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A Probabilistic Functional Atlas of the VIM Nucleus Constructed from Pre-, Intra- and Postoperative Electrophysiological and Neuroimaging Data Acquired during the Surgical Treatment of Parkinson's Disease Patients

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Key Words
Probabilistic functional atlas · Ventrointermediate nucleus · Brain atlas · Electronic atlas · Parkinson's disease

Abstract
We have previously introduced a concept of a probabilistic functional atlas (PFA) to overcome limitations of the current electronic stereotactic brain atlases: anatomical nature, spatial sparseness, inconsistency and lack of population information. The PFA for the STN has already been developed. This work addresses construction of the PFA for the ventrointermediate nucleus (PFA-VIM). The PFA-VIM is constructed from pre-, intra- and postoperative electrophysiological and neuroimaging data acquired during the surgical treatment of Parkinson's disease patients. The data contain the positions of the chronically implanted electrodes and their best contacts. For each patient, the intercommissural distance, height of the thalamus and width of the third ventricle were measured. An algorithm was developed to convert these data into the PFA-VIM, and to present them on axial, coronal and sagittal planes and in 3-D. The PFA-VIM gives a spatial distribution of the best contacts, and its probability is proportional to best contact concentration in a given location. The region with the highest probability corresponds to the best target. The PFA-VIM is calculated with 0.25-mm^3 resolution from 107 best contacts in two situations: with and without lateral compensation against the width of the third ventricle. For the PFA-VIM compensated laterally, the anterior, lateral and dorsal coordinates of the mean value are (in mm) 6.24, 13.83, 1.68 for the left VIM and 6.54, –13.84, 2.10 for the right VIM. The coordinates of the mean value of the highest probability region along with the highest number of the best contacts (P) are: 6.25, 14.25, 1.75, P = 16, for the left VIM, and 6.0, –14.0, 1.00, P = 18, for the right VIM. The coordinate system origin is at the posterior commissure. For the PFA-VIM not compensated laterally, the coordinates of the mean value are 6.24, 13.99, 1.68 for the left VIM and 6.53, –14.13, 2.10 for the right VIM. The coordinates of the mean value of the highest probability region along with the highest number of the best contacts are 5.58, 13.67, 1.33, P = 14, for the left VIM, and 6.36, –14.03, 1.11, P = 17, for the right VIM. The PFA-VIM atlas overcomes several limitations of the current anatomical atlases and can improve targeting of thalamotomies and thalamic stimulations. It is dynamic and can easily be extended with new cases.

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Introduction

The existing stereotactic atlases are constructed based on a few brains only and population information is very limited or lacking completely. These atlases are anatomical, while the actual stereotactic targets are functional. Moreover, these atlases are not consistent in 3-D. A probabilistic functional atlas (PFA) overcomes these limitations and opens new possibilities. By collecting data from numerous patients, the PFA with a functional distribution of cerebral structures can be constructed and potentially new knowledge extracted from it.

We proposed the concept of PFA in a previous study [7]. Subsequently, an algorithm for PFA calculation has been devised [8]. In addition, a web-based public domain portal has been developed allowing the neurosurgeon to calculate the PFA from his/her own data [9]. The calculation of PFA for the subthalamic nucleus (PFA-STN) is addressed in a study by Nowinski et al. [10], while another study by the same group [11] analyzes a PFA-STN created from bilateral cases and extracts new knowledge.

The PFA aggregates knowledge gathered from numerous stereotactic surgeries and presents it in an image form representing the distribution of the best stereotactic contacts. The probability at a given point is proportional to the best contact frequency at this point. The point (or any point if there are more than one) with the highest probability is taken as the best target.

The goal of this work was to build the PFA for the ventrointermediate nucleus (VIM) of the thalamus (PFA-VIM) and study its properties. The PFA-VIM parameters are calculated for the left and right VIM in two situations: with and without lateral compensation against the width of the third ventricle. The calculated parameters include the location of mean value, standard deviation, volume, and coordinates of the mean value of atlas maximum region.

