NeuroImage 119 (2015) 262–271

Contents lists available at ScienceDirect

NeuroImage

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

White matter atlas of the human spinal cord with estimation of partial volume effect

S. Lévy [a,b], M. Benhamou [a], C. Naaman [a], P. Rainville [b,c], V. Callot [d,e], J. Cohen-Adad [a,b,*]

[a] Neuroimaging Research Laboratory (NeuroPoly), Institute of Biomedical Engineering, Polytechnique Montreal, Montreal, QC, Canada
[b] Functional Neuroimaging Unit, CRIUGM, Université de Montréal, Montreal, QC, Canada
[c] Department of Stomatology, Université de Montréal, Montreal, QC, Canada
[d] Aix-Marseille Université (AMU), CNRS, CRMBM UMR 7339, 13385 Marseille, France
[e] APHM, Hôpital de la Timone, CEMEREM, 13005 Marseille, France

ARTICLE INFO

Article history:
Received 21 March 2015
Accepted 13 June 2015
Available online 19 June 2015

Keywords:
MRI
Spinal cord
Atlas
Template
White matter

ABSTRACT

Template-based analysis has proven to be an efficient, objective and reproducible way of extracting relevant information from multi-parametric MRI data. Using common atlases, it is possible to quantify MRI metrics within specific regions without the need for manual segmentation. This method is therefore free from user-bias and amenable to group studies. While template-based analysis is common procedure for the brain, there is currently no atlas of the white matter (WM) spinal pathways. The goals of this study were: (i) to create an atlas of the white matter tracts compatible with the MNI-Poly-AMU template and (ii) to propose methods to quantify metrics within the atlas that account for partial volume effect.

The WM atlas was generated by: (i) digitalizing an existing WM atlas from a well-known source (Gray's Anatomy), (ii) registering this atlas to the MNI-Poly-AMU template at the corresponding slice (C4 vertebral level), (iii) propagating the atlas throughout all slices of the template (C1 to T6) using regularized diffeomorphic transformations and (iv) computing partial volume values for each voxel and each tract. Several approaches were implemented and validated to quantify metrics within the atlas, including weighted-average and Gaussian mixture models. Proof-of-concept application was done in five subjects for quantifying magnetization transfer ratio (MTR) in each tract of the atlas.

The resulting WM atlas showed consistent topological organization and smooth transitions along the rostro-caudal axis. The median MTR across tracts was 26.2. Significant differences were detected across tracts, vertebral levels and subjects, but not across laterality (right–left). Among the different tested approaches to extract metrics, the maximum a posteriori showed highest performance with respect to noise, inter-tract variability, tract size and partial volume effect.

This new WM atlas of the human spinal cord overcomes the biases associated with manual delineation and partial volume effect. Combined with multi-parametric data, the atlas can be applied to study demyelination and degeneration in diseases such as multiple sclerosis and will facilitate the conduction of longitudinal and multi-center studies.

Introduction

The spinal cord (SC) white matter (WM) is organized into bundles of myelinated axons. Each of these bundles, or pathways, conveys ascending or descending signals that are essential to ensure adequate communication between the central and the peripheral nervous systems. For example the corticospinal tracts send motor signals to the peripheral system and the cuneatus and fasciculus gracilis (dorsal column) convey sensory input to the somatosensory cortex for our perception of touch. Damage to spinal axon bundles can have dramatic impact on the quality of life as it can lead to motor (paralysis) and sensory deficits and, in some cases, neuropathic pain (Dijkers et al., 2009). Axon damage can have various causes, such as SC injury, autoimmune and neurodegenerative diseases (e.g., multiple sclerosis), cancers and vascular diseases. Because each spinal pathway has a very specific role within the central nervous system, the prognosis of functional recovery will strongly depend on the type of pathways that have been damaged, the extent of damage, and the functional integrity of spared pathways.

Magnetic resonance imaging (MRI) of the spinal cord has tremendous potential for providing non-invasive biomarkers of white matter pathology. In particular, diffusion-weighted imaging and magnetization transfer were shown to be sensitive to demyelination and degeneration (Wheeler-Kingshott et al., 2014). Apart from the challenges related to

* Corresponding author at: Institute of Biomedical Engineering, Polytechnique Montreal, 2900 Edouard-Montpetit Bld, Montreal, QC H3T1J4, Canada. Fax: +1 514 340 4611.
E-mail address: jcohen@polymtl.ca (J. Cohen-Adad).

http://dx.doi.org/10.1016/j.neuroimage.2015.06.040
1053-8119/

data acquisition in the SC (Stroman et al., 2014), it remains difficult to quantify MRI metrics within specific WM tracts, given the small cross-sectional size of the SC (around 1 cm diameter in the axial plane at the cervical level) and the absence of visible anatomical landmarks that separate individual tracts. Currently, the standard procedure is to manually draw binary regions of interest (ROI) on each axial slice. These ROI are specific to a given tract (e.g., left fasciculus cuneatus) or to an ensemble of tracts (e.g., dorsal column). Once all ROIs are drawn, metrics can be extracted by averaging them across the ROI. Although widely used (Ciccarelli et al., 2007; Cohen-Adad et al., 2008; Gullapalli et al., 2006; Klawiter et al., 2011; Lindberg et al., 2010; Narayana et al., 2004; Onu et al., 2010; Qian et al., 2011; Smith et al., 2010; Xu et al., 2013), this approach has major limitations: (i) the identification of the tract location is biased by the user experience and knowledge of the anatomy, (ii) the manual delineation of ROIs is long and tedious, especially for large populations and (iii) ROIs consist of binary masks and hence do not account for partial volume effect, e.g., between the SC and the cerebrospinal fluid (CSF) where metrics can have very different values. By analogy to brain neuroimaging methods, the combination of a generic template and atlas can provide unbiased quantification of metrics (Desikan et al., 2006; Yendiki et al., 2011). A similar framework would be a step forward for processing SC data, although it has never been addressed so far, notably due to the absence of a common frame of reference (template).

