Segmenting the substantia nigra in ultrasound images for early diagnosis of Parkinson`s disease

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Abstract. Early diagnosis of Parkinson's disease (PD) is of immense importance, since clinical symptoms do not occur until substantial parts of the substantia nigra (SN) in the brain stem have been irreparably damaged. Recent work suggests, that by means of transcranial sonography (TCS) it is possible to determine PD even in the preclinical state. In images of the mesencephalon, the SN shows a distinct hyperechogenic pattern on TCS, which is currently manually segmented. To remove this investigator dependence, we develop a semi-automatic algorithm to segment SN in TCS images. After some preprocessing steps, the actual segmentation works intensity-based with morphological operations, taking anatomical information into account. The resulting size of the SN serves as a risk factor for PD manifestation.

Keywords: Early Diagnosis; Investigator Independence; Parkinson's Disease; Substantia Nigra; Segmentation; Transcranial Sonography.

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1. Introduction

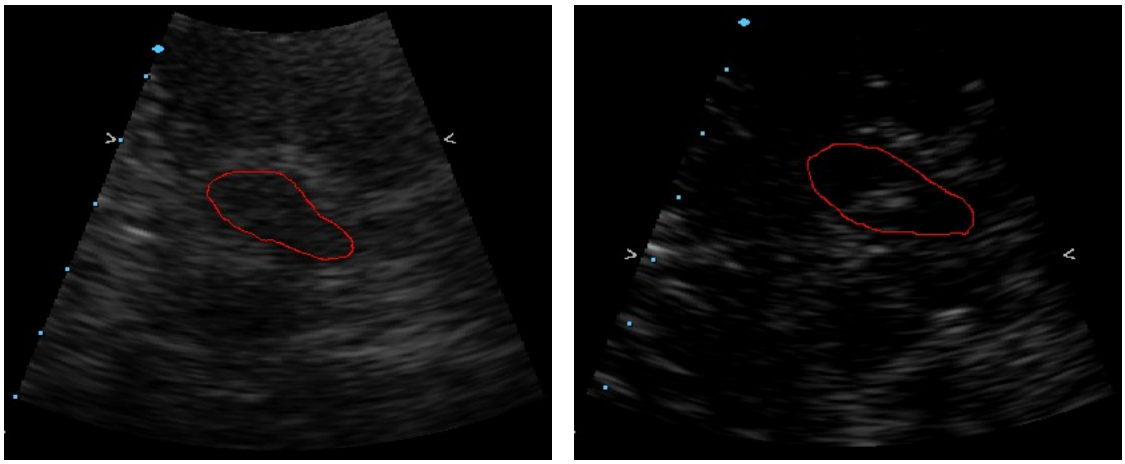
Early diagnosis of Parkinson's disease (PD) is of immense importance, since clinical symptoms do not occur until substantial parts of the substantia nigra neurons in the brain stem have been irreparably damaged. Furthermore, large parts of the population are affected by this disease [1] and although PD is currently regarded as incurable, the symptoms can be alleviated by the administration of drugs. Neuroprotective drugs could shelter neurons of the SN when used at the beginning of the disease in the preclinical state. Therefore a technology to detect early SN damage is wanted for the identification of individuals at risk for PD.

Recent work suggests, that by means of transcranial sonography (TCS) it is possible to determine the formation of idiopathic PD as well as monogenic forms of parkinsonism at a very early state. In ultrasound (US) images of the mesencephalon, the substantia nigra (SN) shows a distinct hyperechogenic pattern on TCS in about 90% of patients with PD, despite its normal appearance on CT and MRI scans [2, 3]. However, this finding is based on manual evaluation of examined images [4]. Nevertheless, the fact that this phenomenon occurs with the use of ultrasound as imaging method is very promising, since US is fast, cheap, and tolerable to immoveable patients compared to other clinical imaging methods. To develop and validate an early, observer-independent PD indicator, a (semi-)automatic algorithm for analysis of brain stem TCS images is necessary. With this algorithm, the size of the region with increased tissue response should be automatically determined.