Material and Method

Material

Multimodal data were acquired pre-, intra-, and postoperatively during the surgical treatment of Parkinson's disease patients. The stereotactic environment for data acquisition [1] (fig. 1) and the surgical procedure [2, 3] have been described previously. Preoperatively, two perpendicular projections, lateral and anteroposterior, were acquired from X-ray ventriculography showing the anterior commissure (AC), posterior commissure (PC), thalamus and third ventricle (fig. 2). The distance between the AC and PC, height of the thalamus (HT) and width of the third ventricle (V3) were measured on these X-rays [4]. These values along with the coordinates of the best contacts (obtained intraoperatively and updated

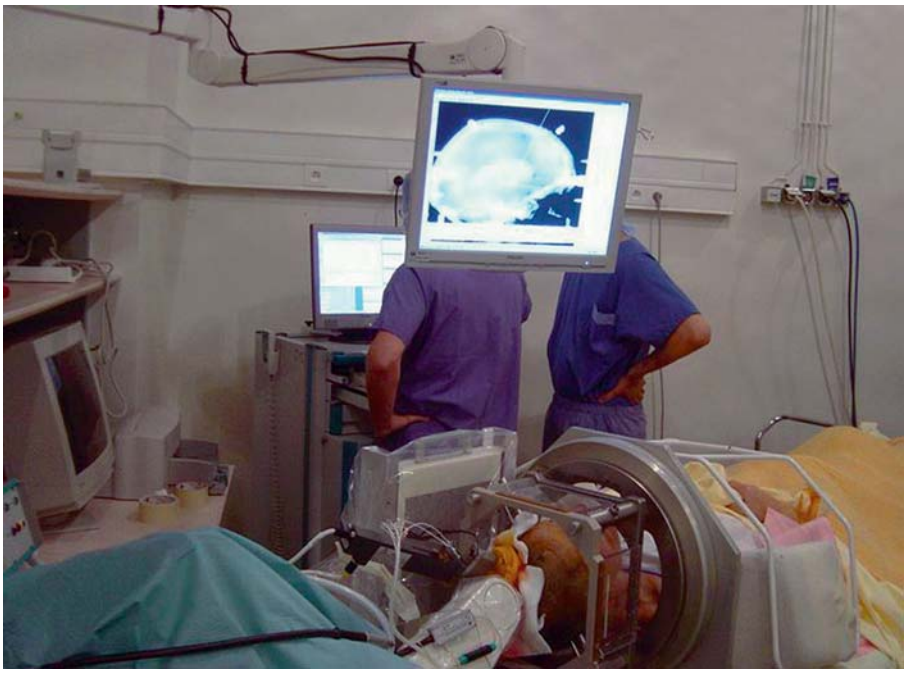

Fig. 1. The stereotactic environment.

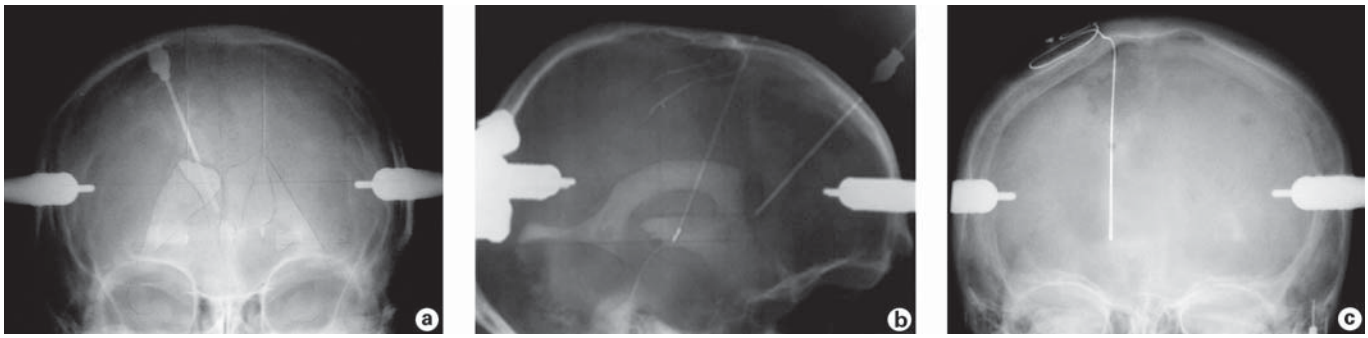

Fig. 2. X-rays: preoperative (**a**) and intraoperative (**b**, **c**).

postoperatively during a 3-month neurological follow-up) were used to calculate the PFA-VIM.

