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Atlas selection for hippocampus segmentation: Relevance evaluation of three meta-information parameters☆

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ABSTRACT

Current state-of-the-art methods for whole and subfield hippocampus segmentation use pre-segmented templates, also known as atlases, in the pre-processing stages. Typically, the input image is registered to the template, which provides prior information for the segmentation process. Using a single standard atlas increases the difficulty in dealing with individuals who have a brain anatomy that is morphologically different from the atlas, especially in older brains. To increase the segmentation precision in these cases, without any manual intervention, multiple atlases can be used. However, registration to many templates leads to a high computational cost. Researchers have proposed to use an atlas pre-selection technique based on meta-information followed by the selection of an atlas based on image similarity. Unfortunately, this method also presents a high computational cost due to the image-similarity process. Thus, it is desirable to pre-select a smaller number of atlases as long as this does not impact on the segmentation quality. To pick out an atlas that provides the best registration, we evaluate the use of three meta-information parameters (medical condition, age range, and gender) to choose the atlas. In this work, 24 atlases were defined and each is based on the combination of the three meta-information parameters. These atlases were used to segment 352 vol from the Alzheimer's Disease Neuroimaging Initiative (ADNI) database. Hippocampus segmentation with each of these atlases was evaluated and compared to reference segmentations of the hippocampus, which are available from ADNI. The use of atlas selection by meta-information led to a significant gain in the Dice similarity coefficient, which reached 0.68 ± 0.11, compared to 0.62 ± 0.12 when using only the standard MNI152 atlas. Statistical analysis showed that the three meta-information parameters provided a significant improvement in the segmentation accuracy.

1. Introduction

The analysis of morphometric characteristics of the hippocampus or its subfields is an important process in the diagnosis of many neurological and neuropsychological diseases, including temporal lobe epilepsy [1], Alzheimer's disease (AD) and mild cognitive impairment (MCI) [2], schizophrenia [3], major depression [4], bipolar disorder [5], and post-traumatic stress syndrome [6], among others [7].

Manually segmenting the hippocampus and calculating its volume are laborious tasks and are prone to subjective interpretation by health professionals. Automated methods that can reduce the subjectivity and increase the segmentation accuracy are highly desirable. However, automatic segmentation of the hippocampus in magnetic resonance images (MRI) presents some challenges. In a T1-weighted image, the pixel (or voxel) intensities of the hippocampus are similar to the intensities from other nearby brain structures, such as the amygdala, caudate nucleus, and thalamus [8]. Also, well-defined borders of the hippocampus with its neighboring structures are not easily identifiable, partial volume effects make pixel classification at the border more difficult, and the non-uniformity of intensities hinders the process of segmenting the hippocampus [9].

When performing a manual segmentation, the radiologist benefits

☆ Data used in preparation of this article were obtained from the Alzheimer's Disease Neuroimaging Initiative (ADNI) database (adni.loni.usc.edu). As such, the investigators from ADNI contributed to the design and implementation of ADNI and/or provided data but did not participate in the analysis or writing of this report. A complete listing of ADNI investigators can be found at http://adni.loni.usc.edu/wp-content/uploads/how_to_apply/ADNI_Acknowledgement_List.pdf.

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from his or her previous knowledge, such as the position of the hippocampus in the brain, the relative positions of neighboring structures, and knowledge about the usual shape of the hippocampus, which allows the professional to overcome those limitations. In automated methods, these high-level features cannot be obtained directly from pixel intensities. However, these features can be incorporated by other means, such as by the usage of atlases [10]. An atlas is an image in which there is reference segmentation for structures of interest, obtained through manual or automatic methods.

The simplest technique of atlas usage for hippocampus segmentation consists of registering a single atlas to the target image. With the deformation map acquired through this registration, it is possible to warp the existing segmentation in the atlas to the target image to obtain the final segmentation. The quality of the segmentation achieved through the **single-atlas** based method is strongly dependent on the choice of atlas and the registration accuracy. To obtain acceptable results, the method must use an atlas that has been created from individuals with anatomies similar to that of the individual in the target image, since the available registration techniques cannot align individuals with large anatomical differences with the required precision [11].

As a way to overcome this problem, many current methods use **multi-atlas** based techniques. Several different techniques have been used for applying multiple atlases in hippocampus segmentation. One of the most common ways is to individually segment the target with all the available atlases. Then, the creation of the final segmentation is done through label fusion techniques [12]. Many methods have been presented within the last years in this field of research [10,13–27].[1] However, despite showing good accuracy, this kind of segmentation method based on multiple atlases has a high computational cost, since the target image must be registered separately with each atlas used. Consequently, it is desirable to use a smaller number of atlases as long as this does not impact on the segmentation quality.