2. Methods

The ultrasound examination is performed from the temporal acoustic bone window in a standardized axial mesencephalic imaging plane (landmark: butterfly-shaped brainstem). Due to a decreased signal-to-noise-ratio with increasing insonation depth, only the closer half of the mesencephalon is analysed, which requires acquiring two images per examination.

In the images, the mesencephalon can be identified as a dark butterfly-shaped structure with the SN lying in the middle part of each wing. In about 90% of healthy subjects, the maximal area of SN hyperechogenicity in an axial imaging plane is below the threshold of 0.2 cm^2, whereas in PD affected persons the SN appears as a bright region interrupted by speckle noise with an area of more than 0.2 cm^2 in more than 90% of patients [5] as shown in Fig. 1.



(a) **(b)**

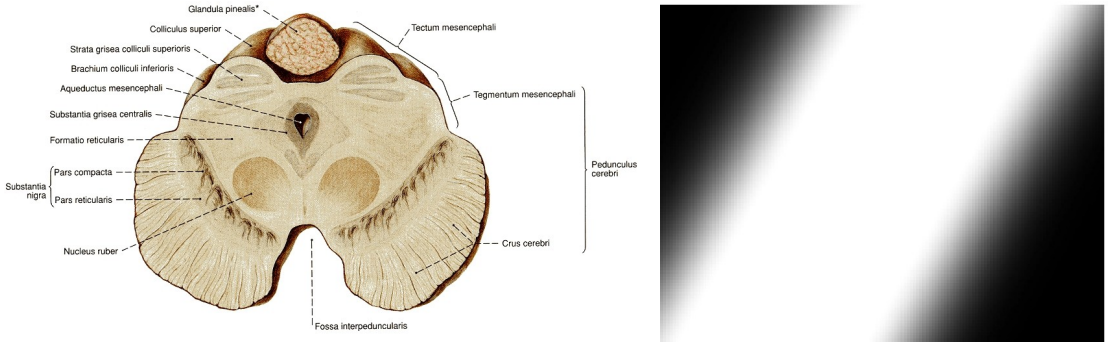
Fig. 1. Manually segmented half of the mesencephalon (red) with SN not visible in a healthy subject (a) and substantia nigra visible in the middle part in a PD affected person (b).

To omit a fault-prone automatic segmentation of the targeted mesencephalon half (ROI), we follow a semi-automatic approach, where the ROI is first manually segmented by a clinical expert. This step is followed by an automatic part whose steps are depicted in the work flow diagram in Fig. 3.

Depending on the accuracy of the manual segmentation it can happen that the ROI border area contains bright pixels from the surrounding tissue which might mislead the automatic intensity-based segmentation of the substantia nigra. To lessen the influence of the manual segmentation, the ROI is pixel wise multiplied with an attenuating mask image generated from the original manual segmentation. To generate this mask image, the binary segmentation image (pixel values 1 for object and 0 for background) is low-pass filtered with a 17x17 average filter and then pixel wise squared resulting in pixel values between 0 and 1.

From the anatomical facts it is known, that the SN lies in the middle third of the ROI (Fig. 2 (a)). To avoid locating the SN in outer parts of the ROI the manually segmented image is pixel wise multiplied with an attenuating mask reducing the image intensity in these ROI parts. This mask is generated from the ellipse which is fitted onto the ROI by second order central moments. The values of the mask pixels are calculated from their

distance *d* to the minor ellipse axis. For *d < 1/6*l* (with *l* the length of the major axis) the value is 1 (no attenuation). For *1/6*l <= d <= 1/2*l* the value degrades from 1 to 0 following a Gaussian curve. Fig. 2 (b) shows a sample attenuation image whose size is that of the ROI surrounding rectangle. An exemplary result of the preprocessing steps is shown in Fig. 3 (b).



(a) **(b)**

Fig. 2. Anatomical position of the substantia nigra in the mesencephalon [6] (a). Exemplary attenuating mask used for preprocessing the manually segmented ROI image (b).

Since the SN is usually the largest bright spot in the ROI, the ROI is thresholded with a heuristically determined threshold. This results in a binary image (Fig. 3 (c)), where the SN is still interrupted by black spots because of speckle noise. Additionally, smaller bright spots in the ROI but outside the SN also remain in this image.

