



The Distribution Of White Matter Hyperintensities Differs Between Subcortical And Cortical 4-repeat Tauopathies

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BACKGROUND

Progressive supranuclear palsy (PSP) syndromes and corticobasal syndrome (CBS) are two 4-repeat (4R) tauopathies presenting with atypical parkinsonism. They target a common network of brain regions, although the relative involvement of cortical and subcortical regions differs. White matter hyperintensities (WMHs) are common in neurodegenerative disorders, however, little is known about their distribution in 4R-tauopathies.

OBJECTIVES

To evaluate the distribution of WMHs in the cortical and subcortical predominant 4R-tauopathies using venous territory-based and the derivative layer designed atlases.

METHODS

- Ninety-five participants with clinical variants of PSP or CBS were recruited by the Neurodegenerative Research Group, Mayo Clinic, and were classified as cortical (n=64) or subcortical (n=31) predominant.
- WMH volume was calculated for superficial, deep cerebral venous territory, and the periventricular (PV) region.
- Additionally, a layered atlas was created to assess WMH volume from the lateral ventricles (LV) to the brain surface. WMH volumes and clinical tests were compared across groups and to 50 age-matched controls.

RESULTS

TABLE 1: Demographic and clinical features of the cortical and subcortical groups

Variable	Cortical (n=64)	Subcortical (n=31)	p-value
Female, %	28 (43.8%)	18 (58.1%)	0.22
Encounter age, years	69.44, 7.03	69.54, 8.65	0.73
Onset age, years	64.97, 6.75	63.68, 8.55	0.46
Time from onset to scan, years	4.00, 2.03	5.41, 3.43	0.15
MoCA (/30)	21.64, 5.22	24.10, 3.44	0.04
PSP Rating Scale (/100)	34.81, 14.93	32.13, 12.17	0.59
MDS-UPDRS III (/132)	37.13, 17.32	37.67, 15.11	0.88
PSIS (/5)	1.61, 1.13	1.82, 1.53	0.66
TULIA (/12)	6.64, 3.64	11.39, 1.03	<.001

Data shown as mean, standard deviation. Chi-squared test was used for categorical variable, and Mann-Whitney-U-test was used for continuous variables. MRPI = MR Parkinsonism index; MoCA = Montreal Cognitive Assessment Battery; MDS-UPDRS III = Movement Disorders Society sponsored revision of the Unified Parkinson's disease Rating Scale, part III; PSIS = PSP saccadic impairment scale; TULIA = Test for Upper Limb Apraxia.