For **atlas selection**, the most common methods are based on image similarity and patient meta-information. Selection by image similarity gives excellent results but still has a high computational cost. On the other hand, selection by meta-information has the advantage of having a significantly low computational cost but may not lead to the selection of an ideal atlas [28].

Thus, the usage of mixed approaches in which a pre-selection is made through meta-information and a selection by similarity is performed later for a reduced group of atlases may combine the best of each technique: the low computational cost of the meta-information selection and the effectiveness of the selection by image similarity techniques. Aljabar et al. [29], for example, selected a subset of a database with 275 atlases based on global characteristics of the image and meta-information, such as the age and sex of the patient. Local similarity metrics for the structure of interest can also be used [28,30–35]. Methods for segmenting other structures have also used similar approaches to select the ideal smallest number of atlases [36–38].

Taking the meta-information selection approach in isolation, the minimal number of atlases needed is equal to the product of the total number of possible values of each parameter used in the selection, that is, an atlas for each combination of the characteristics used. Therefore, knowing the relevance of selection parameters is important, since non-relevant parameters may be excluded from the selection process, thus reducing the total number of atlases needed.

In this context, the presented paper evaluates the relevance of three meta-information parameters in the selection of atlases for hippocampus segmentation in a dataset from the Alzheimer's Disease Neuroimaging Initiative (ADNI). For this purpose, we performed a large-scale experiment, in which 352 vol were segmented with 25 different atlases, (24 specific atlases plus the MNI152 atlas), representing different characteristic combinations of the following parameters: gender, age group, and clinical situation. Each target image and atlas pair was evaluated through the use of the DSC (Dice Similarity Coefficient) precision index [39] so that the influence of each of the three parameters on the result of the hippocampus segmentation could be evaluated.

[1] For a more complete reference, a review of hippocampal segmentation methods is presented in Dill et al. [52].

2. Materials and methods

The experiment was conducted on T1-weighted MRI data obtained from the ADNI database (adni.loni.usc.edu). The ADNI was launched in 2003 as a public–private partnership, led by Principal Investigator Michael W. Weiner, MD. The primary goal of ADNI has been to test whether serial magnetic resonance imaging (MRI), positron emission tomography (PET), other biological markers, and clinical and neuropsychological assessment can be combined to measure the progression of mild cognitive impairment (MCI) and early Alzheimer's disease (AD).

The following sections describe the segmentation method used (Section 2.1), atlases (2.2), test data (2.3), evaluation procedure (2.4), and execution details (2.5).

2.1. Segmentation method

Fig. 1 shows a schematic overview of the applied segmentation method. Initially, the atlas selection is performed through meta-information matching. Using the parameters gender, clinical situation, and age group, an atlas that corresponds exactly to these three characteristics of the target volume is chosen as a template.

Details about the atlases used in this experiment are presented in Section 2.2. The method assumes the existence of a set generated in such a way that there is one atlas for each combination of possible values of parameters used (sex, age, and clinical condition). The values used for each selection parameter are presented in Table 1. Thus, to cover the full range of possible combinations of these values, 24 atlases are needed.

The target volume and the atlas are converted to the same coordinate space through a linear registration technique [40] using the MNI152 as the template [41]. This procedure is found to be necessary since it normalizes the images for future steps of skull stripping and allows the usage of non-linear registration techniques, which are designed for the fine alignment of internal structures and cannot handle large shifts.

After the linear registration, a skull stripping technique is applied on the target volume [42,43]. The BET (Brain Extraction Tool), which is part of the FSL toolkit (http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/) [44], is used in this process. This execution step removes the skull from the image volume, keeping only the brain mass, thus increasing the non-linear registration precision which will be applied later. This also reduces the computational cost of the process, since a smaller number of pixels are used in the computation.

With the brain mass segmented, the non-linear registration algorithm is applied, aligning the atlas with the target volume. The result of the non-linear registration process is a deformation map that, when applied to the target image, aligns the brain as a whole, including the cerebral substructures. In Fig. 2, examples of these steps are presented. To acquire the final hippocampus segmentation, the linear and non-linear deformation maps are inverted and applied over the hippocampus segmentation from the atlas, generating a segmentation of the hippocampus of the target image.

For this experiment, two non-linear registration techniques were tested: **ART** (Automatic Registration Tool) [45,46], and **SyN** (Symmetric Diffeomorphic Image Registration) [47]. These techniques were mentioned in a previous study [48] as the most precise with regard to hippocampal region alignment. The SyN implementation used here is provided by the author through the ANTs tool (http://stnava.github.io/ANTs/) and ART was used through the tools available at the Neuroimaging Informatics Tools and Resources Clearinghouse (NITRC, https://www.nitrc.org/projects/art).