Original article

Stereotactic localization and visualization of the subthalamic nucleus

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Keywords: *subthalamic nulcleus; visualization; stereotaxis; brain atlas*

Background The subthalamic nucleus (STN) is widely recognized as one of the most important and commonly targeted nuclei in stereotactic and functional neurosurgery. The success of STN surgery depends on accuracy in target determination. Construction of a digitalized atlas of STN based on stereotactic MRI will play an instrumental role in the accuracy of anatomical localization. The aim of this study was to investigate the three-dimensional (3D) target location of STN in stereotactic space and construct a digitalized atlas of STN to accomplish the visualization of the STN on stereotactic MRI, thus providing clinical guidance on the precise anatomical localization of STN.

Methods One hundred and twenty healthy people volunteered to be scanned by 1.5 Tesla MRI scanning with 1-mm-thick slice in the standard stereotactic space between 2005 and 2006. One adult male was selected for 3D reconstruction of STN. The process of 3D reconstruction included identification, manual segmentation, extraction, conservation and reconstruction.

Results There was a significant correlation between the coordinates and age (P <0.05). The volume of left STN was significantly larger than the right STN, and there was a significant negative correlation between volume and age (P <0.05). The surface of the STN nucleus after 3D reconstruction appeared smooth, natural and realistic. The morphological feature of STN on the individual brain could be visualized directly in 3D. The 3D reconstructed STN could be rotated, zoomed and displayed at any direction in the stereotactic space. The anteroposterior diameter of the STN nucleus was longer than the vertical and transverse diameters in 3D space. The 3D reconstruction of STN manifested typical structure of the “dual lens”.

Conclusions The visualization of individual brain atlas based on stereotactic MRI is feasible. However, software for automated segmentation, extraction and registration of MR images need to be further developed.

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Among surgical treatments for advanced Parkinson’s disease (PD), the subthalamic nucleus (STN) has become the preferred target for high-frequency deep brain stimulation (DBS). It is widely recognized as one of the most important and commonly targeted nuclei of the motor thalamus in stereotactic and functional neurosurgery.[1] The success of STN surgery for PD depends on accuracy in target determination.[2,3] Given the small size of the STN, its oblique orientation, and its ovoid shape, it is crucial that the anatomic localization be as accurate as possible.

In stereotactic and functional neurosurgery, brain atlases would be useful for preoperative planning, intraoperative support and post-operative assessment.[4] Schaltenbrand-Wahren (SW) brain atlas is the most widely and frequently used at present. The optimal anatomical coordinates of STN target is often indirectly determined by neurosurgeons with coordinate transformations in stereotactic space. In addition, an intra-operative electrophysiological analysis is essential to finally confirm the optimal functional target of STN. However, there are several limitations when using this target-positioning method:[5-7] (1) In the Schaltenbrand′s atlas, sampling intervals in the direction of the slices are uneven and crude (0.5 mm–4 mm), which impedes their spatial interpolation. Furthermore, the horizontal microscopic series were erroneously sliced parallel to Reid’s line, which in the specimen analyzed was approximately 6°–8° oblique to the AC–PC plane, and thus not orthogonal to the other series.[8] (2) Notable variability of human brains exist between individuals, especially among different races. Specimens from Caucasians were collected in S-W atlas, which are not completely suitable for Asians. (3) Repeated adjustments of the defective anatomical target by intraoperatively electrophysiological confirmation would increase the duration of operation and also the risk of bleeding.[9] (4) Nowinski et al[10] have shown the three dimensional

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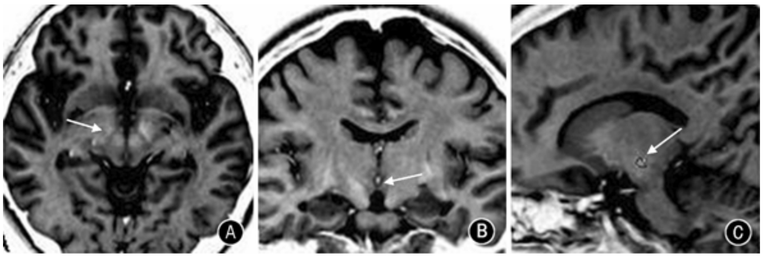

Figure 1. STN images on three different axes in stereotactic MRI. **A:** axial view; **B:** coronal view; **C:** sagittal view.

