IMG08

Comparing Neuroradiologist Qualitative Rating of Atrophy to Normative Brain Volume Measures

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Introduction

Detecting the presence of brain atrophy is a key factor in monitoring disease progression in Multiple Sclerosis (MS). Brain atrophy is commonly assessed in patients with MS (pwMS) by neuroradiologists' (NRs) MRI reports, often using qualitative descriptions such as mild, moderate, severe, or none. Studies in other patient populations such as dementia have found discrepancies between NR visual interpretation of brain atrophy and volumetric normative percentiles. Understanding the relationship between qualitative assessments and quantitative atrophy measures in MS may aid the incorporation of quantitative atrophy measures into clinical practice.

Objectives

To compare NRs qualitative atrophy ratings (NQR) to quantitative, normative brain volumetrics in pwMS to understand how objective brain volumetrics relate to subjective atrophy ratings in an MS population.

Methods

- 86 pwMS were selected from a retrospective database and assessed by 3 NRs. Each pwMS had 2 MRI scans, on average 1 year apart, with 3D T1, 3D T2 FLAIR, and 3D T1-post contrast series.
- Each NR categorically rated each pwMS for atrophy (mild, moderate, severe, and none), resulting in a total of 258 ratings.
- Then, 3D T1 and 3D T2 FLAIR MRI series images from each patient were processed using a commercially available, FDA cleared software for automated volumetric brain segmentation.
- Processing with software returned brain segmentation masks and associated volume measures including volume (cm^3), percent of intracranial volume, and normative percentiles of volume compared to age and sex-matched healthy controls. The segmentation masks were manually reviewed by a trained specialist.
- Normative percentiles of whole brain volume and total ventricle volume were used in this analysis, as they reflect the features NRs visually assess to generate the NQR.
- NQR and brain volumetrics data were correlated in a linear model with NR as a covariate. NR was included as a covariate to determine how much inter-NR variability affects the dependent variable (brain volume measured), with NQR held constant.

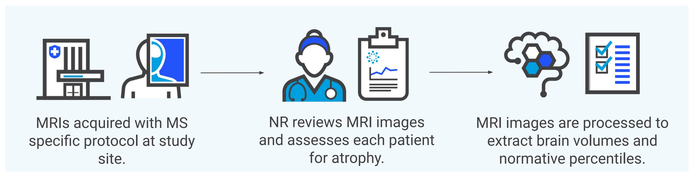

Figure 1: Illustration of the workflow performed to obtain NQR ratings and brain volumetrics for each pwMS, requiring the following: patient scanning,, NR review and rating of qualitative atrophy, processing of MS MRIs through automated software, and review of the software's brain segmentation mask outputs for accuracy.

Disclosures: FXF AK, AS, and KML are employees of Octave Bioscience, Inc.

Results

NQR	Count	Whole Brain Volume Normative Percentile			Total Ventricle Volume Normative Percentile		
		Mean	Median	Std Dev	Mean	Median	Std Dev
None	109	38.9%	33.0%	27.7%	67.5%	71.0%	24.5%
Mild	114	23.3%	15.0%	24.9%	78.7%	87.0%	22.8%
Moderate	31	8.3%	1.0%	13.9%	91.2%	99.0%	13.4%
Severe	4	5.3%	3.0%	5.9%	96.8%	99.0%	4.5%

Table 1: Distribution (mean, median, and standard deviation) of brain volume normative percentiles within each categorical rating of atrophy (NQR).

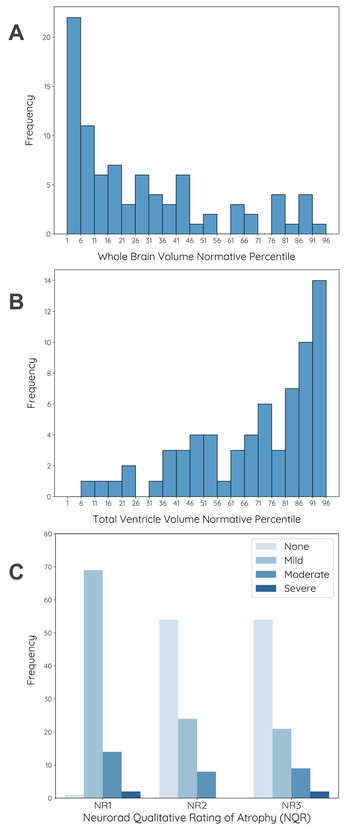

Figure 2: (A) Frequency of normative percentiles for individual patients for Whole Brain Volume and (B) Total Ventricle Volume. (C) Frequency of NQR by NR. NR2 and NR3 were found to more closely resemble one another than NR1.

