

## CERES: A new cerebellum lobule segmentation method

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### ABSTRACT

The human cerebellum is involved in language, motor tasks and cognitive processes such as attention or emotional processing. Therefore, an automatic and accurate segmentation method is highly desirable to measure and understand the cerebellum role in normal and pathological brain development. In this work, we propose a patch-based multi-atlas segmentation tool called CERES (CEREbellum Segmentation) that is able to automatically parcellate the cerebellum lobules. The proposed method works with standard resolution magnetic resonance T1-weighted images and uses the Optimized PatchMatch algorithm to speed up the patch matching process. The proposed method was compared with related recent state-of-the-art methods showing competitive results in both accuracy (average DICE of 0.7729) and execution time (around 5 minutes).

### 1. Introduction

The human cerebellum is a neuroanatomical structure within the human brain located below the cerebrum and connected to the brainstem through the cerebellar peduncles. Although it represents a small percentage of the total intracranial volume, about 10%, it plays a key role in motor coordination and learning (Manto et al., 2013). The cerebellum acts as a modulator for the motor cortex signals to perform fine and precise movements through the integration of the inputs signals from the somatosensory system and cerebellar cortex. It has been shown that cerebellar damage leads to important motor dysfunctions such as limb ataxia, balance alterations and other deficits in motor coordination (Kase et al., 1993; Compston and Coles, 2008; Davie et al., 1995; Klockgether, 2008). Recent neuroimaging studies indicate that cerebellum is also involved in many cognitive functions (Stoodley, 2012) such as attention, emotion or behavior (Timmann et al., 2010).

Despite the cerebellum being involved in many brain functions, it has been widely understudied. Lately, several publications have focused on the study of the cerebellum and its implication in several

neuropsychiatric pathologies. For example, patients with schizophrenia showed a reduced vermis (Okugawa et al., 2002) and subjects with Alzheimer's disease presented smaller posterior lobes (Thomann et al., 2008). Nevertheless, there exist publications with inconclusive results regarding the role of the cerebellum in different neuropsychiatric disorders (Nenadic et al., 2010; James et al., 2004). This could be explained by the fact that accurately segmenting the cerebellum is quite challenging due to its complex anatomy.

Cerebellar anatomy consists of a white matter tree structure located behind the pons. It is divided into two hemispheres (left and right), with each white matter branch surrounded by a layer of grey matter that creates folds called foliations. These grey matter folds are denominated cerebellum lobules. The size, position and number of (visible) lobules is highly variable between subjects which makes the segmentation process challenging.

Manual segmentation (delineation) by an expert requires a huge effort since it is a time consuming and tedious process. Delineation by non-expert raters may be faster but still impractical for studies applied to a large cohort of subjects. Further, both alternatives require dealing with inter and intra-rater variability. A few semi-automatic methods

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have been developed offering large structure parcellation as the brainstem, white matter and grey matter (Weier et al., 2012). These methods intend to reduce the time required by a human rater while keeping the reliability of manual delineation. However they are still time consuming.

An alternative to the manual segmentation is using multi-atlas based segmentation (Aljabar et al., 2009) which consists of transferring and combining multiple manual segmentations to the case to be segmented. One of the first automated algorithms specifically developed for cerebellum segmentation is SUIT (Diedrichsen, 2006). In this method, a set of manually labeled images was used to build a probabilistic atlas that was then warped into the target image space. However, SUIT is not able to capture all the anatomical variability due to the use of a single atlas approach. In addition, the method developed by Diedrichsen is semi-automatic since it includes a cerebellum extraction step that is suggested to be manually corrected for optimal results.

Fully automatic methods appeared in the last years. Bogovic et al. (2013) published a method called ACCLAIM using deformable models and random forest boundary classification. Recently Yang et al. (2016) proposed a segmentation method combining multi-atlas label fusion and tissue/boundary classification in a graph-cut segmentation framework to address the high variability of the cerebellum anatomy achieving good results at the expense of a high computational burden (execution time of several hours per case). Also recently, a new approach based on multi-atlas segmentation called MAGEt Brain (Chakravarty et al., 2013; Park et al., 2014) has been proposed for cerebellum lobule segmentation. This new approach aims at solving the problem of having very few exemplar cases (manual segmentations) of a given segmentation protocol. It uses the estimation of a large set of non-linear deformations to map the example cases to a set of unlabeled templates increasing the number of candidate segmentation to apply a final majority vote based label fusion. MAGEt Brain demonstrated better results than single atlas and classical multi-atlas label fusion using majority voting methods at the expense of a high computational cost in terms of both memory and execution time. Finally, Weier et al. (2014) published another multi-atlas segmentation method named RASCAL based on a multi-atlas patch-based label fusion. It utilizes a library of manually segmented cases that is non-linearly registered into the target image space to perform the labeling process.