Three types of electrodes were used: monopolar, quadpolar with 1.5-mm gap (Medtronic 3387) and quadpolar with 0.5-mm gap (Medtronic 3389). The numbers of the best contacts were: 50 for the left VIM: 20 (mono), 29 (3387) and 1 (3389); 57 for the right VIM: 29 (mono), 26 (3387) and 2 (3389).

Method

The PFA-VIM is calculated in the atlas space. This atlas space is Cartesian with the coordinate system origin at the PC. The directions of axes are: x, from posterior to anterior; y, from right to left (hemisphere); z, from ventral to dorsal. The x axis is in AC-PC units such that the AC-PC distance is divided into 12 units. The y axis is in millimeters and the z axis in HT units, each unit being HT/8. The method has the following steps:

1 Normalize all contacts and place them in the atlas space (fig. 3a). The contacts are normalized in 3-D as follows: posteroanteriorly by scaling them proportionally to the AC-PC distance; ventrodorsally by scaling them proportionally to HT; laterally (left and right) in two situations: without lateral compensation against the third ventricle (i.e., with no change in the lateral coordinates), and with lateral compensation against the width of the third ventricle by shifting its lateral coordinate by $(V3_{average} - V3)/2$, where $V3_{average}$ is the average width of V3 over all cases.
2 Select the best contacts (fig. 3b). The best contacts are initially determined intraoperatively and then fine tuned in a neurological follow-up.
3 Discretize contacts (fig. 4a). The volume of each cylindrical contact (deformed due to normalization) is converted into isotropic volumetric elements (voxels). The size of a voxel is user defined. A fast algorithm for contact voxelization is detailed in Nowinski et al. [8].
4 Calculate atlas function. The value of atlas function in a given point (the center of the voxel) is calculated as the number of best contacts in this point.
5 Replace each contact with its corresponding voxels (fig. 4b). This changes the atlas representation from geometric to volumetric.
6 Calculate probability. The atlas probability is a linear function of the atlas function. The user specifies it to convert the range of atlas function values into [0,1], for examples see [8].

