Tractometry-based Anomaly Detection for Single-subject White Matter Analysis

Editors: Under Review for MIDL 2020

Abstract

There is an urgent need for a paradigm shift from group-wise comparisons to individual diagnosis in diffusion MRI (dMRI) to enable the analysis of rare cases and clinically-heterogeneous groups. Deep autoencoders have shown great potential to detect anomalies in neuroimaging data. We present a framework that operates on the manifold of white matter (WM) pathways to learn normative microstructural features, and discriminate those at genetic risk from controls in a paediatric population.

Keywords: Diffusion MRI, Tractometry, Anomaly Detection, Autoencoder

1. Introduction

Considerable effort has gone into designing methods for group comparisons in dMRI (Jones and Cercignani, 2010) (i.e., $N$ patients vs $M$ controls) and as such, single-subject analysis frameworks are currently lacking (i.e., 1 patient vs $M$ controls). For clinically-heterogeneous groups, normative modeling (Marquand et al., 2016) has been proposed, but still relies on voxel-based methods, and hence is suboptimal for dMRI since WM tracts offer a more suitable manifold. In this work, we investigate individual differences in children with copy number variants (CNVs) at high genetic risk of neurodevelopmental and psychiatric disorders (Chawner et al., 2019), which are relatively rare and challenging to recruit for imaging (Villalón-Reina et al., 2019). We propose the following unsupervised framework for anomaly detection: First, we learn a normative set of features derived from tract profiles obtained from typically developing (TD) young people using an autoencoder. Second, we apply the framework to unseen tract profiles, to determine whether these deviate from TD children (based on the hypothesis that deviations will stand out from the normal distribution).

2. Methods

2.1. Data acquisition & preprocessing

Diffusion data from 90 TD (age 8-18) and 3 children with a CNV and no apparent WM lesions (age 13-15) were acquired on a Siemens 3T Connectom MRI scanner with 14 $b_0$ images, 30 directions at $b = 500$, 1200 s/mm$^2$, 60 directions at $b = 2400$, 4000, 6000 s/mm$^2$ and $2\times2\times2$ mm$^3$ voxels. Data were preprocessed (Veraart et al., 2016; Vos et al., 2017; Andersson and Sotiropoulos, 2016; Andersson et al., 2003; Glasser et al., 2013; Kellner et al., 2016) and rotationally-invariant spherical harmonic (R0, Mirzaalian et al. (2015)) features were derived for each subject. Automated white matter tract segmentation was performed using TractSeg (Wasserthal et al., 2018) to obtain 20 bundles of interest (Fig. 1, left). For each bundle, Tractometry (Bells et al., 2011) was performed (sampling at 20
locations, Cousineau et al. (2017); Chamberland et al. (2019)) and the resulting 20 tract profiles were concatenated to form a feature vector \((n = 20 \text{ tracts} \times 20 \text{ locations} = 400 \text{ features})\) for each subject. A validation set \((n = 6)\) was generated and held-out by combining the individuals with a CNV \((n = 3)\) with a random subset of TD \((n = 3)\). The rest of the TD \((n = 87)\) data was used to establish a normative distribution. Age regression and feature normalization were performed on the training set and subsequently applied to the validation set.

**2.2. Anomaly detection**

Our autoencoder implementation consists of 5 fully connected layers \((400 \times 128 \times 64 \times 128 \times 400 \text{ units})\) with \(\text{tanh}\) activation between the layers. 10% of the TD data was held out for testing during the training phase \((\text{epochs: 100, batch size = 87, learning rate: } 1.5e^{-3}, \text{ optimiser: Adam, loss: mean squared error})\), where the goal was to generate an output \((\hat{x})\) similar to the input \((x)\) by minimising the reconstruction error. We then compared our implementation with 1) a conventional Z-score distribution; and 2) PCA combined with the Mahalanobis distance (Yeatman et al., 2018; Sarica et al., 2017) computed over tract-profiles. For all methods, anomaly thresholds were set at the tail of the probability density functions (Fig. 1, right).

**3. Results**

The autoencoder approach identified 2 CNV subjects as outliers (Fig. 2, right) in contrast with the other methods that did not detect any. Feature inspection (i.e., R0 profiles) highlighted discrepancies along various association pathways for the CNV subject with the highest reconstruction error (Fig. 3).
4. Discussion & future work

The framework enabled subject- and tract-specific characterisation of WM microstructure. By training only healthy paediatric data, our findings revealed that clinical cases (CNVs) were classified as outliers, but not unseen TDs. The framework also outperformed traditional outlier detection mostly due to its ability to handle high-dimensional data non-linearly. This extends the possibility of using anomaly detection in extremely rare cases (as little as n = 1), where group comparisons are otherwise impossible. The tool will be made freely-available to the community (e.g., via Github). However, further exploration of input features and hyper-parameters remains to assess the generalizability of the framework and its application to other pathology. We believe that our Tractometry-based anomaly detection framework paves the way to progress from the traditional paradigm of group-based comparison of patients against controls, to a personalised medicine approach, and takes us a step closer in transitioning microstructural MRI from the bench to the bedside.
References