inconsistency of STN on the traditional SW atlas in their recent study. This demonstrates that the simple use of stereotactic coordinates directly derived from SW atlas is unreliable and unsafe. Therefore, many researchers have become more aware of the limitations of conventional atlases and consider the better alternative of individualized and functional computerized visualization of targeted nucleus in stereotactic surgery.[11]

The localization and reference of the structure and nucleus are mainly based on the brain atlas and two-dimensional (2D) image materials such as MR or CT, while three-dimensional (3D) reconstruction of the intracranial structures based on MRI can help neurosurgeons to obtain much more information than 2D image.[12,13] Therefore, stereotactic anatomical study and digitalized atlas of STN based on MRI will play a considerable role on the accurate anatomical localization in the functional neurosurgery. However, to our knowledge, a stereotactic individualized and digitalized atlas of STN on MRI has not been reported yet.

On the basis of our previous works,[14-16] we carried out a stereotactic anatomical study of STN based on MRI. And STN was recognized, segmented and 3D reconstructed in stereotactic space by using computerized techniques. The aim of this study was to investigate the 3D target location of STN in stereotactic space and construct a digitalized atlas of STN to accomplish the visualization of the STN on stereotactic MRI, providing clinical guidance to precise anatomical localization of STN.

METHODS

Stereotactic MRI acquisition of specimen

One hundred and twenty healthy Chinese people volunteered to be scanned by stereotactic MRI between 2005 and 2006. The group was composed of 60 males (age ranging from 21 years to 80 years, mean (43.32±14.15) years), and 60 females (age ranging from 21 years to 78 years, mean (45.27±15.83) years). The subjects were assigned to six groups as follows: A: 21–30 years; B: 31–40 years; C: 41–50 years; D: 51–60 years; E: 61–70 years; F: 71–80 years. Twenty cases were in each group.

High-resolution MR imaging of the brains was performed with a Siemens 1.5 Tesla scanner (Siemens, Germany). Prior to imaging, the brains were fixed according to our previously described method.[17] The detailed steps or measures of MR image acquisition were the same as our previous study.[18] Prior to scanning, determined AC, PC and the length from midpoint of AC posterior edge to midpoint of PC anterior edge was measured, which was called LI. Midpoint of LI was viewed as an origin in the coordinate system. Z axis was defined as the axis through the origin that is parallel to the median sagittal plane. X axis was perpendicular to the sagittal plane at AC-PC plane. Y axis was perpendicular to both axes through the origin. The directions of axes are: x, from left to right (hemisphere); y, from posterior to anterior; z, from ventral to dorsal. The AC-PC plane was considered as H0 plane. The coronal plane and sagittal plane, which were vertical with the H0 plane at the original point, were considered as F0 and S0 plane, respectively. We scanned axial MRI with T2 weighting series (layer thickness 1 mm, interval distance 0 mm) after setting H0 plane as the center. The MRI sections upper-down H0 plane were marked as Hd and Hv, respectively. And the distance to H0 plane was marked as Hd1, Hd2, Hd3…Hd20 and Hv1, Hv2, Hv3…Hv20. Figure 1 shows STN images on three different axes in stereotactic space. T2-weighted sequence (TR = 4200 ms, TE=100 ms, FOV=192×256) was performed for the visualization of 3D reconstruction for STN.

Analysis of MRI data

On the successive scanning of T2-weighted sequence, the MR section with maximum transverse diameter of STN was selected from each specimen. With computerized techniques and software developed in our group, the centroid coordinates of STN on both hemispheres were measured automatically. Comparative analysis was studied on the centroid coordinates of STN between six groups. Data were analyzed by *t* test with SPSS 13.0. A probability of less than 0.05 was considered significant. Contours of the STN nucleus were delineated manually. The areas and volumes of STN were calculated automatically with computer.

Three-dimensional reconstruction of STN

Among all the volunteers, one adult healthy male was selected to be scanned by stereotactic MRI for 3D reconstruction of STN. The 3-D reconstructing process included identification, manual segmentation, extraction, conservation and reconstruction of STN.