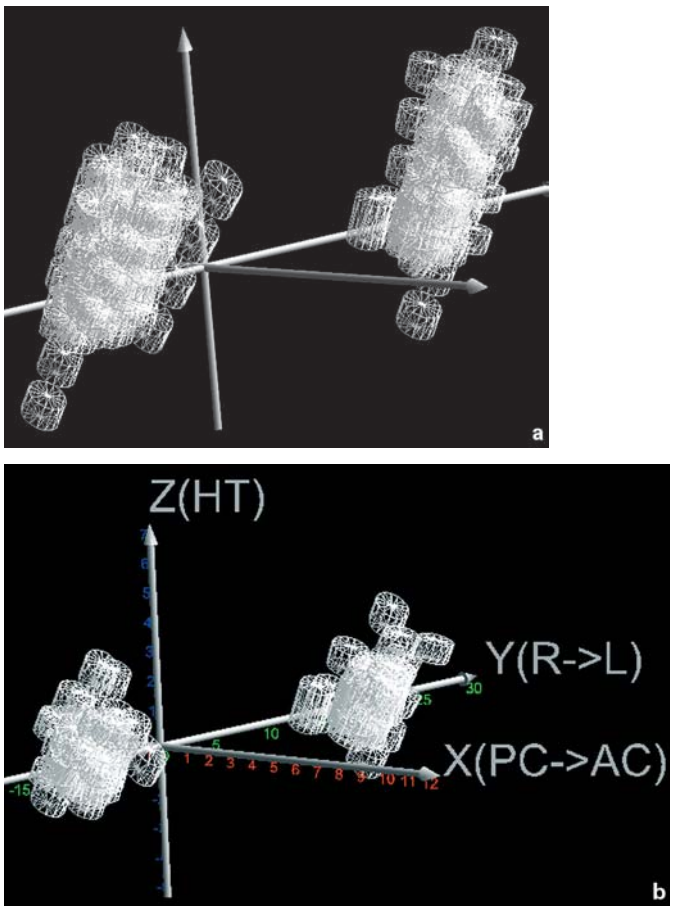

Fig. 3. Processing of stereotactic contacts. **a** All contacts normalized to the atlas space. **b** Best contacts selected.

To facilitate PFA-VIM use, it has been recalculated in millimetres along all three axes assuming that the AC-PC distance in the atlas space is 24 mm (the AC-PC unit is 2 mm) and the height of the thalamus is 16 mm (the HT unit is 2 mm).

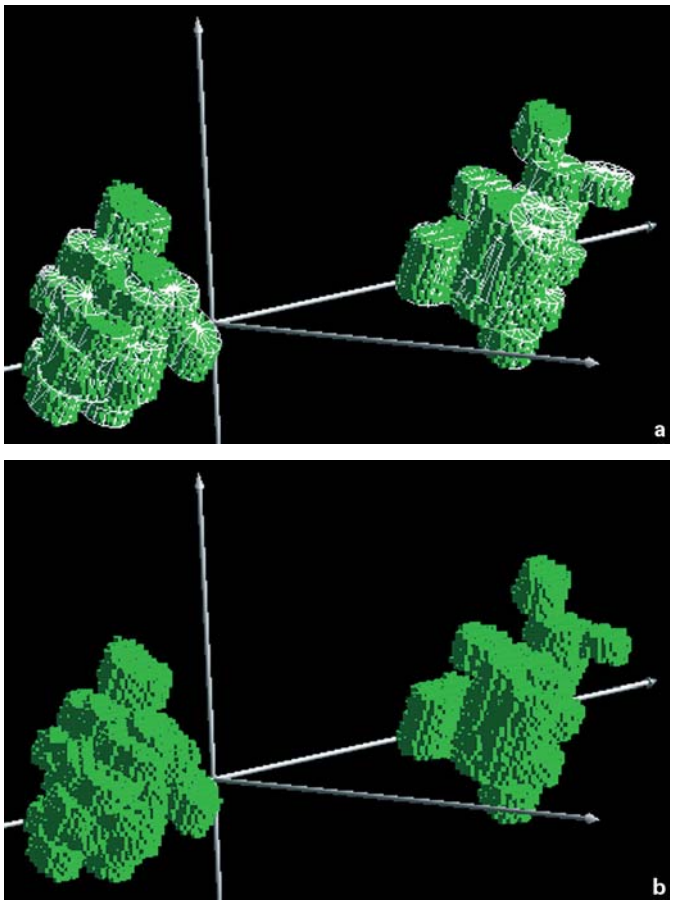

Fig. 4. Contact voxelization. **a** Best contacts converted into voxels (both cylindrical contact outlines and voxels are shown). **b** 3-D PFA-VIM in volumetric representation (as a set of voxels).

