones like the caudate nucleus, hippocampus or thalamus; and its conception as an easy-to-use tool developed to work in standard PC Windows environment.

Keywords: MRI, PET, multimodality registration, Talairach grid, brain, segmentation, normalization, volumetric data, metabolic activity, schizophrenia.

1. INTRODUCTION

This paper addresses a common problem in studies involving brain intersubject comparisons as it is the requirement of a standard coordinate space common to all subjects, independent of size, position, or shape of the individual brains. The problem is more complex when two image modalities like PET and MRI are being used, since the normalization process involves both intra- and inter-subject registration. The ideal procedure for quantitative studies should feature brain normalization and also a standardized and repeatable segmentation method. The problem with most segmentation algorithms is the considerable amount of labor involved in the process, which makes impracticable the analysis for large series of patients. Automatization of the segmentation process would not only enable the analysis of large samples, but also improve the precision and repeatability of volumetric measurements.

The Talairach atlas was originally conceived to provide a standardized coordinate system for location of brain structures in stereotactic space, and has been widely used in neuro-clinical procedures[1-3]. The Talairach grid has also been proposed as a tool for automatic segmentation, following the idea of defining brain structures as series of 3D volume 'boxels' or Talairach grid cells[4, 5]. Basically, the Talairach normalization consists of a piecewise linear transformation that produces a tessellation of the brain into a grid of 1,056 cells. These volume cells can be considered to represent homologous measuring units of volume or activity rates across subjects. Segmentation of the brain upon grid cells offers the advantage of providing a fully standardized protocol based on the widely accepted anatomical reference of the Talairach atlas. Inter-subject comparisons could be made by using information from single grid cells, though preferably sets of cells encompassing brain structures should be used for quantification. In the trade-off between degree of deformation and maximum repeatability, the Talairach method provides a reasonable solution compared with other methods because involves a minimal modification of the brain morphology at the expense of a limited spatial resolution. Maximum resolution depends on the size of the 1,056 cells (actual values range from 1-2.5 cc of brain tissue), thus determining the minimum volume suitable for analysis.

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Because of its limited spatial resolution, the use of the Talairach grid for segmentation and measuring has only been attempted for large anatomical structures like the frontal or temporal lobes[4]. The aim of this paper is to present a new implementation of the Talairach grid system to be used as an automatic segmentation and brain measuring method. The computer application presented has the asset of its conception as an easy-to-use tool for the medical community, developed to work in standard PC Windows environment.

To illustrate the potentialities of the program, we show the results of a comparative study of volume and activity rate patterns in MRI and PET images in a group of 51 schizophrenic patients and 24 healthy volunteers.

2. METHOD DESCRIPTION

To perform the metabolic and volumetric measurements of the different brain structures, a two-step procedure was adopted. The first step involved editing the MRI to remove skull and extra cranial tissue, registration of PET and MRI, and an initial segmentation of cerebral tissues into Gray Matter (GM), White Matter (WM) and Cerebrospinal Fluid (CSF). In a second stage, we apply the Talairach method to define ROIs and to obtain volume and metabolic activity data. The software developed is part of a Multimodality Workstation running on IDL® (Interactive Data Language, Research Systems Inc.).[6]

2.1. Removal of Extra Cranial Tissue from the MRI

Our implementation of the Talairach normalization system uses images of cerebral tissue only, requiring MRI edition to remove the scalp, sagittal sinus, cerebellum, and brainstem. Available image segmentation tools like region growing, thresholding and manual tracing are applied by an experienced user on each MRI.

2.2. Fusion of PET and MRI

After removal of extracranial tissue, the edited MRI image was co-registered with the PET study. Fusion of these two images implies finding the transformation matrix necessary to rotate, translate, scale, and reslice the PET image to match its corresponding MR. Co-registration was made using the AIR algorithm[7], which optimizes volume matching between the two images. Only rigid linear transformations were allowed in the registration since both MRI and PET volumes came from the same subject. Fusion results were visually checked in all cases and the observed fit was always optimal.

2.3. Initial Segmentation

Initial segmentation of cerebral tissue into GM, WM, and CSF is obtained by using an automatic method based on expectation maximization algorithm[8]. This method produces a set of three 3D volume masks, one for each tissue type and MRI. All of these automatically generated 3D masks are checked for inconsistencies and manually corrected whenever necessary by an experienced radiologist.