Building upon the recent development of a standard SC template that includes a probabilistic map of white and gray matter (Fonov et al., 2014), this study aims at: (i) creating an atlas of the WM tracts compatible with the MNI-Poly-AMU template and (ii) proposing methods to quantify metrics within the atlas that account for partial volume effect.

The paper is organized as follows. The Material and methods section describes the creation of the WM atlas and its integration into the MNI-Poly-AMU template. Then, different approaches are compared and validated for extracting metrics within specific WM tracts using a synthetic phantom and bootstrapping approach. A proof-of-concept application is presented to quantify magnetization transfer ratio in each individual WM tracts in five healthy subjects. The Results section presents the atlas and the performance of each extraction method with respect to accuracy and reproducibility as a function of noise, tract variability, tract size and partial volume effect with CSF. The Discussion section addresses limitations, applications and future works.

Material and methods

Atlas creation

The overall procedure for creating the MRI atlas of WM tracts consisted in (i) identifying and extracting anatomical information from an existing atlas (Gray's Anatomy), (ii) registering this atlas to the MNI-Poly-AMU WM template at the corresponding slice (C4 vertebral level), (iii) propagating the atlas throughout all slices of the template (C1 to T6) and (iv) computing partial volume values for each tract at each voxel. Fig. 1 illustrates the procedure. The detailed steps are described hereafter.

Extraction of Gray's Anatomy atlas

The atlas was built from the Gray's Anatomy (Standring, 2008), which illustrates the position of the following 15 different WM tracts of both left and right sides at the mid-cervical level in human: fasciculus gracilis, fasciculus cuneatus, lateral corticospinal tract, spinocerebellar tract, rubrospinal tract, lateral reticulospinal tract, spinal lemniscus (spinothalamic and spinoreticular tracts), spino-olivary tract, ventrolateral reticulospinal tract, lateral vestibulospinal tract, ventral reticulospinal tract, ventral corticospinal tract, tectospinal tract, medial reticulospinal tract and medial longitudinal fasciculus. Each tract was digitalized and assigned a gray-level value per tract. This single gray-level image of the WM was then split into 30 different binary images, each representing one tract. A binary mask representing the WM was also created for the purpose of registration to the MNI-Poly-AMU template.

Initial registration to the MNI-Poly-AMU template

The MNI-Poly-AMU template is a straight and symmetric T_2-weighted template of the spinal cord that covers C1 to T6 vertebral levels (504 slices along z direction) and has a resolution of $0.5 \times 0.5 \times 0.5$ mm^3 (Fonov et al., 2014). The MNI-Poly-AMU T_2w template includes a probabilistic template of the WM (Taso et al., 2014), which was used here to register the atlas to. The WM template was

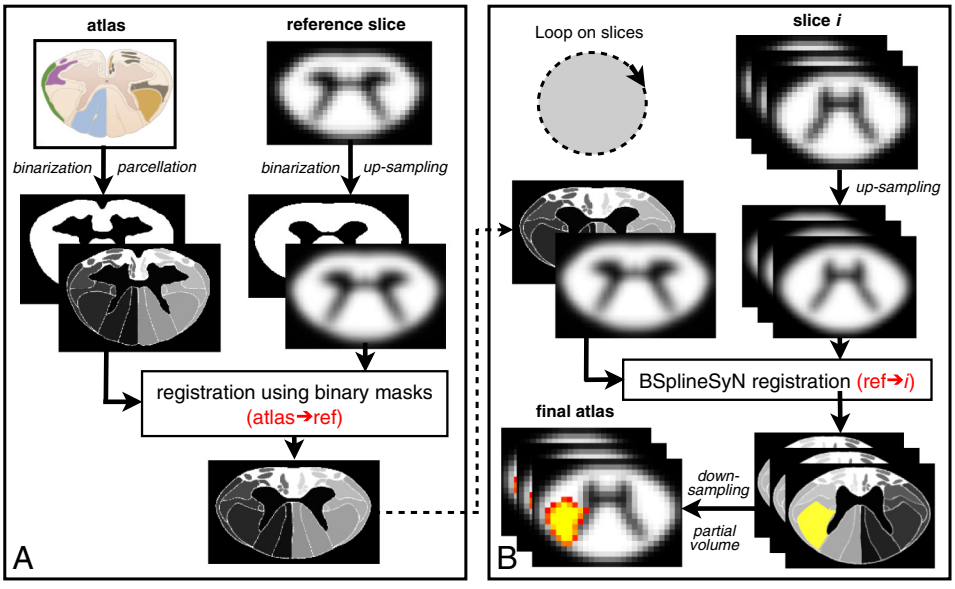

Fig. 1. Overview of the WM atlas creation and registration to the MNI-Poly-AMU template. A. The Gray's Anatomy atlas was manually segmented, then the binary mask was registered to the mid-C4 slice (reference slice) of the up-sampled MNI-Poly-AMU WM template using SyN transformation. B. Propagation of the atlas to other slices of the template was done by registering each slice to the reference slice using BSplineSyN transformations. The resulting backward warping fields were then applied to the resulting atlas from step A, yielding one registered high-resolution atlas per slice. The atlas was then down-sampled to the native resolution of the MNI-Poly-AMU template (0.5 mm isotropic) by computing partial volume values.