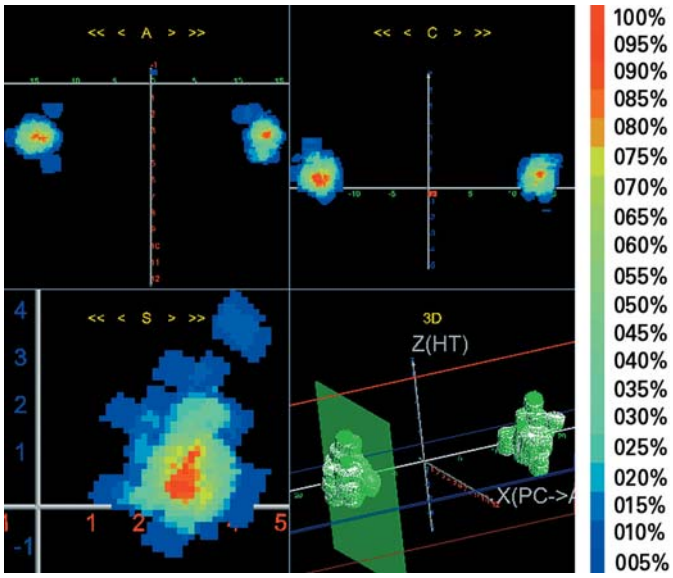

Fig. 5. Presentation of PFA-VIM as 2-D axial A, coronal C and sagittal S probabilistic maps (with the color bar on the right) and in 3-D (along with the locations of the orthogonal A, C, S planes).

Table 1. Atlas calculation time versus its resolution

Resolution, mm^3	Time of calculation, s
0.5	2
0.25	14

PFA-VIM Presentation

The PFA-VIM can be presented in two ways (fig. 5): (1) in 3-D as a set of voxels (bottom right), and (2) on 2-D orthogonal axial A (top left), coronal C (top right) and sagittal S (bottom left) images generated from the voxelized contacts by fixing one coordinate. The 3-D presentation gives the overall shape of the functional VIM. The 2-D maps show probability distribution and they are more suitable for warping and overlaying onto a patient-specific scan. The 2-D maps can be presented as color or gray scale images. Color images require a color bar (palette) representing probability value. We used typically cold colors to represent a low range of probabilities and hot colors to represent a high range of probabilities (fig. 5). When using gray scale images, the gray scale is proportional linearly to probability such that the white color corresponds to probability zero and the black color to probability one.

Results

The PFA-VIM is calculated rapidly from the data with high 0.25-mm^3 resolution. The time of atlas calculation is resolution dependent. The algorithm performance on a Pentium 4 (3 GHz, 1 GB RAM) is given in table 1.

The following parameters are calculated and analyzed for the left and right PFA-VIM:

- maximum value of atlas function;
- anterior, lateral (left and right) and dorsal coordinates of the mean atlas value (in mm);
- standard deviation;
- volume in mm^3 (formed by all voxels for which the atlas function value is ≥ 1);
- anterior, lateral (left and right) and dorsal coordinates of the mean value of the region with the maximum atlas value (the highest probability).

Table 2. PFA-VIM parameters with the lateral compensation against the third ventricle

Parameter	PFA-VIM		Difference right/left
	left	right	
Best contacts	50	57	7
Maximum value	16	18	2
Location of mean value, mm	6.24, 13.83, 1.68	6.54, –13.84, 2.10	0.51
Standard deviation	1.59, 1.22, 1.72	1.56, 1.27, 1.78	0.08
Volume, mm^3	182.23	214.84	17.89%
Coordinates of mean value of atlas maximum region, mm	6.25, 14.25, 1.75	6.0, –14.0, 1.00	0.83

Table 3. PFA-VIM parameters without the lateral compensation against the third ventricle

Parameter	PFA-VIM		Difference right/left
	left	right	
Best contacts	50	57	7
Maximum value	14	17	3
Location of mean value, mm	6.24, 13.99, 1.68	6.53, –14.13, 2.10	0.53
Standard deviation	1.59, 1.57, 1.72	1.55, 1.49, 1.78	0.11
Volume, mm^3	205.09	232.83	13.52%
Coordinates of mean value of atlas maximum region, mm	5.58, 13.67, 1.33	6.36, –14.03, 1.11	0.89

The PFA-VIM parameters with lateral compensation are given in table 2, while table 3 contains these parameters without lateral compensation.

Discussion

Lateral Compensation

Figure 6 shows 3-D and 2-D PFA-VIM images with and without lateral compensation against the third ventricle. Qualitatively, each situation (i.e. with and without lateral compensation) looks similar, although there are visible differences in the lateral position of the PFA-VIM. Quantitatively, laterally compensated volume of PFA-VIM is smaller (by 11.15% for the left PFA-VIM and 7.73% for the right PFA-VIM) and the lateral component of the standard deviation is lower (1.22 vs. 1.57 for the left PFA-VIM and 1.27 vs. 1.49 for the right PFA-VIM; (tables 2 and 3). This may be interpreted that the lateral compensation makes the functional VIM more compact. In addition, for the laterally compensated PFA-VIM the region of atlas maximum contains a single voxel only for each hemisphere, while that for the PFA-VIM noncompensated laterally is composed of multiple voxels (see the section PFA-VIM-Based Surgery Planning).

