

QUANTIFYING THE VOLUME OF BRAINSTEM NUCLEI IN NEURODEGENERATIVE DISEASES ASSOCIATED WITH DEMENTIA

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INTRODUCTION

Brainstem atrophy occurs in several neurodegenerative diseases^{1,2}. Sleep dysfunction is common in dementia and several brainstem nuclei, such as the parabrachial, periaqueductal grey, ventral tegmental area and midbrain reticular formation help to regulate sleep and working memory³⁻⁷. Smaller volumes of the midbrain, locus coeruleus and raphe nuclei are associated with poorer attention and executive function in people with mild cognitive impairment (MCI) and Parkinson's disease^{8,9}. This study investigated volumetric differences in brainstem nuclei in people with Alzheimer's disease/amyloid positive MCI (AD/MCI), dementia with Lewy bodies (DLB), frontotemporal dementia (FTD), corticobasal syndrome (CBS), progressive supranuclear palsy (PSP) and controls.

METHODS

1238 people recruited to various studies through memory clinics

762 had recon all MRI that underwent AAN segmentation using Freesurfer

85 duplicate MRIs removed

7 scans removed due to failed segmentation

Combat harmonisation with age, sex and diagnosis as modulating factors.

72 excluded due other diagnosis, additional 26 due to missing age and sex and additional 4 due to missing scanner type.

568 people included with AD/MCI, DLB, PSP, CBS, FTD and controls.

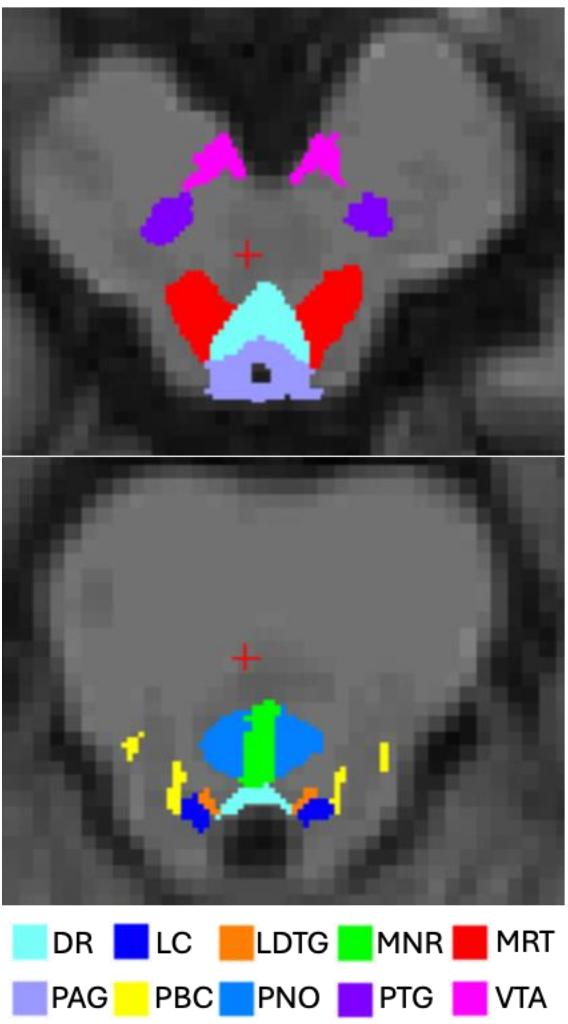


Fig 2: Freesurfer brainstem (AAN) output¹⁰

Freesurfer segments the brainstem into 10 nuclei; ventral tegmental area (VTA), locus coeruleus (LC), dorsal raphe (DR), median raphe (MNR), pontis oralis (PNO), laterodorsal tegmental nucleus (LDTG), parabrachial complex (PBC), periaqueductal grey (PAG), midbrain reticular formation (MRT) and pedunculotegmental nucleus (PTG).

RESULTS

Fig 3: Volumes of all brainstem nuclei were significantly smaller in PSP and CBS compared to controls. Volumes of all nuclei except the LC were significantly smaller in FTD compared to controls. Volumes of the PBC, MNR, PNO, MRT, PTG and VTA were significantly smaller in DLB and AD compared to controls. Volumes of PAG were significantly smaller in DLB compared to controls.