2.4. Talairach based Segmentation

2.4.1. Proportional Grid Division

Division of the brain volume is centered upon the position of the anterior and posterior commissures, AC and PC, following the principles of the Talairach atlas[9]. This is basically a two-step division: a major brain-region partition followed by a within-region subdivision into cells or 'boxels', (Fig. 1). At the end of this process each brain consists of a set of 1,056 cell boxes, which, according to the Talairach rationale, represent homologous parts of the brain that can be directly compared across subjects.

2.4.2. Selection of Commissures and Talairach Grid Construction

In order to apply the Talairach coordinate system the MR image must have the AC and PC in the same plane, perpendicular to the midsagittal plane. The process of Talairach normalization begins on the edited brain MRI by manually selecting the position of the AC and PC points and a third point in the midsaggittal plane (Fig. 2). The coordinates of these points are then transformed to comply with the Talairach system. The transformation matrix is calculated using the algorithm proposed by Arun[10] based on Singular Value Decomposition (SVD). The resulting parameters describe a rigid body transformation of the image volume, composed of three translations and three rotations in the space. In the reslicing process, the image voxels

are interpolated using nearest neighbor interpolation in order to preserve total volume of the MR image for the quantification process.

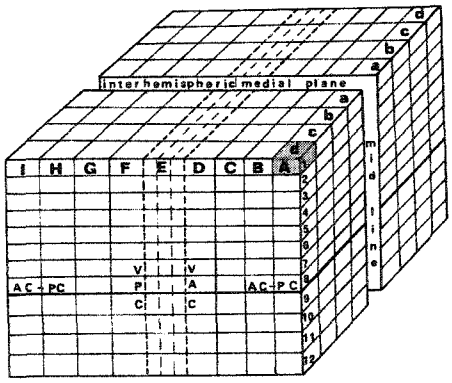

Figure 1. Description of the grid system used in the Talairach atlas of the brain[9]. The system produces a division of the brain into a set of 1,056 grid cells, centered upon the anterior and posterior commissures, AC and PC. A first major division yields 6 different regions on each hemisphere, three below and three above the AC-PC plane: anterior to AC, between AC and PC, and behind PC. A second division of those six hemispheric regions into grid cells originates four boxes on each side of the coronal plane. On the axial plane, the portion of the brain anterior to the AC and the one posterior to the PC are also divided into four boxes, whereas the tissue between commissures is divided into three. Each of the 1,056 cells resulting from this process is labeled to identify its position in the brain (modified from Talairach and Tournoux[9]).

