



Quasi-conformal statistical shape analysis of hippocampal surfaces for Alzheimer's disease analysis



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ABSTRACT

Alzheimer's disease (AD) is a no-cure disease that has been frustrating the scientists for many years. Analyzing the disease has become an important but challenging research topic. The shape analysis of the sub-cortical structure of AD patients has been commonly used to understand this disease. In this paper, we assess the feasibility of using shape information on the hippocampal (HP) surfaces to detect some sub-structural changes in AD patients. We propose a quasi-conformal statistical shape analysis model, which allows us to study local regional geometric changes in the HPs amongst normal control (NC) and AD groups. A shape index defined by the quasi-conformality and surface curvatures is used to characterize region-specific shape variations of the HP surfaces. Feature vectors can be extracted for each HPs, with which a classification model can be built using machine learning methods to classify HPs into NC and AD subjects. Experiments have been carried out on 99 normal controls and 41 patients with AD. Results demonstrate that the proposed quasi-conformal based model is effective for classifying HPs into NC and AD groups with high classification accuracy (with highest overall classification accuracy reaching 87.86% in a leave-one-out experiment using the whole dataset).

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1. Introduction

The Alzheimer's disease (AD) is a chronic neurodegenerative disease characterized by a decline in cognitive functions. The cause of AD is poorly understood. It usually starts slowly, gets worsen over time and eventually leads to death. Early detection of AD is thus an important but a challenging task.

Amongst the various subcortical structures, the hippocampus (HP) has demonstrated pronounced shape changes in the early stages of AD. For example, the hippocampal atrophy has been recognized to be more aggressive in AD in comparison with the normal aging [1–6]. The HP surface is therefore amongst the most important biomarker for the early diagnosis of the disease.

HP shape analysis has usually been carried out by studying its global and local shape changes. For global shape analysis, the overall HP volumes are usually evaluated to study global shape differences amongst AD patients. It is believed that HP volumetric decline is correlated to the memory lost [7]. Tissue losses in the HP have also been found in the AD [8]. As a matter of fact, HP

volumetry on MR images has been widely used and found helpful for the diagnosis of AD.

Although the HP volume can provide significant information to discriminate AD from normal control subjects, significant regional shape changes in the HP have been observed in the neurodegenerative process of AD [9,10]. For example, neuron loss has commonly been found in CA1 and subiculum subfields [11–13]. In view of this, the examination of the local regional shape changes in the HPs is expected to provide better information to analyze the disease and classify HPs between AD and NC groups. Besides, another potential limitation of the global shape analysis approach is that geometric differences between AD and NC groups may only occur at some specific local regions. Taking into account the overall shape change of the whole HP volume may average out or diminish the discriminative power of the geometric differences amongst the normal and diseased groups, which hinder the shape analysis accuracy. It is therefore desirable to design local shape analysis model that can measure regional shape changes effectively.

In order to analyze the localized pattern of HP shape changes, surface-based morphometry can be employed. A shape index that quantifies regional shape changes is often defined, with which statistical shape analysis can be performed for the HP classification. In this work, we propose a quasi-conformal based shape analysis approach, which allows us to study local regional shape

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differences of the HP amongst NC and AD groups. A shape index based on the quasi-conformality and surface curvatures is applied to characterize region-specific shape variations of the HP surfaces amongst different subjects. The shape index is a positive real-valued function defined on every vertices of the HP. Feature vectors for each HP can be extracted from their shape indices using statistical methodologies. A classification model can then be built using the extracted feature vectors. The proposed quasi-conformal based model is found to be an effective approach to classify HPs into NC and AD groups.

Our experiments are performed on 99 normal controls and 41 patients with AD. The data is obtained using 1.5 T magnetic resonance imaging (MRI) scanner. Using our method, we can accurately achieve a high accuracy of classification between NC and AD groups.

The rest of the paper is organized as follows. In Section 2, we review some previous literatures closely related to this work. Our proposed quasi-conformal shape analysis model will be described in detail in Section 3. Experimental results will be shown in Sections 4 and 5. The paper is concluded in Section 6, in which possible future works are discussed.