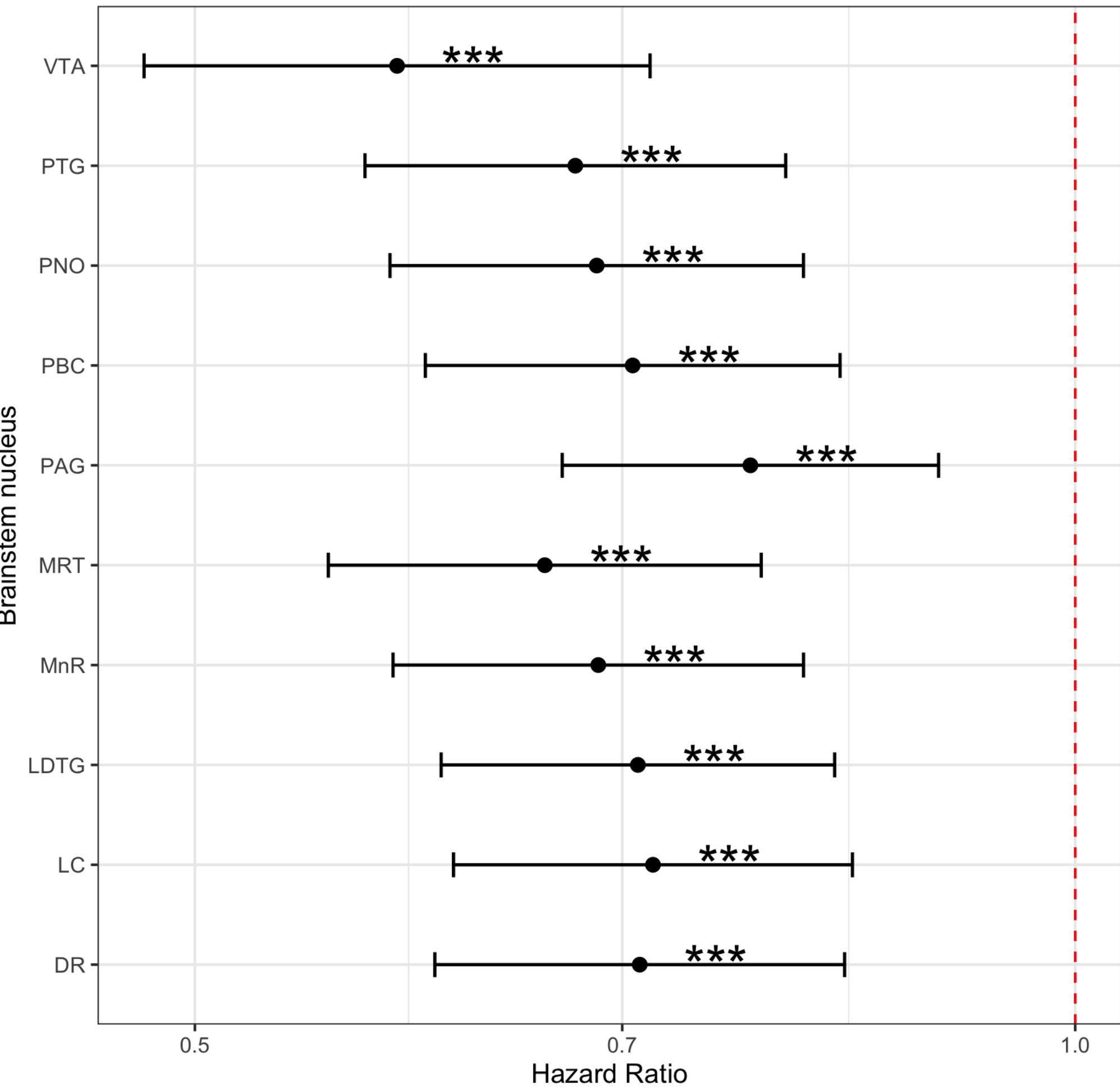