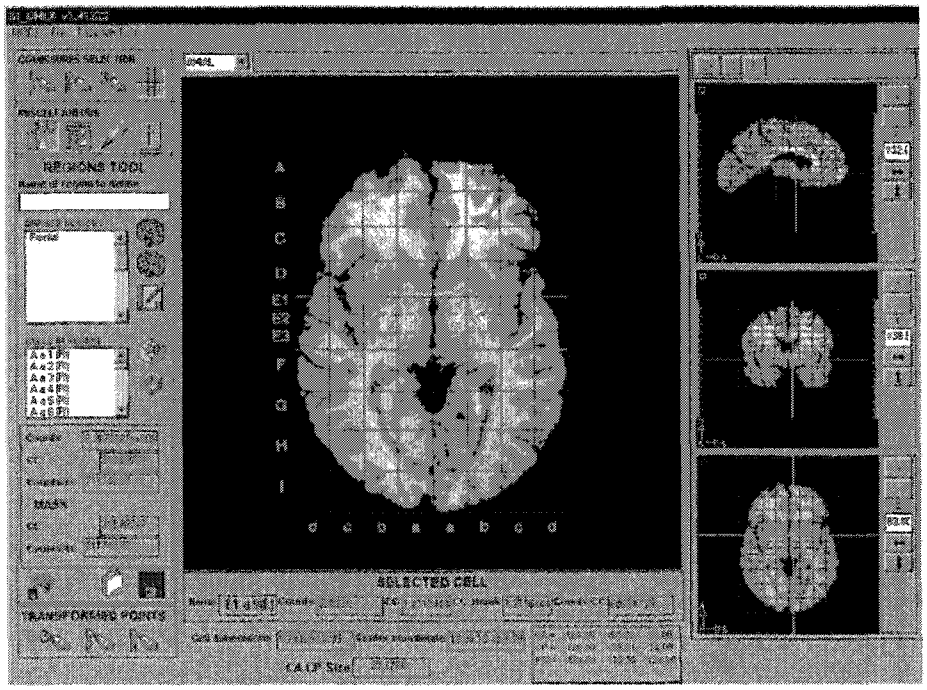

Figure 2 A sample screen of our computer application. Precise selection by the user of the anterior an posterior commissures can be made using a tri-planar view of the brain. Upon selection of commissures and image transformation, the 3D grid is automatically fitted to the outer limits of each edited MRI.The program allows 3D navigation through the brain in the Talairach space for each particular brain. The segmentation program also features tools for defining ROI's as sets of cells, show quantitative data for ROI's or individual cells and producing report files.

Next, the program automatically finds the boundaries of the brain tissue searching through planes perpendicular to the coordinate system axes, and finding the planes in which the maximum pixel value is smaller than a certain threshold. The resulting orthogonal planes define the left, right, top, bottom, anterior and posterior margins of the brain. This set of planes

constitutes the limits of the Talairach grid. After construction of this Talairach grid, co-registered PET or segmentation masks are superimposed onto the grid for visualization and quantification (Fig. 3).

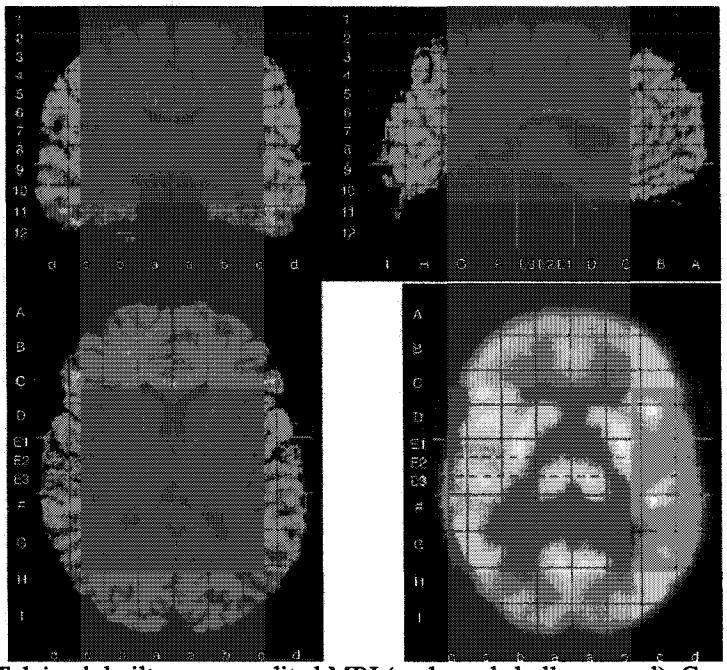

Figure 3. An example of a Talairach built upon an edited MRI (scalp and skull removed). Coronal, sagittal and axial views of the resulting brain image. Bottom right: After the Talairach grid has been calculated for a particular brain, a co-registered PET is superimposed for quantification

2.4.3. ROI Definition, Segmentation and Quantification

ROIs are delineated by adding up particular grid cells that, according to the Talairach atlas[9], encompass the desired brain structure (Fig. 4).

