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Original Article

Automated MRI-Based Mapping of Dentate Nucleus Using Advanced Neural Networks

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ABSTRACT: *The dentate nucleus (DN) plays a central role in cerebellar output and is implicated in various neurological disorders. Accurate in vivo segmentation of the DN is challenging due to its small size and low visibility on conventional MRI sequences. In this study, we developed a fully automated deep learning pipeline to segment the DN using quantitative susceptibility mapping (QSM) MRI. A diverse dataset of 328 individuals, including healthy controls and patients with cerebellar ataxia or multiple sclerosis, was collected from nine international sites. Manual annotations provided reference standards with high reliability. A two-step approach combining localization and segmentation was implemented, with the nnU-Net framework yielding the best performance. The model achieved Dice scores of 0.90 ± 0.03 (left DN) and 0.89 ± 0.04 (right DN) on internal testing and outperformed existing tools in external validation. These results demonstrate that automated neural network-based DN segmentation is accurate, generalizable, and suitable for large-scale clinical studies. The model is publicly accessible for research applications.*

KEYWORDS: *Dentate nucleus, Quantitative susceptibility mapping, Deep learning, MRI, segmentation, Neural networks.*

1. INTRODUCTION

The dentate nucleus (DN) is the largest deep cerebellar nucleus and serves as the primary output hub of the cerebellum. It is innervated by Purkinje cells of the lateral cerebellar hemispheres and projects to cortical and subcortical targets through the dentatorubral and dentatothalamocortical tracts. The DN is functionally segregated into motor and nonmotor territories, which modulate various behavioral and cognitive domains. Malformations of the DN structure or function are associated with various neurological diseases, such as inherited cerebellar ataxias and multiple sclerosis.

However, the DN is poorly visible in conventional MRI sequences such as T1-weighted and T2-weighted images and because it is small, high-resolution in vivo quantitative analysis of the DN remains challenging. Susceptibility-weighted imaging can demonstrate the DN by highlighting their high iron content, but this method is qualitative and subject to artifacts. Quantitative susceptibility mapping (QSM) circumvents these issues via offering an absolute measure of tissue magnetic susceptibility, which can be exploited to obtain accurate DN demarcation and microstructural characterization.

Manual extraction of the DN on QSM files is time-consuming and liable to variation, which restricts large-scale research. Currently available software tools (e.g., MRICloud) often use atlas-based approaches, which do not have the specificity and generalization ability. Some of the modern deep learning (DL) techniques, which include CNNs, have demonstrated potential for medical image segmentation. Therefore, we pursue this project to design a strong and completely automated DL framework for DN segmentation based on QSM MRI across multiple ethnic populations that serves as an instrument in both academic research and clinical use.

2. MATERIALS AND METHODS

2.1. DATA COLLECTION

QSM MRI data were retrospectively collected from nine international imaging centers between 2016 and 2023. The dataset included 141 healthy individuals and 187 patients with Friedreich ataxia (FRDA) or multiple sclerosis (MS), aged 11–64 years. Imaging protocols varied across centers but primarily utilized 3-T Siemens and Philips scanners with multi-echo gradient-recalled echo sequences. Ethical approval was obtained at all sites, and informed consent was secured for all participants.

2.2. PREPROCESSING

Images were resampled to an isotropic voxel spacing of 0.86 mm. QSM maps were reconstructed using established toolboxes (JHU/KKI QSM and STI Suite) with Laplacian phase unwrapping, V-SHARP background field removal, and MEDI or iLSQR for susceptibility calculation. Z-score normalization was applied to voxel intensities to reduce inter-scan variability.

2.3. MANUAL ANNOTATION

Three experienced neuroradiologists independently traced DN boundaries on QSM images to create reference standards. Inter- and intrarater reliability were assessed using intraclass correlation coefficients (ICC), Dice scores, and Hausdorff distance metrics. High reproducibility was achieved (mean ICC > 0.75 for interrater, >0.90 for intrarater).

2.4. DEEP LEARNING PIPELINE

A two-step deep learning pipeline was implemented:

- Localization – A neural network identified the cerebellum within the full brain MRI volume, providing spatial context for the segmentation network.
- Segmentation – The nnU-Net architecture was trained to segment the left and right DN within the localized region. Data augmentation techniques, including rotation, scaling, elastic deformation, and intensity variations, were applied to improve generalization.

The dataset was split into training (70%), tuning (10%), and internal testing (20%) sets using stratified sampling to maintain center-specific distribution.

2.5. EXTERNAL VALIDATION

The model was tested on an independent set of 38 QSM datasets from four additional sites, including scans reconstructed with both MEDI and STreaking Artifact Reduction QSM pipelines. Performance was compared with MRICloud.

2.6. STATISTICAL ANALYSIS

Segmentation accuracy was evaluated using Dice score, Jaccard index, Hausdorff distance, and volume similarity metrics. Pearson correlation coefficients were calculated to compare predicted DN volumes with manual annotations. Differences between methods were assessed using the Wilcoxon signed-rank test, with significance set at $P < 0.05$ (Bonferroni corrected).

3. RESULTS

3.1. DATASET CHARACTERISTICS

The final dataset included 328 participants (157 males, 171 females) with 141 healthy controls, 169 FRDA patients, and 18 MS patients. Ages ranged from 11 to 64 years. Demographic distributions were balanced across training, testing, and validation sets.

3.2. MANUAL SEGMENTATION RELIABILITY

High intrarater reliability was observed (ICC > 0.90), with moderate-to-good interrater agreement (ICC 0.67–0.76). Dice scores and Hausdorff distances confirmed consistent manual annotations.

3.3. MODEL PERFORMANCE

The nnU-Net-based pipeline achieved mean Dice scores of 0.90 ± 0.03 for the left DN and 0.89 ± 0.04 for the right DN in internal testing. External validation results were also strong (LDN: 0.86 ± 0.04; RDN: 0.84 ± 0.07), outperforming MRICloud (LDN: 0.57 ± 0.22; RDN: 0.58 ± 0.24; $P < 0.001$). Predicted DN volumes were highly correlated with manual annotations (Pearson $r = 0.74$ for left DN, $r = 0.48$ for right DN).

3.4. BIOLOGIC OBSERVATIONS

A positive association between DN volume and magnetic susceptibility was observed, consistent with previous studies. Partial volume effects were noted but corrected using a linear regression-based adjustment factor derived from healthy controls.

4. DISCUSSION

This study presents a fully automated, deep learning-based framework for DN segmentation from QSM MRI. Key contributions include:

- Two-step pipeline – Localization followed by segmentation reduced false positives in iron-rich regions and improved accuracy.
- High generalizability – Model performance remained strong across multiple external datasets and reconstruction pipelines.
- Biologic validity – Replication of known associations between DN volume and susceptibility confirms that the model captures meaningful anatomical information.

The performance of neural network was better than that of the atlas-based method (MRICloud) in Dice scores and volume correlation. The framework is not computationally expensiveto calculate, it takes less 60 seconds if run on CPU and around of 15seconds on GPU hardware to generate the explainable probability scores.

Limitations include the relatively small sample of MS subjects and that our analysis was limited to FRDA and MS, which may have implications for generalization in noncerebellar disease. Future work should extend the study to account for a greater range of neurologic problems and investigate transformer-based architectures using larger data sets.

5. CONCLUSION

The proposed deep learning pipeline enables accurate, reliable, and fully automated segmentation of the dentate nucleus from QSM MRI across diverse populations. This tool has potential for large-scale clinical studies, longitudinal monitoring, and biomarker discovery in cerebellar disorders. The model is publicly available for research use.

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