2. Related works

The shape analysis of the HP for the disease analysis of AD has been widely studied by various research groups. Different approaches have been developed. For global shape analysis, HP volume has been used for classifying AD subjects and AD diagnosis [5,6,14–17]. In particular, by studying the HP volumes, [18] has reported the classification result between AD and cognitively normal subjects with a success rate of about 72–74% over an Alzheimer's Disease Neuroimaging Initiative (ADNI) database. To further improve the accuracy for the analysis of AD, local shape changes in the HP have been taken into account. Surface-based morphometry of the HP surfaces has been extensively studied. The spherical harmonic (SPHARM) representation of the HP surface has been exploited to extract shape features to quantify shape changes caused by AD [18–22]. Longitudinal approaches which study the HP atrophy rates over times have been proposed for AD classification problems [23,24]. These approaches can often achieve higher classification accuracy than the volumetric approaches (e.g. 82% on 568 images of the ADNI dataset by Wolz et al. [24]). Younes et al. [25] applied the large deformation diffeomorphic metric mapping method for HP surface registration and successfully detected the changing point that indicated the AD. Wang et al. [26] proposed the tensor-based surface morphometry on the HP to analyze shape changes in HPs of AD subjects. To better examine the regional shape changes of the HP, algorithms which segment subfields of the HP have been proposed to detect the local atrophy pattern [27,28]. Lui et al. [29] also proposed to obtain HP registration using Beltrami holomorphic flow. Using the registration, vertex-wise shape changes can be detected and statistically significance map (p-map) can be computed to visualize the regions with significant shape differences.

Statistical shape analysis methods to analyze AD have also drawn much attention recently. For instance, Miklossy et al. [30] used Koch's and Hill's criteria in finding the AD. The analysis of the reviewed data following Koch's and Hill's postulates shows a probable causal relationship between neurospirochetosis and AD. Comelli et al. [31] combined the univariate tests and logistic regression in proposing a therapy for AD. Thompson et al. [32] used the statistical region-of-interest method in assessing the twelve-month metabolic declines in probable AD and Amnesic Mild Cognitive Impairment. It is noteworthy that both the statistical analysis and surface mapping take an important role in human brain analysis especially for the study of AD. Recently,

multidimensional classification methods have been widely used for disease classification [19,33–38].

In order to perform local shape analysis, surface registration that captures the one-to-one vertex-wise correspondence between different HP surfaces is crucial. Harmonic surface registration has been widely used [39,40], which produces smooth surface mapping by simply solving an elliptic PDE. Landmark-matching optimized harmonic map has also been proposed to obtain an optimal harmonic map that matches the corresponding landmark features [41–44].

Quasi-conformal theory will be applied in this work. Computational quasi-conformal mapping has been studied recently and applied successfully in the medical imaging field. Lui et al. [29] proposed to obtain quasi-conformal surface registration using the Beltrami holomorphic flow method. The method has been applied to compute HP surface registration [45]. Quasi-conformality has also been utilized to quantify non-isotropic deformations, which can be used to detect abnormal growth or deformation [46]. To deal with higher genus surfaces, different methods have been developed to compute quasi-conformal mappings of surfaces with general topologies [47,48]. Landmark-based surface quasi-conformal registration has also been investigated [47,49].

3. The proposed model

In this section, we will describe our proposed quasi-conformal statistical shape analysis model in detail. Suppose we are given a collection of hippocampal (HP) surfaces of normal controls (NCs) and diseased subjects suffering from Alzheimer's disease (AD). Our goal is to learn a classification model using their shape information, with which a new input HP surface can be classified into either normal or diseased subject. This can potentially assist physicians for the diagnosis of the AD. For this purpose, we propose to combine quasi-conformal theories and statistical tools to develop a shape classification machine. Shape deformation measurement is firstly obtained through quasi-conformal theories, which provide accurate measurement of local geometric differences amongst subjects. A shape classification model can then be learnt through statistical tools and machine learning procedures.

Denote the collection of HP surfaces of m normal controls and n diseased subjects by $\tilde{N} = \{S_i^t\}_{i=1}^m$ and $\tilde{A} = \{S_i^t\}_{i=m+1}^{m+n}$, respectively, where $t = 0$ or 1 . The HP surface of each subject was captured at the base-time $t = 0$ and after one year $t = 1$. Their surfaces are denoted by S_i^0 and S_i^1 , respectively. Our proposed quasi-conformal statistical shape analysis can be summarized as follows, which consists of five main steps.

1. *Surface registration*: For each subject i , the deformation $f_i : S_i^0 \rightarrow S_i^1$ of subject i is obtained. Also, surface registrations $g_{ij} : S_i^0 \rightarrow S_j^0$ are computed. These registrations give point-wise correspondence between subjects for further shape analysis.
2. *Shape deformation measurement*: For each subject i , measure the shape deformation at each vertex of the HP from $t = 0$ to $t = 1$ using quasi-conformal theories. A shape index $E_{shape}^i : S_i^0 \rightarrow \mathbb{R}^+$ is obtained that measures the degree of deformation at each vertex.
3. *Extraction of statistically significant regions*: Statistically significant p-map is obtained based on the shape index computed for each subject. A statistically significant region Ω can be extracted to obtain more accurate classification results.
4. *Extraction of feature vector*: The shape index E_{shape}^i together with the statistically significant region Ω gives rise to a discriminative feature vector \tilde{c}_i for each subject. A mean feature \tilde{c}_{mean}^{NC} amongst the normal control group can also be extracted. Distance d_i between each feature vector \tilde{c}_i and the mean feature

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