First, the MRI data was extracted from the compact disk and the DICOM form was transformed into the Bitmap form to preserve pixel resolution. The image was saved in

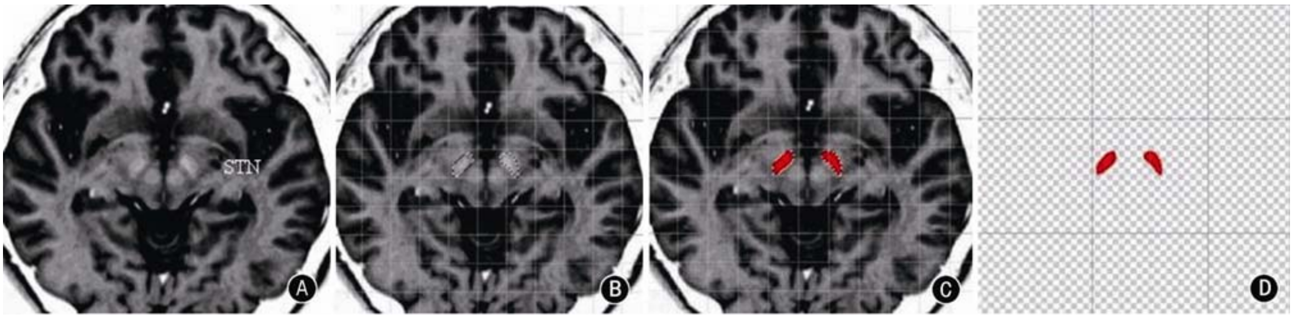

Figure 2. Process of three-dimensional reconstruction of STN. **A:** identification; **B:** segmentation; **C:** filling; **D:** extraction.

the RGB mode. Second, the RGB mode MR image was extracted with specific software and STN was identified at the axial image. The contour of STN was outlined by manual segmentation at slices, using minor adjustments where necessary. Then colors were filled in and most other structures were neglected (Figure 2). Finally, each slice was numbered and saved. In this study, we segmented and saved the amygdaloid nucleus (AM), lateral cerebral ventricle and corpus callosum to demonstrate the spatial localization for STN (Figure 3).

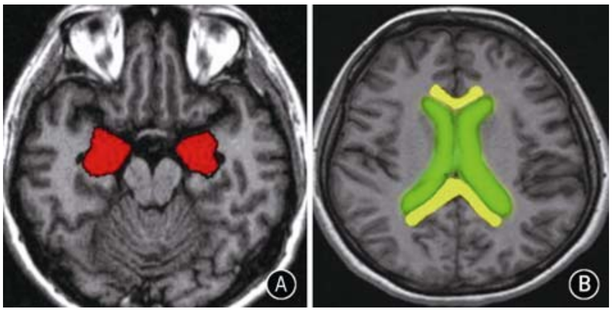

Figure 3. Segmentation of amygdaloid nucleus, lateral cerebral ventricle and corpus callosum. **A:** amygdaloid nucleus; **B:** corpus callosum and lateral cerebral ventricle.

We used the software package TriPlanar MedViewer developed by a collaborator (Harbin Institute of Technology, China) to 3-D reconstruct the image saved above. This software can identify the boundaries of STN, AM, lateral cerebral ventricle and corpus callosum, and reconstruct the structure automatically.

RESULTS

The stereotactic coordinates and volumes of STN

The centroid coordinates of STN nucleus in different groups were seen in Table 1. After statistical analysis, there was significant correlation between the coordinates and age (P <0.05). Significant difference could be seen between group D and E (P <0.05). However, there was no significant difference among other groups (P >0.05).

The volumes of STN in different age and gender groups were seen in Table 2. From statistical analysis, the volume of male STN was significantly larger than female STN (P <0.05). Simultaneously, the volume of left STN was significantly larger than the right STN, and there was a significant negative correlation between volume and age (P <0.05).

Table 2. The volumes of STN in different groups (mean±SD, mm^3)

Groups	No.	Male		Female	
		Right	Left	Right	Left
A	20	136±6.23	143±6.27	129±5.37	133±6.30
B	20	131±5.87	145±7.54	128±6.28	136±7.37
C	20	142±7.17	148±9.32	131±8.37	136±8.48
D	20	133±8.26	141±7.85	131±6.93	134±6.72
E	20	123±6.54	134±9.26	118±7.54	126±7.83
F	20	120±7.66	129±5.74	117±5.32	122±5.97
Total	120	130±5.58	140±7.67	125±6.64	132±7.11

Three-dimensional reconstruction of STN

Figure 4 shows the 3D reconstruction of STN in stereotactic space. In the image reconstructed, the yellow straight line is AC-PC (Y), and the red one stands for the straight line (Z) that perpendicular to mid AC-PC in the midsagittal plane, while the green represents the line (X) that perpendicular to mid AC-PC through original point in the H0 plane.