Next, the image is dilated with a horizontal line-shaped structural element (7x2 pixel) to reduce speckle noise. In the resulting image (Fig. 3 (d)), the largest object (connected pixels) is selected and again dilated to include also smaller objects which are close to the largest object, since they may have been separated from it by remaining speckle noise. The structural element used is a circle of radius 5.

The resulting image (Fig. 3 (e)) is used to mask the thresholded image Fig. 3 (c). This generates an image containing the largest objects after the threshold step together with those smaller objects lying close to it (Fig. 3 (g)). As the last step, closing is applied to this image, since the anatomical structure searched for does not contain any holes. The structural element for this step is a circle of radius 10, since the SN has a smooth contour without sharp corners (Fig. 3 (h)).

Results

The result of our algorithm is the segmentation of that part of the substantia nigra, that shows increased tissue response. With this result the area of the ROI can easily be calculated and used as a diagnostic measure.

As long as there is a ROI with increased tissue response – presumably PD affected tissue – our algorithm works very reliable in segmenting it, even when the ROI is only slightly distinguishable from the surrounding tissue in the manually segmented region. For an exemplary SN segmentation see Fig. 3 (i).

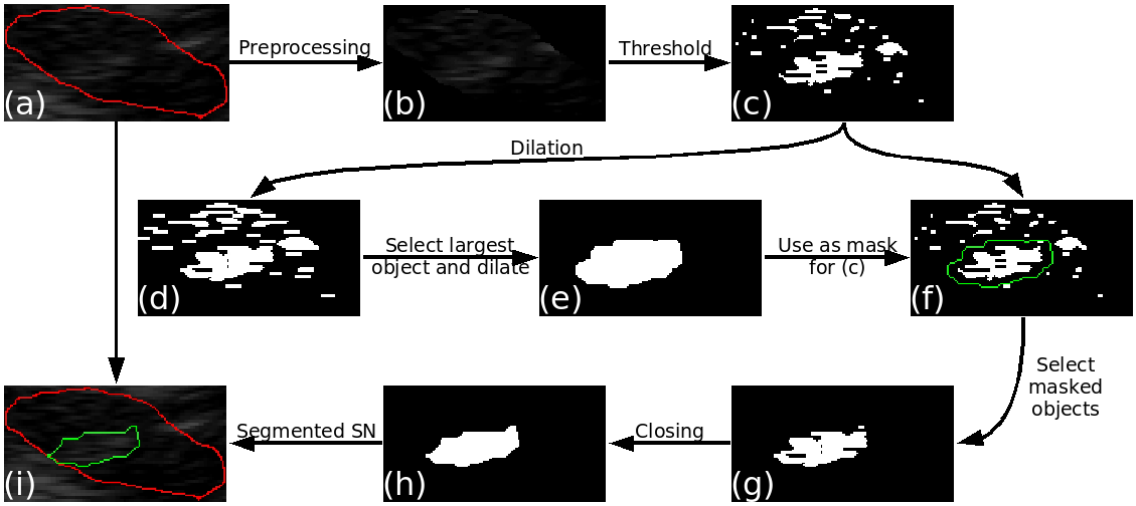


Fig. 3. Steps in segmenting the substantia nigra in an ultrasound image.

Conclusions

The proposed algorithm for segmenting affected parts of the substantia nigra in ultrasound images paves the way for an automatic, reliable, and reproducible measure for early Parkinson diagnosis. Furthermore, by using ultrasound this measure would even be fast, non-expensive, and uncomplicated to use on immobile patients. Preliminary results in comparing automatically segmented regions with those manually segmented by a clinical expert are very promising. To further reduce the observer-dependence of this method, automatic segmentation of the mesencephalon would be ideal, which proves to be a difficult task. Moreover, additional features could be calculated either on the segmented SN or on the complete ROI to describe the information contained in the images. These could be form- or texture-based or could originate from the theory of moments (e.g. inertia, Hu-moments).

However, to be used in diagnostic routine, this measure of course firstly has to be validated by a study to prove its correctness and secondly it has to be used to confirm the relationship between the occurrence of increased tissue echo response in the substantia nigra and Parkinson's disease.

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