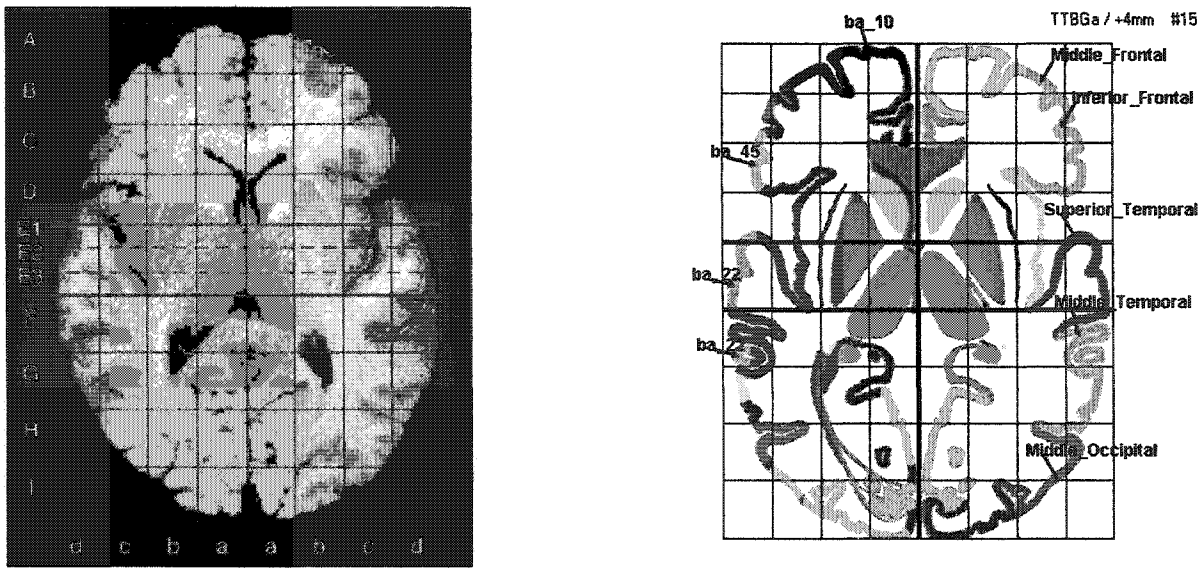

Figure 4. Axial view of a Talairach grid built upon an MRI and its corresponding description by the Talairach atlas. Definition of ROIs can be easily made by following the atlas[9]. ROIs are defined as series of cells encompassing each brain region. Large brain regions, like the frontal lobe, are better defined than small structures like the caudate or the thalamus.

Definition of small structures like the thalamus, hippocampus or caudate nucleus is more difficult because the relevant Talairach boxels may include other brain structures as well. Selection of appropriate boxels is made after detailed examination of the location of the structures in the atlas and in the MRI's. For those small structures that can't be entirely defined as a set of grid cells, volume measurements are not possible since values simply reflect the size of the few Talairach cells involved.

Measuring is done in a boxel-wise manner. Once the PET image is fused with the MRI, measuring is performed by selectively adding up data from selected boxels or grid cells defining each ROI. On each grid cell, volume and count rate activity data from the superimposed PET image are collected. The software recognizes tissue GM - CSF boundaries within each cell, allowing ventricular and sulcal CSF to be excluded for volume and activity estimations. Precise discrimination between brain tissue and CSF is critical for correct measurements of total and per cc activity estimates[4].

The method also allows to use segmented masks of a given tissue (GM, WM, CSF), instead of the whole PET image (Fig. 5). For instance, by using 3D volume masks of GM we obtain more specific and localized data, equivalent to cortex-only measurements. Superimposing this mask onto the Talairach grid, we are able to produce regional quantification of volume and activity of the GM (cortex) in the whole brain.