Advantages of PFA-VIM

The constructed probabilistic functional VIM has the following advantages. It:

- aggregates knowledge from the previously operated cases;
- shows quantitative distribution of the best contacts in image representation;
- is population based;
- is consistent in 3-D;
- has high resolution of 0.25 mm^3; generally, the PFA-VIM can be calculated with a user-specified resolution;
- is dynamic: new cases can be added or various PFAs can easily be merged;
- can be calculated rapidly, which enables its quick updates or use in remote operations (web-enabled applications; table 1).

It has to be emphasized that knowledge aggregation can be done individually by the neurosurgeon, or within a group of users, or over the entire neurosurgical community.

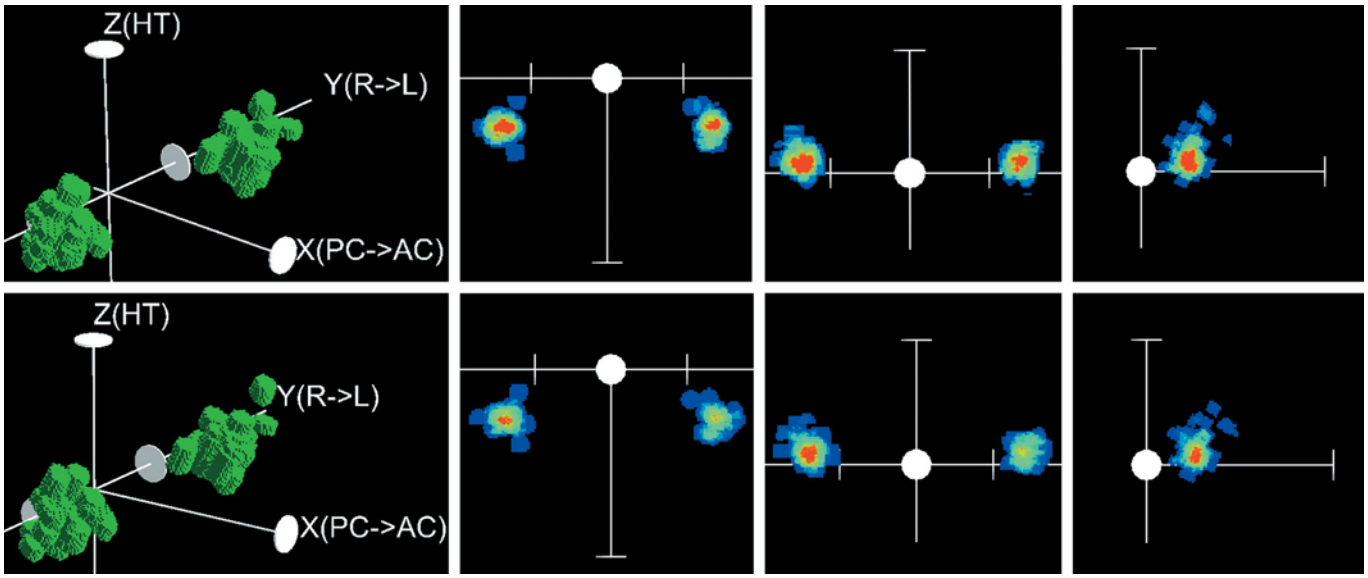

Fig. 6. 3-D and 2-D PFA-VIM images with and without lateral compensation against the third ventricle. The top row shows 3-D, axial, coronal and sagittal images with the lateral compensation, and the bottom row the corresponding images without the lateral compensation. The disks on the axes are located at the HT (dorsally), AC (anteriorly) and at 10 mm (left and right).