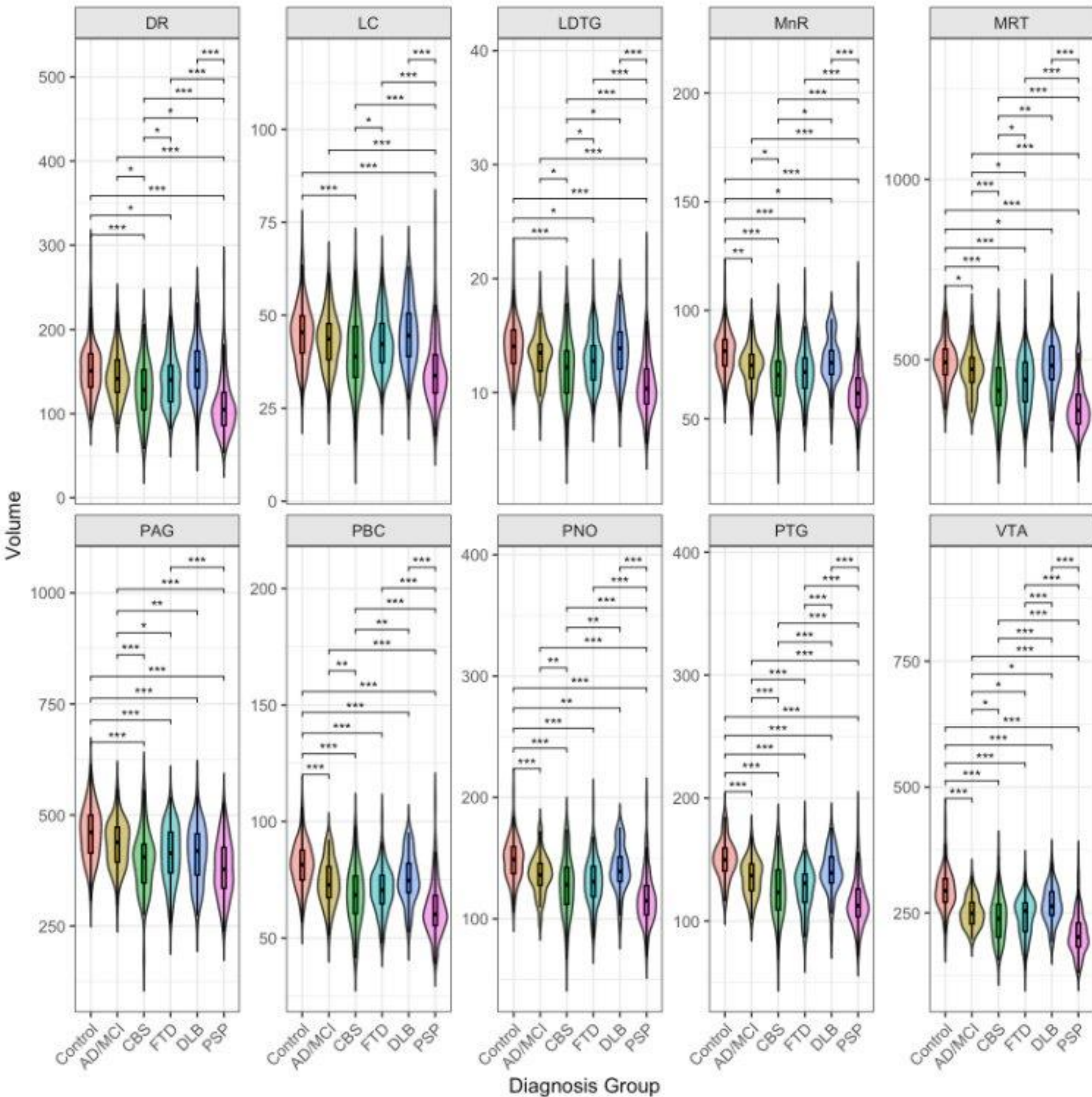


