Journal of Neuroscience Methods 262 (2016) 1–13

Contents lists available at ScienceDirect

Journal of Neuroscience Methods

journal homepage: www.elsevier.com/locate/jneumeth

Computational neuroscience

Improved segmentation of cerebellar structures in children

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HIGHLIGHTS

- The probabilistic Cape Town Pediatric Cerebellar Atlas (CAPCA18) provides accurate assignment of 16 hemispheric regions.
- In a pediatric dataset (age 9-13 years), automated CAPCA18 atlas based segmentation performs better than SUIT segmentation.
- Multi atlas based label fusion using the 18 training atlases improves spatial overlap with manual tracings, compared to CAPCA18 segmentation.

ARTICLE INFO

Article history:
Received 13 January 2015
Received in revised form 9 December 2015
Accepted 17 December 2015
Available online 29 December 2015

Keywords:
Pediatric probabilistic atlas
Cerebellum
Multi atlas segmentation
CAPCA18

ABSTRACT

Background: Consistent localization of cerebellar cortex in a standard coordinate system is important for functional studies and detection of anatomical alterations in studies of morphometry. To date, no pediatric cerebellar atlas is available.
New method: The probabilistic Cape Town Pediatric Cerebellar Atlas (CAPCA18) was constructed in the age-appropriate National Institute of Health Pediatric Database asymmetric template space using manual tracings of 16 cerebellar compartments in 18 healthy children (9-13 years) from Cape Town, South Africa. The individual atlases of the training subjects were also used to implement multi atlas label fusion using multi atlas majority voting (MAMV) and multi atlas generative model (MAGM) approaches. Segmentation accuracy in 14 test subjects was compared for each method to 'gold standard' manual tracings.
Results: Spatial overlap between manual tracings and CAPCA18 automated segmentation was 73% or higher for all lobules in both hemispheres, except VIIb and X. Automated segmentation using MAGM yielded the best segmentation accuracy over all lobules (mean Dice Similarity Coefficient 0.76; range 0.55-0.91; mean Hausdorff distance 0.9 mm; range 0.8-2.7 mm).
Comparison with existing methods: In all lobules, spatial overlap of CAPCA18 segmentations with manual tracings was similar or higher than those obtained with SUIT (spatially unbiased infra-tentorial template), providing additional evidence of the benefits of an age appropriate atlas. MAGM segmentation accuracy was comparable to values reported recently by Park et al. (Neuroimage 2014;95(1):217) in adults (across all lobules mean DSC = 0.73, range 0.40-0.89).
Conclusions: CAPCA18 and the associated multi-subject atlases of the training subjects yield improved segmentation of cerebellar structures in children.

1. Introduction

The human brain is a complex structure and mapping its functional organization presents an ongoing challenge. Recent findings suggest that the cerebellum is functionally heterogeneous, with different topological regions subserving sensory, motor, cognitive, and affective processing (Stoodley and Schmahmann, 2009; Schlerf

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http://dx.doi.org/10.1016/j.jneumeth.2015.12.010
0165-0270/

et al., 2010; Strick et al., 2009; Schmahmann and Sherman, 1998; Makris et al., 2005). As such, it has become increasingly important to identify precisely which lobule is activated in functional imaging studies. Efforts to map cerebellar function have, however, been limited by the fact that available cerebellar atlases are generally limited to gross morphologic relationships (Crosby et al., 1962; Carpenter, 1976; DeArmond et al., 1989; Waddington, 1984; Roberts et al., 1987; Kretschmann and Weinrich, 1992), that the individual cerebellar lobules are generally not labeled, and only limited sections are depicted in either one or two of the cardinal planes with large gaps between these. Furthermore, the terminology used to identify the fissures and lobules in these atlases is not uniform and is often contradictory.

Schmahmann et al. (1999) presented a human cerebellar atlas with sections at 2 mm intervals in three cardinal planes based on high-resolution T1-weighted Magnetic Resonance (MR) images of a single human cerebellum that was coregistered to the Montreal Neurological Institute (MNI) template (Evans et al., 1993) and annotated using a revised and simplified nomenclature. Using the above MR image atlas of the human cerebellum as a basis for identification of landmarks and fissures, Makris et al. (2005) developed a manual method aided by a set of computer-assisted algorithms to facilitate the parcellation of the cerebellar cortex into 32 parcellation units (PUs) per hemicerebellum in a manageable period of time. In their implementation, the fissures divide the cortex into lobules, while longitudinal divisions separate the vermis from the hemispheres, and subdivide the hemispheres into medial and lateral zones. The large lateral hemispheric region of Crus I and II is divided into a further two zones. The authors found that intraclass correlation coefficients (McGraw and Wong, 1996; Shrout and Fleiss, 1979) for both intra- and inter-rater reliability were significantly improved by clustering PUs according to either lobar divisions, anatomical connectivity, or functional connectivity. Lobar clusters are widely used (Pierson et al., 2002) and divide the cerebellum into anterior, posterior and flocculonodular lobes that are separated by the primary and the posterolateral fissures, respectively. In all these studies only data acquired from adults were used.