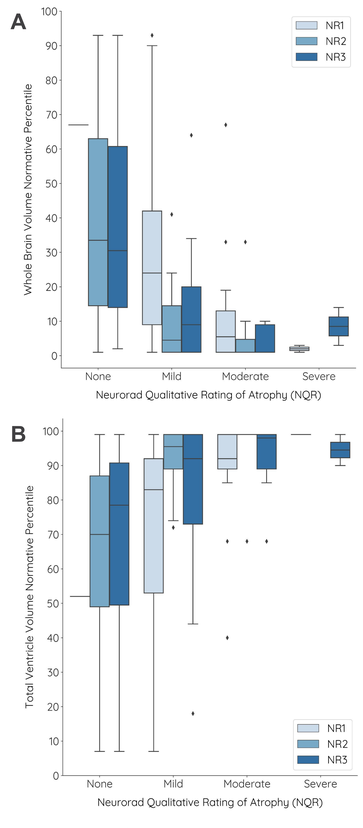

Figure 3: Box plot of NQR distribution by NR and associated range in normative volume for A: Whole Brain and B: Total Ventricles. Inverse relationship between whole brain and total ventricle percentiles is consistent with NQR.

- The level of NQR agreement for individual patients (N=86) was measured: Full Agreement: 10, One NR Disagrees: 73, All NRs Disagree: 3.
- The distribution of normative percentiles for whole brain volume & total ventricle volume are shown in Figures 2A & 2B, respectively. As expected, there was an inverse relationship between whole brain and total ventricular volume normative percentiles.
- Inter-NR variability was demonstrated, shown by two NRs in this study varying substantially from a third NR in the frequency of "No Atrophy" and "Mild Atrophy" ratings. (Figure 2C)
- Table 1 shows the distributions of whole brain and total ventricle volume normative percentiles across NQRs. Box plots (Figure 3) visualize individual NR's patterns of NQR in relation to the pwMS' normative percentile.
- NRs reported non-severe NQRs for patients with very low normative whole brain volume percentiles. 22 pwMS had normative whole brain volume percentile of ≤ 5%, yet only 3 NQRs of "severe" quality were recorded.
- Results of OLS linear regression showed that a one-step increase in NQR severity was associated with a statistically significant decrease in whole brain volume normative percentile of 18.4% (p=1.4e-13) and a statistically significant increase in total ventricular volume normative percentile of 14.3% (p=1.2e-10).
- When comparing to NR1, and with NQR held constant, there was a 12.4%(p=2.5e-3; NR2) or 13.5%(1.9e-5; NR3) decrease in norm whole brain volume and a 10.5%(p=5.3e-3; NR2) or 9.6%(9.2e-3; NR3) increase in norm total ventricular volume. This result is consistent with NR1 having more ratings of Mild, and fewer ratings of No Atrophy. (Table 2)

Region of Interest	Predictor Variable	p Value	Coefficient	2.5 CI	97.5 CI
Whole Brain (Normative Volume Percentile)	Intercept	1.1e-29	49.8%	42.2%	57.4%
	NQR	1.4e-13	-18.4%	-23.0%	-13.8%
	NR 2 (compared to NR1)	1.2e-3	-13.5%	-21.6%	-5.4%
	NR 3 (compared to NR1)	2.5e-3	-12.4%	-20.4%	-4.4%
Total Ventricles (Normative Volume Percentile)	Intercept	5.2e-43	58.6%	51.7%	65.5%
	NQR	1.2e-10	14.3%	10.1%	18.5%
	NR2 (compared to NR1)	5.3e-3	10.5%	3.1%	17.8%
	NR3 (compared to NR1)	9.2e-3	9.6%	2.4%	16.9%

Table 2: CI= Confidence Interval. Results of the OLS regression model, highlighting the degree with which increasing NQR severity predicts Whole Brain and Total Ventricle volume normative percentiles consistent with increasing brain atrophy in a pwMS.

Conclusions

The results of the OLS regression suggest that NRs thresholds for brain and ventricle appearance vary when determining a pwMS' qualitative brain atrophy. The data show that increasing NQR severity is associated with reduced brain volumes, yet discrepancies between NRs qualitative atrophy ratings and volumetric percentiles persist. Since detecting the presence and change of brain atrophy is a key factor in monitoring disease progression in MS, pairing clinician expertise with quantitative data may provide a more precise & actionable MRI report, leading to improved patient outcomes.

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