The 3D reconstructed STN has smooth surface vivid appearance and clearly shows the individual localization in the standard stereotactic space for directly observing the shape of STN. The surface of the STN nucleus after

Table 1. The centroid coordinates values of STN in different groups (mean±standard deviation (SD), mm)

Groups	No.	Right			Left		
		X	Y	Z	X	Y	Z
A	20	10.50±2.43	−1.85±0.40	−3.50±0.34	−10.77±2.03	−1.50±0.46	−3.58±0.67
B	20	10.78±2.84	−1.16±0.14	−5.94±1.21	−10.82±2.83	−1.33±0.33	−5.04±1.21
C	20	11.16±3.05	−1.13±0.28	−4.98±1.37	−11.22±1.55	−1.40±0.21	−4.81±0.87
D	20	10.17±2.03	−1.41±0.32	−5.28±1.23	−10.87±2.62	−1.12±0.32	−4.53±1.19
E	20	12.85±3.20	−0.73±0.21	−3.50±0.74	−12.94±2.12	−0.51±0.12	−2.72±0.26
F	20	12.90±3.90	−0.66±0.13	−3.59±1.02	−12.97±2.07	−0.49±0.08	−2.80±0.32
Total	120	11.38±1.19	−1.18±0.31	−3.95±0.94	−11.59±1.20	−1.05±0.21	−3.05±0.25

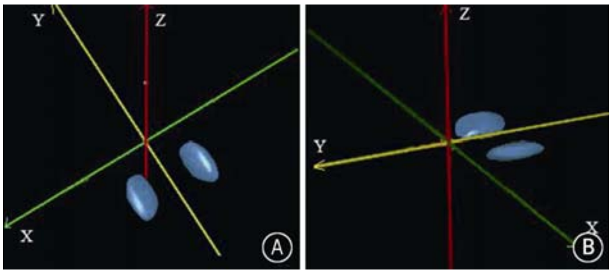

Figure 4. Effect of three-dimensional reconstruction of STN. **A:** superior view; **B:** lateral view.

3D reconstruction appeared smooth, natural and realistic. The morphological feature of STN on the individual brain could be visualized directly in 3D. The anteroposterior diameter of the STN nucleus was longer than the vertical and transverse diameters in 3D space. The 3D reconstruction of STN manifested typical structure of the "dual lens". The result of 3D reconstruction for STN, AM, lateral cerebral ventricle and corpus callosum can be seen in Figure 5. The 3D reconstructed structures and nucleus can be rotated, zoomed and displayed at any direction in the stereotactic space.

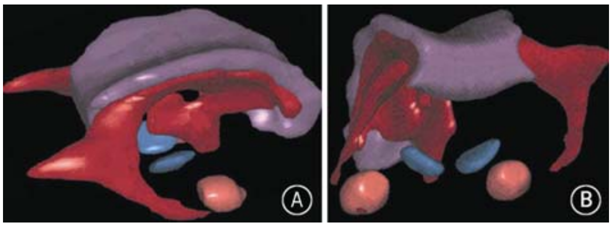

Figure 5. Three-dimensional reconstruction of STN, amygdaloid nucleus, lateral cerebral ventricle and corpus callosum. **A:** lateral view; **B:** posterior view.

DISCUSSION

The STN is a major stereotactic target structure for the surgical treatment of Parkinson's disease. Many studies on the STN have been carried out, including anatomical, imaging, electrophysiological and clinical studies.[19-21] In this study, we carried out a stereotactic anatomical study of STN based on MRI. The STN nucleus was recognized, segmented and 3D reconstructed in stereotactic space by using computerized techniques. A stereotactic individualized and digitalized atlas of STN on MRI has been constructed. The aim was to explore a creative way for the individualization of stereotactic and functional neurosurgery. With the development of the atlas registering, the technique of segmentation and associated computer software, there is no doubt this will make a significant contribution to the formulation of a successful stereotactic operation procedure. This method allows the intracranial structure to be rapidly 3D reconstructed by the imageology.