Subsequently, Diedrichsen (2006) developed the high-resolution spatially unbiased infra-tentorial template (SUIT) of the cerebellum by normalizing individual cerebella of 20 healthy adults non-linearly to each other before averaging, which improved specificity when labeling regions in functional MRI data.

Although atlases are widely used to assign anatomical labels to locations, there is a high risk for error due to high spatial variability of individual cerebellar anatomy, and even more so between different populations. Probabilistic atlases enable the assignment of labels to specific regions while also providing a quantitative measure of the uncertainty of such assignments. Currently, whole brain probabilistic atlases typically treat the cerebellum as a single structure without any lobular divisions (Hammers et al., 2003; Shattuck et al., 2008). In 2009, the first probabilistic cerebellar SUIT atlas was created (Diedrichsen et al., 2009) based on manual tracings of lobules on T1-weighted MRI scans (1 mm isotropic resolution) of 20 healthy adult participants (10 male, 10 female, age range 19-27 years). The SUIT atlas defines twenty-eight compartments: lobules I-IV and V divided into left and right hemispheres; lobules VI, Crus I, Crus II, VIIb, VIIIa, VIIIb, IX, and X divided into vermal sections in addition to left and right hemispheres. This atlas aims specifically to improve inter-subject co-registration of cerebella to yield improved specificity of cerebellar activations and valid assignments of functional activations to specific cerebellar lobules.

We were interested in examining cerebellar anatomy in children (age 9-13 years) from the Cape Coloured (mixed ancestry) community in Cape Town, South Africa. Since manual tracing is both time intensive and subjective, we wanted to perform automatic cerebellar segmentation. It has been noted previously, however, that a specialized atlas should be created for research in children (Diedrichsen, 2006) as the shape and ratio of gray matter to white matter in the cerebella of children differ significantly from that of adults (Fonov et al., 2011). To our knowledge, no pediatric cerebellar atlas is currently available.

In developing an atlas, an important decision relates to the registration target (template). A template closer to the study population reduces morphometric bias and the amount of nonlinear deformation required to establish spatial alignment (Yoon et al., 2009) between the template and subject. Wilke et al. (2008) developed the 'Template O Matic' toolbox for SPM that creates an age specific whole brain template by initially using linear co-registration of subjects and regressing for age and sex in pediatric populations. The resulting template, however, appears smoothed and lacks anatomical detail in the regions of greatest variability.

The unbiased nonlinear National Institutes of Health Pediatric Database (NIHPD) template created by Fonov et al. (2011) provides better spatial resolution and improved contrast compared to the classical International Consortium for Brain Mapping (ICBM152) template. NIHPD templates are available for different age ranges for normal brain development; the pediatric population was grouped into five categories between the ages of 4.5 and 18.5 years. For each category, two templates were constructed, one that preserves asymmetry and another with symmetric hemispheres. Deformation studies using these five different templates have shown that the average magnitude of deformation increases with increasing difference in age between the template used and the subject being studied (Fonov et al., 2011). In the present study we used the NIHPD unbiased nonlinear template that preserves asymmetry closest to the age range of our subject population (7.5-13.5 years).

Although recent advances in image segmentation have demonstrated that multi atlas segmentation improves accuracy over standard atlas based approaches, these have rarely been applied to cerebellar segmentation, possibly due to the need for a large number of manually segmented atlases, which is both time intensive to construct and requires extensive expertise. Pipitone et al. (2014) recently developed the Multiple Automatically Generated Templates (MAGeT-Brain) algorithm, which minimizes the number of atlases needed by propagating the atlas segmentations to a template library constructed from a subset of the target images. Using this approach and manually segmented atlases of only 5 adult cerebella, Park et al. (2014) demonstrated good accuracy using voxel wise majority voting compared to "gold standard" manual segmentations in the identification of all lobules (mean Dice Similarity Coefficient [DSC] = 0.73; range 0.40-0.89) and the entire cerebellum (mean DSC = 0.93; range 0.90-0.94) in 20 adults (10 healthy controls; 10 patients with schizophrenia). Bogovic et al. (2013) demonstrated superior performance compared to SUIT atlas based and multi atlas fusion approaches using multiple object geometric deformable models. To the authors' knowledge, no multi atlas cerebellar segmentation pipeline is available that has been tailored to pediatric datasets and is based on training data from children. Further, the parametric generative model (Iglesias et al., 2012; Iglesias et al., 2013) has not been applied to cerebellar segmentation.

In this work, we present the probabilistic Cape Town Pediatric Cerebellar Atlas (CAPCA18) for improved labeling of cerebellar structures in children. The atlas was constructed in the already established age-appropriate NIHPD template space from manual tracings of 16 cerebellar compartments in 18 healthy children (age range 9-13 years, 6 male) according to the nomenclature introduced in the MRI atlas of the human cerebellum (Schmahmann et al., 1999). The probabilistic presentations of each compartment provide a quantitative measure of the spatial variability in that region. In addition, manually traced cerebella of the training subjects were used to implement multi atlas label fusion using both