In this paper, we introduce a new pipeline for cerebellum lobule segmentation that is based on an adaptation of a recently proposed segmentation method called Optimized PatchMatch Label fusion (OPAL) (Ta et al., 2014; Giraud et al., 2015). This method consists of a multi-atlas patch-based (Rousseau et al., 2011) segmentation with a non-local label fusion technique that produces fast and accurate segmentations using a library of manually segmented cases. The original method developed for hippocampus segmentation (Coupé et al., 2011) has been adapted to segment the cerebellum anatomy using a library of non-linearly registered cases instead of using only an affine registration as in the original method. A post-processing step has been added to enforce regularity of the different lobule labels. Also, given the small size of the template library (only 5 cases) we extended the number of templates of the library by adding automatically segmented cases.

## 2. Materials and methods

In the following sections, the data used in this paper and the proposed method details are described. We have called the proposed method CERES (for CEREBellum Segmentation).

### 2.1. Image data

In this work, two datasets have been used. A High Resolution (HR) set of 5 MR T1-weighted images has been used to construct the library of manually labeled cases. A second dataset of 20 standard resolution images has been used to evaluate the proposed method and to compare it with other related approaches. The HR images are publicly available at the CoBrALab website (<http://cobralab.ca/atlas/Cerebellum.html>). Both the HR images used as input and the manually labeled validation dataset are the same as those used in Park et al. (2014).

#### 2.1.1. HR dataset

These cerebellar atlases were created based on HR MR images from 5 healthy volunteers (2 male, 3 female, aged 29–57). We used T1-weighted images that were acquired on a GE Discovery MR 750 3 T system (General Electric, Waukesha, WI) using an 8-channel head coil. High-resolution T1-weighted images were acquired using the 3D inversion-prepared fast spoiled gradient-recalled echo acquisition, FSPGR-BRAVO, in a scan time of ~20 min with the following parameters: TE/TR=4.3 ms/9.2 ms, TI=650 ms,  $\alpha=8^\circ$ , 2NEX, FOV=22 cm, slice thickness=0.6 mm, 384×384 in-plane steps for an approximate isotropic resolution of 0.6 mm dimension voxels. Reconstruction filters, ZIPX2 and ZIP512, were also used resulting in isotropic 0.3 mm<sup>3</sup> voxels with a final matrix size of 489×734×503 voxels (Park et al., 2014). These HR MR images were manually segmented by two expert raters that allowed for both inter- and intra-rater comparisons of segmentations to validate the consistency of the manual segmentation protocol (for details of the segmentation protocol please see Park et al. (2014)). The cerebellum was manually delineated into 26 structures: White matter and Lobules I-II, III, IV, V, VI, Crus I, Crus II, VIIb, VIIIA, VIIIB, IX, and X considering left and right hemispheres as shown in Fig. 1. One of the authors of this manuscript, Min Tae M. Park, was one of the manual raters of these data.

#### 2.1.2. Standard resolution dataset

MR images from 10 healthy control and 10 patients with schizophrenia (15 male, 5 female, average 30.1 years age, range 25–35 years) were used to create a validation set. Imaging data were acquired using an 8-channel head coil on a 1.5 T GE Echospeed system (General Electric Medical Systems, Milwaukee, WI), which permits maximum gradient amplitudes of 40 mT/m. Axial inversion recovery prepared spoiled gradient recall images were acquired: echo time (TE)=5.3 ms, repetition time (TR)=12.3 ms, time to inversion (TI)=300 ms, flip angle=20°, number of excitations (NEX)=1(124 contiguous images, 1.5 mm thickness, 0.78×0.78 mm in plane resolution). These images were linearly registered to the MNI space using MRITotal software (Collins et al., 1994) to perform the manual labeling thus resulting in a 1 mm<sup>3</sup> image resolution and a matrix size of 181×217×181 voxels. The

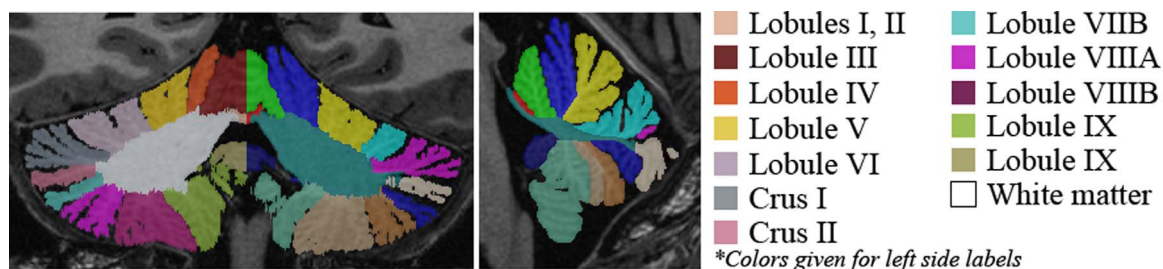


Fig. 1. Example of one HR case and its corresponding manual segmentation.

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