Limitations of PFA-VIM

Limitations of the PFA-VIM include:

- linear scaling and shifting applied for contact normalization; theoretically, nonlinear warping is superior, but practically, within the region between the AC-PC where the target is located, the difference between the linear and nonlinear warping is negligible [5];
- activation region limited to the shape of the contact (a more advanced model requires knowledge of electrophysiological properties of brain tissues and electrical properties of electrode);
- limited number of cases used in this study.

PFA-VIM-Based Surgery Planning

The PFA-VIM can be individualized to a patient-specific scan by performing a transformation inverse to that used for contact normalization. Then, the PFA-VIM can be overlaid on the scan and the probability at any location read. The initial target, based on imaging and/or anatomical atlas, can be enhanced by taking into account the most probable point (or generally the region with the maximal atlas value) of the PFA-VIM. In case when the imaging-based target and the PFA-VIM target overlap, our approach provides an extra degree of confidence in target selection and potentially a further fine tuning of target location, as the PFA-VIM spatial resolution is much higher than that of MRI. In case of mismatch, the PFA-VIM may be employed for setting the second trajectory, if the first one is not optimal.

It should be noted that the location of the mean value of atlas maximum region (tables 2 and 3), in general, may not be the best target. For the data used in this study, only for the PFA-VIM compensated laterally the single best target and the mean value of atlas maximum region are the same. In this situation, the region of atlas maximum is composed of a single voxel, so the best target and the mean value of atlas are the same (i.e. the coordinates of the center of this voxel and those of the mean value are similar). For the left hemisphere, this maximum value is 16 located at 6.25, 14.25, 1.75. For the right hemisphere, the maximum value is 18 located at 6.0, –14.0, 1.0.

However for the PFA-VIM not compensated laterally, the atlas maximum region is composed of multiple voxels. For the left hemisphere, there are three voxels with the maximum value of 14 with coordinates: 5.25, 13.75, 0.5; 5.75, 13.5, 1.75; 5.75, 13.75, 1.75. The location of their mean (5.583333, 13.66667, 1.333333) is inside voxel 5.5, 13.75, 1.25, which is not the best target (its atlas value is 10). For the right hemisphere, there are nine voxels with the maximum value of 17 with coordinates: 6.0, –14.0, 1.0; 6.25, –14.0, 0.75; 6.25, –14.0, 1.0; 6.25, –14.0, 1.25; 6.5, –14.25, 1.0; 6.5, –14.0, 0.75; 6.5, –14.0, 1.0; 6.5,

–14.0, 1.5; 6.5, –14.0, 1.75. The location of their mean (6.361111, –14.027778, 1.111111) is inside voxel 6.25, –14.0, 1.0, which is the best target.

Combination of the PFA-VIM with an anatomical atlas, such as the Schaltenbrand-Wahren atlas (SWA) [16], may provide a more efficient target and trajectory planning. Then, a high spatial resolution PFA-VIM is combined with a highly parcellated SWA, which causes that the target structure can be displayed with high resolution compensating for its sparseness in the SWA, while its surrounding structures are delineated by the SWA. The PFA-VIM was spatially co-registered with the SWA based on the approach presented in Nowinski [12], and subsequently the application [13] containing the PFA-STN has been extended to include the PFA-VIM too [15]. In this application, the zero probability region is displayed as transparent, while the non-zero probability region is in gray scale with a user controlled blending between the scan and PFA-VIM. A combined PFA and SWA atlas should be employed with care and the limitations inherent in the SWA [6, 14] should be taken into account.

Conclusion

The PFA of the VIM nucleus is derived from 107 best stereotactic contacts. The PFA-VIM is based on electrophysiology, neuroimaging and neurological assessment. The resulting atlas is volumetric and of high 0.25-mm^3 resolution. It can be reformatted and warped to match patient-specific data. In addition, it is dynamic and can easily be extended to aggregate knowledge from previously operated cases. The PFA-VIM overcomes several limitations of the current anatomical atlases and can improve targeting of thalamotomies and thalamic stimulations. It may also be useful in neuroscience research to study functional properties of the VIM. The presented method is general and can be applied for constructing human and animal probabilistic functional brain atlases.

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