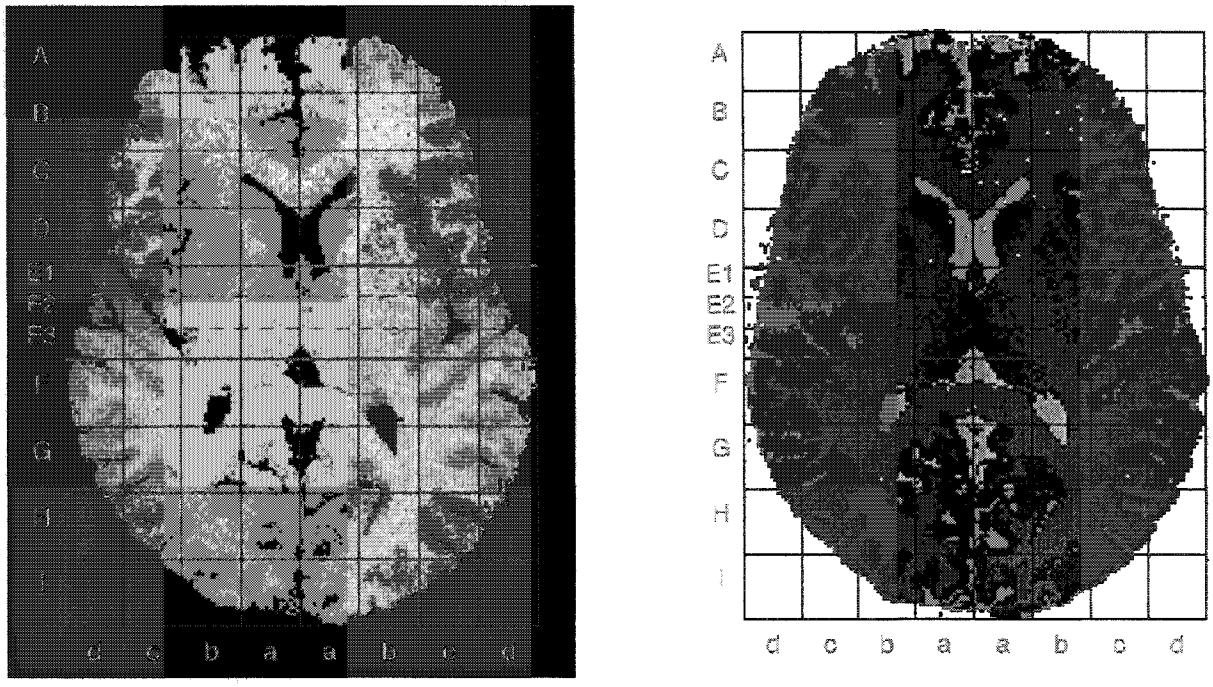

Figure 5. Once the Talairach grid is built for a particular brain, co-registered PET image or masks of CSF, GM, or WM are superimposed on the grid. Then, volume and metabolic activity are calculated for each grid cell and for each tissue type. For instance, using tissue GM masks instead of the whole PET image allows regional-wise analysis of the GM cortex. Total ROI values are obtained by adding up data from those specific cells encompassing the ROI.

3. CLINICAL APPLICATION

To illustrate the method, we show its use in a comparative study of volume and activity rate patterns in a group of 51 schizophrenic patients and 24 healthy volunteers, analyzing MRI and PET images.

3.1. Image acquisition

Image measurements were performed on MRI studies acquired on a Philips Gyroscan 1.5T scanner using a gradient echo T1-weighted 3D sequence with the following parameters: matrix size 256 x 256, pixel size 0.9 x 0.9 mm (FOV about 256 mm), flip angle 30°, echo time 4.6 ms, slice thickness ranging from 1.1 to 1.5 mm.

PET studies were obtained with a Posicam EZL PET scanner 20 min after the injection of 370 MBq of 18-FDG. Matrix size was 256 x 256 x 61, and slices were 2.6 mm thick. Tracer counts obtained in SUV (Standard Uptake Value) were proportionally normalized to the global count rate for each PET[11].

After selection of AC and PC points on each brain, data collection is automatically performed by constructing the Talairach grid and superimposing image masks for quantification using batch processing. One of the advantages of our method is the large amount of data that can be used for analysis of brain variability. Once a raw database of volume and activity rates of WM, GM and CSF is calculated for each cell, a large number of parameters can be easily measured by combining boxel data. In our study, more than 90 different brain parameters were estimated. The total number of variables obtained was much larger because each variable was available bilaterally, for the left and right sides separately. Asymmetry of each structure was also obtained by comparing data from both sides.

Using our methodological approach we were able to show differences between healthy control volunteers and schizophrenic patients in volume and activity rates of the cortex, highlighted in the caudate and right thalamus nuclei (Fig. 6). The results obtained show that schizophrenic patients can be characterized by a pattern of larger CSF and WM volumes, which entails a lower GM volume. Because our method allowed regional analysis, we were able to identify this pattern in the frontal, whereas other brain lobes showed no differences between patients and controls (Fig. 6). Findings similar to these have already been described in the literature[12].

