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## Title

Modelling morphological variability of the hippocampus using manifold learning and large deformations

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## Introduction

The hippocampus is a structure of the temporal lobe of the brain which plays an important role in memory processes and in many neuropsychiatric disorders, including Alzheimer's disease, epilepsy and schizophrenia. Here, we present a method to infer the anatomical variability of the hippocampus, based on the LDDMM (Large Deformation Diffeomorphic Metric Mapping) framework and a manifold learning approach to capture the geometry of the population in the space of shapes.

## Methods

We propose to estimate the anatomical variability of the hippocampus in a population by using Isomap (Tenenbaum et al, 2000) to extract the manifold on which lies our population in the space of shapes. We used as metric between two shapes the length of the deformation which maps one onto the other, based on LDDMM with currents (Glaunès et al, 2008). It consists in deforming regularly the space in which is the shape to be deformed, to obtain a smooth deformation trajectory. We iteratively calculate the centroid with diffeomorphic metric of the hippocampus population: we first register a first hippocampus onto another, and define an initial centroid at  $1/2$  of the trajectory, this initial centroid is then registered onto another hippocampus, which defines a new centroid at  $1/3$  of the trajectory. The process is iterated by taking  $1/i$  of the trajectory between the current centroid and the  $i$ -th hippocampus. We thus obtain a centroid of the population, for the diffeomorphic metric. We then calculated deformation maps between this centroid and every subject, from which we can derive a first-order approximation of the distance between any pair of hippocampi (Yang et al, 2011), Isomap is then applied to the resulting distance matrix to estimate the manifold on which the hippocampi population lies.

We illustrate our approach on 30 controls and 30 patients with Alzheimer's disease selected from the Alzheimer's Disease

Neuroimaging Initiative (ADNI) database ([adni.loni.ucla.edu](http://adni.loni.ucla.edu))

. Hippocampi were segmented automatically used SACHA software (Chupin et al, 2009) and converted to surface meshes. As a preprocessing, all hippocampal meshes were rigidly registered, to cancel global rotations and translations.

## Results

Figure 1 presents the first three dimensions of the Isomap space (AD patients are in red, controls are in blue). Figure 2 presents a moving average (using the diffeomorphic metric) along the first dimension of the Isomap (the blend of colors from red to blue indicate the proportion of AD patients and controls in each average).

The first dimension accounts for 29% of the variance. Coordinates along this first dimension are statistically different between AD patients and controls (Student's t-test,  $p=0,00072$ ).

## Conclusions

We have presented a method to model anatomical variability of the hippocampus in a population. Differences between shapes are defined from large deformations. The structure of the manifold on which lies the population is then learned using Isomap. Preliminary evaluation demonstrates that, although completely unsupervised, the method is able to capture morphological differences between AD patients and controls.