The stereotactic coordinates and volume of STN target

In this study, the centroid coordinates of right STN was as follows: X=(11.38±1.19) mm, Y=(–1.18±0.31) mm and Z=(–3.95±0.94) mm; and the left STN was X=(–11.59±1.20) mm, Y=(–1.05±0.21) mm and Z=(–3.05±0.25) mm. There is a difference between our results and another study.[22] The main reason for the difference may be due to the difference between the anatomical centroid coordinates measured in this study and the functional target coordinates obtained through intraoperative electrophysiological determination. Moreover, other factors may also cause the difference in data acquisition, including the different histological processing method for cadaver brain, the positional identification and determination of AC and PC, and the different location of the origin derived in this way.[14]

In this study, we have found from statistically analysis that the volume of male STN was significantly larger than female STN (P <0.05). Simultaneously, the volume of left STN was significantly larger than the right STN, and there was a significant negative correlation between volume and age (P <0.05). These differences may reflect the concordance between the morphology and the function of human brain. It is also a reflection of the cerebral asymmetry.

The meaning of the stereotactic digitalization and visualization of atlas

At present, the pre-operative localization commonly refers to the original stereotactic brain atlases. However these atlases only obtain anatomical data from a few people's brains. There are many limitations in the use of these atlases for the precise anatomical localization because of the variability of individual anatomy.[6,7] Some brain atlases of print edition have been transformed to electrical pattern in order to make the atlas more direct-viewing, including Schaltenbrand-Bailey atlas, Schaltenbrand-Wahren atlas, Talairach-Tournoux atlas, Ono et al atlas, Afshar atlas, Van Buren-Borke atlas, etc.

Vayssiere et al[23] found that there was a significant difference after comparison of Schaltenbrand atlas and MRI-based stereotactic targeting of the Gpi in the performance of DBS for treatment of dystonia. Neurosurgeons have realized the limitation of the original atlas during the process of stereotactic and functional neurosurgery. Experts in this field have paid much emphasis on the visualization and individualization of the target nucleus.[24] There is a need for the development of the computerized techniques and medical image manipulation.[25]

The study of digitalization and visualization for STN

There are lots of reports on DBS for the therapy of Parkinson's disease. However, there have been fewer studies on the STN visualization atlas. This study has rebuilt the 3D image for STN on MRI with computer technology to carry out the individualization and visualization of STN. To our knowledge, there has no previous study on 3D reconstruction for the STN of

Chinese brain. Our group successfully 3D reconstructed the STN, as well as AM, lateral cerebral ventricle and corpus callosum.

Figure 5 shows the localization of stereotactic space for STN, AM, lateral cerebral ventricle and corpus callosum. It also can be rotated, zoomed and displayed at any direction in the stereotactic space following 3D reconstruction. The digitalization and visualization of these structure and nucleus on MRI has been accomplished based on computerized techniques of image processing.

The problems to be solved for 3D reconstruction of STN

The technology of image segmentation is a general problem in image manipulation and analysis. This technology can help researchers extract the structure which they are interested in from the brain. Additionally, it is also the foundation of 3D reconstruction. The effect of segmentation has direct influence on the accuracy of 3D reconstructed model.

In this study, extraction of STN from MRI is accomplished by manual segmentation. However, it is tremendously hard work to segment nucleus manually because of the large number of MR images. Whether the brain atlas can make a big breakthrough or not depends on the technology of image segmentation, which will shorten the researcher's working time and improve efficiency of the entire process. Scholars have proposed many methods to automatically segment medical images and have succeeded to some extent.[26] However, for such complicate medical images as the brain, it is difficult to automatically segment all structures of the tissue relying just on the image. The currently available image segmentation technology can only automatically dissect cerebral gray matter, white matter and CSF on MRI, and the manual segmentation is still the major procedure for most of the cerebral tissues. To perform 3D reconstruction on an individual basis completely and rapidly, some issues need to be solved, such as automatic recognition, registration and segmentation with computer technology.

The effect of MR technology for 3D reconstruction

Excessively minor size is still a limitation on the effect of reconstruction for STN computerized 3D model. Scanning with 3.0 Tesla MR and 0.5 mm slice interval can demonstrate STN more clearly[20] and then reconstruction of the STN can result in a more satisfying effect. We adopted 1.5 Tesla and 1 mm slice interval to scan image and achieve ideal results.

With the software developed on the basis of surface rendering technology, the AM nucleus has already been 3D reconstructed based on cadaver brain sections.[27] In this study, we used the software explored by Harbin Institute of Technology to 3D reconstruct STN and other structures or nuclei and made progress that built upon previous domestic findings. However, further works and studies on the algorithm and software for the 3D reconstruction of brain structures are needed in the future.

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