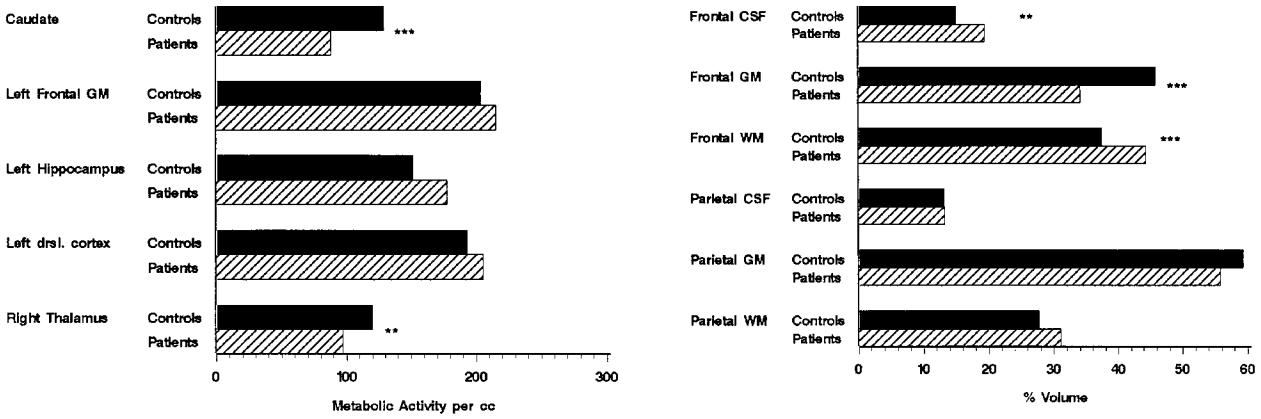

Figure 6. Results of the comparison between schizophrenic patients and control individuals using the Talairach segmentation method. Bars show mean volumes for each ROI studied. Left: metabolic activity data. Right: Relative volume (% of total brain structure). Asterisks show significant differences.

4. DISCUSSION

Used as segmentation method, the Talairach grid is a truly useful tool for exploratory analysis involving large series of images, where the use of manual segmentation is unaffordable. Preliminary results of volumetric variation and PET activity patterns can be obtained within a reasonable short time, showing evidence of potential structures worth of thorough examination using more detailed analysis.

Previous applications of the Talairach normalization system have used nonlinear warping models[4, 13, 14] to fit individual brains to the Talairach atlas. Our strategy strictly follows the division protocol of the original Talairach atlas, doing a piecewise linear fit of the 3D grid to each particular brain. In the trade-off between maximum anatomical correspondence among normalized brains vs. minimal transformation of the characteristic size and shape of each brain, we have selected the minimal geometric transformation, yet achieving a fairly precise anatomical correspondence among normalized brains.

Relative to linear and nonlinear normalization methods designed for PET images[15], the Talairach system offers a number of advantages that call for the development of convenient and easy-to-use applications like the one presented here. The most favorable characteristic of the procedure is the minimal transformation of images, because the normalization process follows

an inverse strategy compared with most normalization protocols. Instead of adjusting each MRI to a standard brain (like in SPM[16]) the Talairach system fits the normalized grid *onto* each brain. Thus, the brain size and shape remain unchanged because the transformation is applied to the normalized structure to fit each brain, differing from most normalization procedures. The only transformation made to the raw MRI consists of an image reformatting, intended to correct for minor spatial deviations in the 3D orientation of the patient's head, relative to the standard assumed in the Talairach atlas. It must be emphasized that minimal alterations of the brain morphology during the normalization process may be particularly important in the study of some diseases like schizophrenia, which involves subtle changes in size and shape of the brain[12, 17]. Other normalization processes in those cases may be flawed by the need to adjust the allegedly abnormal brain of the patient to a template built from normal individuals.

With regard to previous examples of this procedure applied to PET images, our system considerably improves the spatial resolution originally attained from the Talairach grid by enabling multiple levels of segmentation (Fig. 5) and quantification of metabolic activity rates, even for small brain structures (Fig. 6).

Our straight application of the Talairach grid division revealed two main inconsistencies of the published Talairach Atlas with its own tessellation procedure, corrected in our application. Inconsistencies have to do with to the lack of precision in determining the dimensions of the grid cells resulting from the division of brain regions into three, four or eight cell rows and columns[3]. Dimensions of the Talairach cells depicted in the original atlas can show up to 3mm difference in length with the real expected value. Perhaps the most relevant mistake for comparative studies is the false assumption of full bilateral symmetry of the Talairach atlas, which is in contradiction with descriptive studies of the human brain. Our automatic fit of the Talairach grid maintains the level of individual asymmetry relative to the midsagittal plane because external right and left boundaries of the brain are set independently by finding the tissue limits on each side. Our system also makes a precise division of the brain into equally-sized boxels for each of the six hemispheric regions (Fig. 1). Here again our procedure differs from other implementations of the Talairach method, that involve exact fitting of each brain to the Talairach atlas[4, 13, 14]. Unlike our system, the complete matching of the brain to the Talairach atlas distorts the brain by eliminating its natural asymmetry.

New tools and enhancements of the program that are now being tested include automatic brain extraction to reduce manual labor in MRI editing, and full batch operation when second or additional PET studies of the same patient are available. We believe that our system will enable neuroscientists a full exploitation of the Talairach grid as an automatic, standardized, segmentation and quantification method satisfactory for a wide variety of brain structures.

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