q-Space Deep Learning for Alzheimer’s Disease Diagnosis: Global Prediction and Weakly-Supervised Localization

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Synopsis

Most diffusion MRI approaches rely on comparably long scan time and a suboptimal processing pipeline with handcrafted physical/mathematical models. They can be outperformed by recent model-free methods. For instance, q-space deep learning (q-DL) allows unprecedentedly short scan times and optimized voxel-wise tissue characterization. We reformulate q-DL such that it estimates global (i.e. scan-wise rather than voxel-wise) information. We use this formulation to distinguish Alzheimer’s disease (AD) patients from healthy controls based solely on raw q-space data without handcrafted models such as DTI. Classification quality is very promising. Weakly-supervised localization techniques indicate that the neural network attends to AD-relevant brain areas.

Introduction

Most diffusion MRI approaches rely on relatively long scan time and a suboptimal processing pipeline with handcrafted physical/mathematical representations. They can be outperformed by recent handcrafted-representation-free methods.1,2 For instance, q-space deep learning (q-DL) allows unprecedentedly short scan times and optimized voxel-wise tissue characterization.1,2 Here we reformulate q-DL such that it estimates global (i.e. scan-wise rather than voxel-wise) information. We use this formulation of q-DL to distinguish patients with Alzheimer’s disease (AD) from healthy controls based solely on raw q-space data without any handcrafted representations such as diffusion tensor imaging.

Methods

Data: The data were as follows:3,4 47 AD patients, 58 healthy controls, one b=0 image (averaged over 3 repetitions), 45 diffusion directions (b=1200s/mm^2, single-shot SE-EPI, TR=6638ms, TE=73ms, voxels 1.72mm^3, 2.5mm, matrix 128×128, 48 axial slices), motion/distortion-corrected using ExploreDTI.5 Following deep learning terminology, we refer to each of these 45+1 contrasts (diffusion-weighted images) as “channels”. To study the effect of scan time reduction, separate experiments were performed using sets of 46/30/23/15/7/4 randomly selected channels. For convenient neural network training, so-called feature scaling was performed by dividing each channel by the corresponding channel mean taken over all scans. To prevent overfitting on intensity values, each scan was additionally divided by its mean intensity, and during each training iteration multiplied by a random value between 0.5 and 1.5.

Network: Five-fold cross-validation was performed: The dataset was split into five equally-sized subsets, and in each fold three of the subsets were used for training, one was used for validation (early stopping) and one for testing (results are reported on the test set of each of the five folds). The neural network architecture was C128-P-C256-P-C512-GP-FC2000-FC1, where Cn is a convolutional layer with n filters sized 3×3×3, P is a 2×2×2 max-pooling layer, GP is a global-pooling layer, and FC is a fully-connected layer with n units. Hidden-layer nonlinearity: ReLU(z) = max(z, 0), output nonlinearity: sigmoid, trained with binary-cross entropy loss, Adam algorithm,6 learning rate 2·10^{-5}, to distinguish AD patients from healthy controls.

Results

Figure 3 shows the receiver operating characteristic (ROC) for the test sets from the five cross-validation folds. Area under the curve (AUC) in the five cross-validation folds ranges between 0.85 and 0.96. Dependency of AUC on channel number is illustrated in Fig. 4.

Gradient-based class activation mapping7 (Grad-CAM) is a “weakly-supervised localization” technique to visualize on what spatial image area the network bases its decision. Its combination with saliency maps (e.g. guided backpropagation8) that model which inputs strongly influence the prediction, is called Guided Grad-CAM.7 We use these techniques to examine which brain areas drive the network’s decision. Visualization of Guided Backpropagation8 and (Guided) Grad-CAM7 for an AD patient that the network correctly classified are shown in Fig. 5.

Discussion

We can thus report that one can train a network directly on q-space data, without any handcrafted representations needed when classifying AD. The network can compensate for missing channels, i.e. providing good predictions for relatively short scan times. AUC drops substantially only when extremely few channels are exposed to the network.

Conclusions

We conclude, (1) that it is possible to directly use raw q-space data as inputs for a convolutional neural network and obtain good classification results when detecting AD, and (2) that the convolutional neural networks seem to learn with weak supervision which areas of the brain are affected by AD.
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References

Figures

2D slice of random elastic deformations of a 128×128×48 checkerboard image using deformation vectors with different coarse-grid densities and standard deviations. Grid density 8×8×4 and standard deviation of 1 voxel were used for MRI data augmentation.

Original 128×128 2D MRI slice (left) and randomly elastically deformed version for training with data augmentation (right).
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ROC for Alzheimer's disease classification using global q-DL.

Dependency of AUC on selected number of channels (diffusion-weighted images) that are exposed to the network. Even though AUC remains stable relatively long with less channels, AUC drops substantially when the network is trained on very few channels.

Visualization of Grad-CAM, Guided Grad-CAM and Guided Backpropagation overlaid with the b=0 channel of an AD patient. Highlighted regions mark brain areas that were important for the network's classification decision.