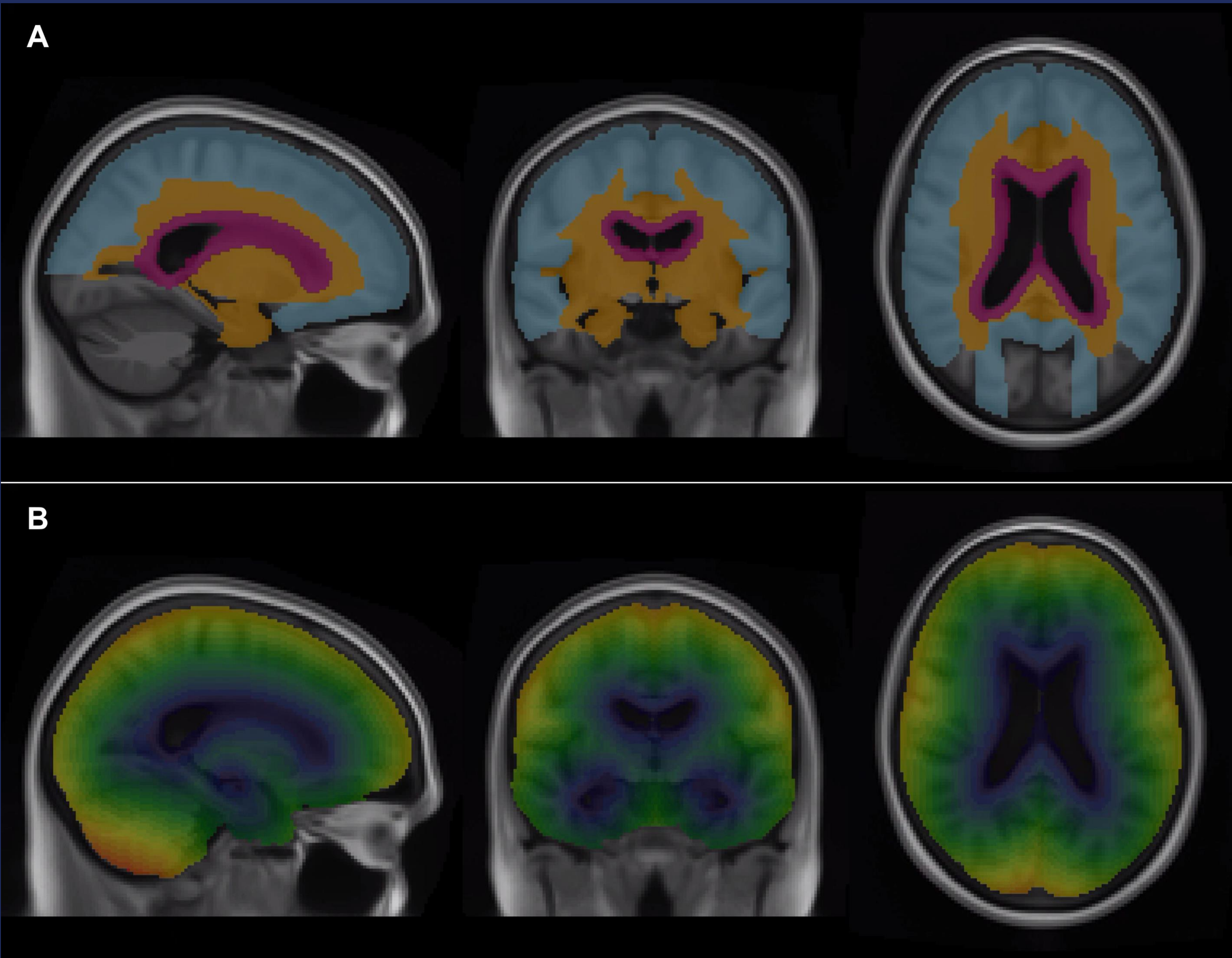


Figure 1: Representative three-plane views of two atlases in the template space. (A) Anatomical design-venous territory atlas. Purple, periventricular; orange, deep; blue, superficial. (B) Mechanical design-layered atlas. Twenty layers from deep to surface of brain.

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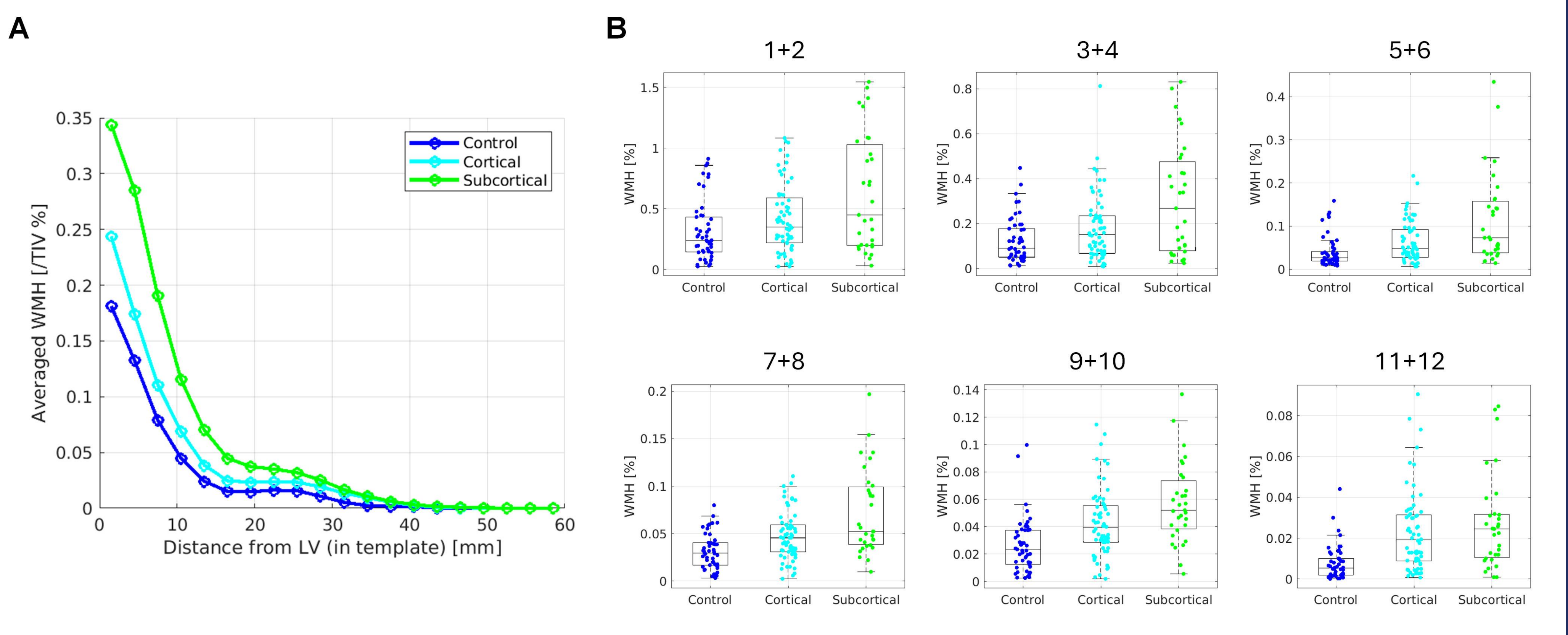


Figure 2: WMHs distribution in layered version of atlas among control, cortical, and subcortical group. (A) Average WMHs distribution in the control, cortical, and subcortical group. (B) Scatterplot of WMHs distribution in the control, cortical, and subcortical group in each two layers.

CONCLUSIONS

The distribution of WMHs in the deep cerebral venous territory and the presumed watershed zone suggests that dysfunction of the venous system may play a role in the pathomechanism of 4R-tauopathies, particularly subcortical variants.