Association Between Clinical Progression in Multiple System Atrophy and Brain Volume Changes Evaluated via Deep Learning Segmentation

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OBJECTIVE

Assess **brain volume changes** in patients with **multiple system atrophy (MSA)** over one year.

INTRODUCTION

Identifying **biomarkers for disease progression** is essential for advancing MSA treatment.

- Previous longitudinal MRI studies of brain atrophy in MSA have faced methodological challenges, limiting conclusions about MRI's utility in assessing and monitoring disease progression.
- Novel post-processing techniques, particularly deep-learning segmentation, offer improved precision and have the **potential to enhance tracking of MSA progression**.

Our study **monitored changes in brain volumes over 12 months**, aiming to establish a correlation between brain volume changes and disease progression.

METHODS

Seventeen participants meeting criteria for clinically probable MSA were enrolled in the bioMUSE natural history study, with fluid biomarkers (α-synuclein SAA in CSF, and NfL in CSF and plasma), 3T MRI, and neurological exams conducted at baseline, 6 and 12 months.

- Clinical assessments included **UMSARS and NNIPPS rating scales**.
- Age-matched healthy controls (HC, n=19) and Parkinson's disease (PD, n=17) patients were enrolled as controls for single MRI scan.
- **3D T_1-weighted images were segmented using AssemblyNet**, a deep-learning technique. Regions of Interest (ROIs), including cerebellar grey matter, cerebellar white matter, putamen, globus pallidus, and brainstem, were normalized to intracranial volume (ICV).

Group differences were evaluated using a least squares model, adjusting for age and sex, and longitudinal volumetric changes were analyzed with a linear mixed-effects model. Associations between volumetric changes and disease progression were explored.

RESULTS:MSA PARTICIPANTS

For participants enrolled in bioMUSE, fluid and imaging biomarkers, along with clinical manifestations, were used to classify patients as MSA (n=10: 6 MSA-P, 4 MSA-C) or PD/DLB (n=5). Patients who tested negative for alpha-synuclein (n=2) were excluded from the analyses.

	MSA	PD/DLB	PD-controls	HC
N	10	5	17	19
Sex (M/F)	4/6	4/1	12/5	9/10
Age (years), mean ± std	60 ± 8	67 ± 7	63 ± 6	65 ± 7
UMSARS Total, mean ± std	34 ± 11	25 ± 9		
PPS Total score, mean ± std	59 ± 20	50 ± 27		

Table 1. Demographic and Clinical Data at baseline

RESULTS:BRAIN VOLUMES AT BASELINE

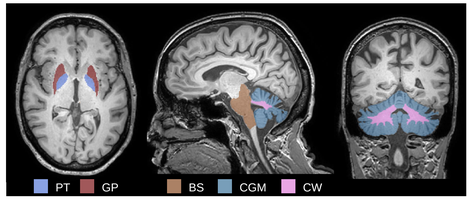

Fig. 1. Regions of Interests.

Example of ROIs segmented using AssemblyNet, including the putamen (PT), globus pallidus (GP), brainstem (BS), cerebellar grey matter (CGM), and cerebellar white matter (CWM).

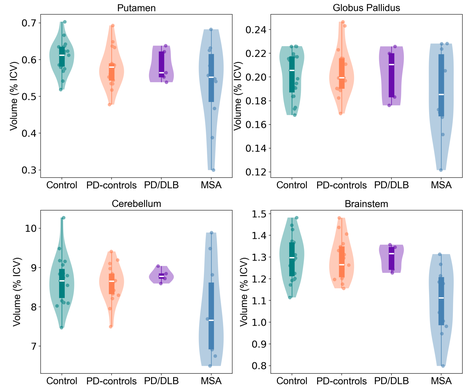

Fig. 2. Group differences.

Violin plots are displaying the volume distribution across different ROIs for each group. Least squares model fitting indicate that MSA patients had significantly lower volumes in the cerebellar grey matter, cerebellar white matter, putamen, globus pallidus, and brainstem compared to both healthy controls (HC) and Parkinson's disease (PD) controls (all p-values < 0.01).

RESULTS: LONGITUDINAL CHANGES

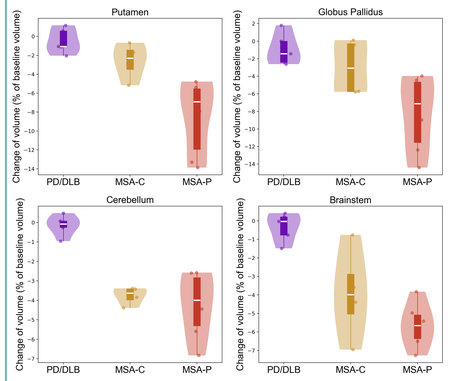

Fig. 3. Longitudinal brain volume changes over 12 months.

Over the 12-month period, PD-like patients showed no significant brain volume changes. In contrast, both MSA-C and MSA-P patients exhibited significant volume reductions in the cerebellum, globus pallidus, and brainstem, with MSA-P patients additionally showing significant volume loss in the putamen.

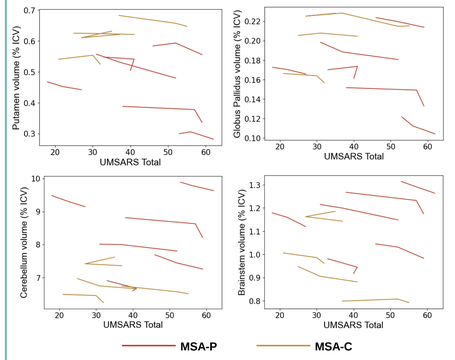

Fig. 4. Association with clinical scores.

The plot shows the relationship between brain volumes and UMSARS scores over time. Individual patient trajectories are shown as lines connecting data points at baseline, 6 months, and 12 months. These lines illustrate the progression of brain volume reduction in relation to increasing UMSARS scores, providing a visual representation of disease progression, highlighting the variability among patients. Mixed-effects models confirmed these relationships as statistically significant.

CONCLUSIONS

- Over the course of one year, MRI with deep-learning segmentation **revealed significant brain volume reduction in MSA patients**.
- Structural MRI plays a critical role in both diagnosing MSA and monitoring disease progression.
- Subcortical brain volume shows potential as a biomarker for evaluating disease-modifying therapies.

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