Fig 4: Larger volumes of all brainstem nuclei were significantly associated with lower mortality in all disease groups. This effect remained even after removing PSP from the disease group.

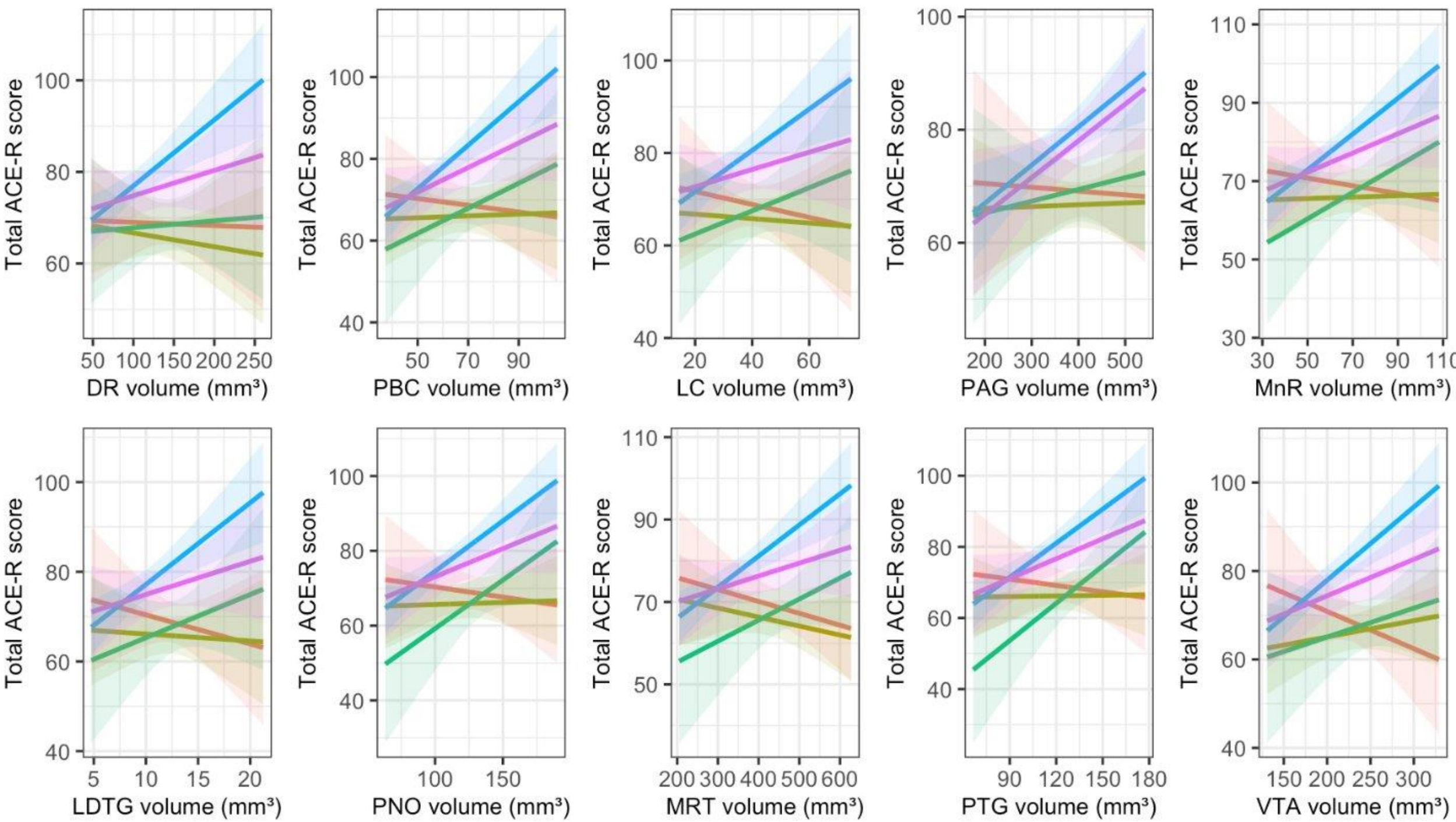
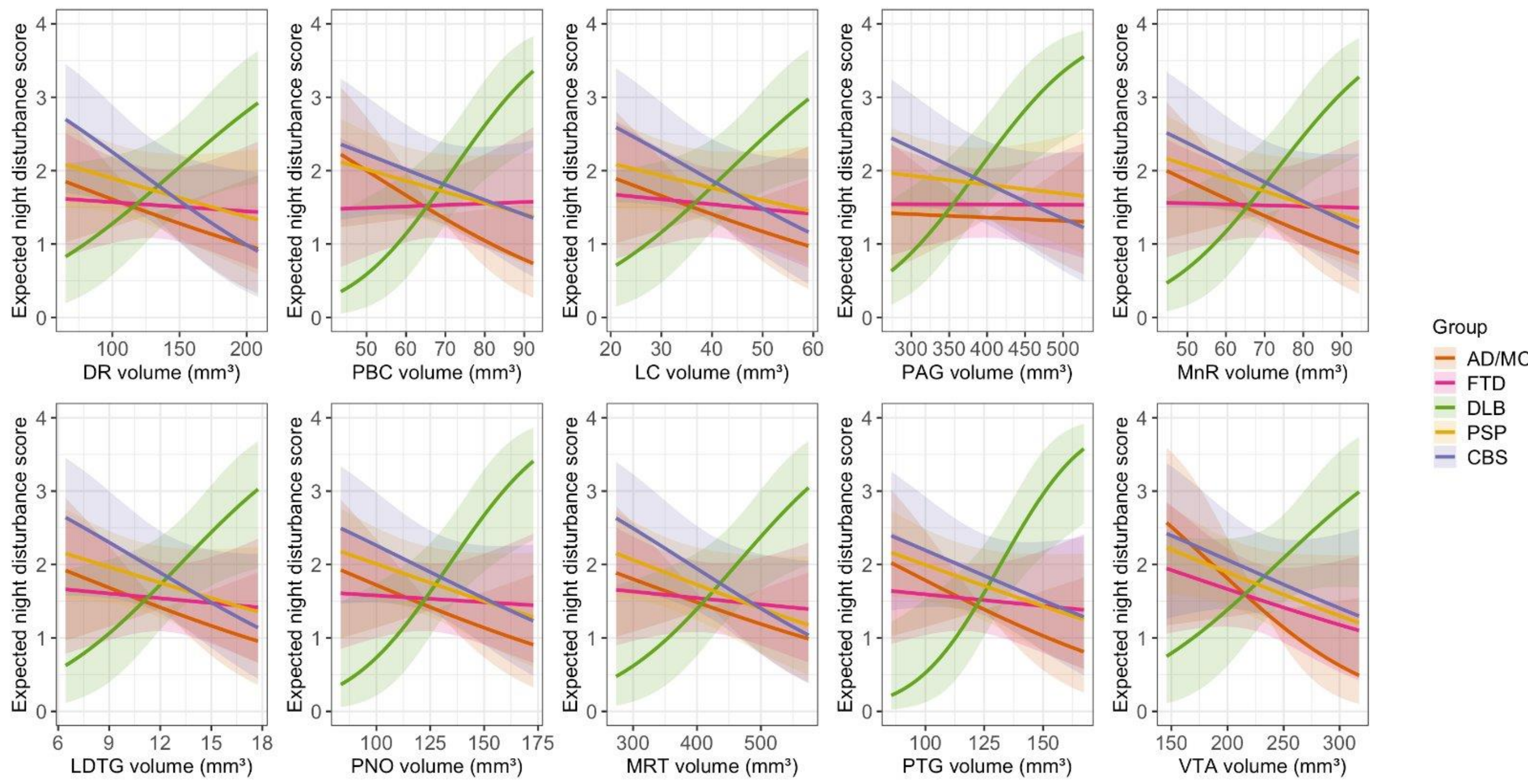


Fig 5: Larger volumes of all brainstem nuclei were associated with significantly higher total ACER scores in PSP. ACER = Addenbrooke's Cognitive Examination Revised.

Fig 6: Larger volumes of the PBC, PAG, MNR, PNO and PTG were associated with significantly greater frequency of nighttime sleep disturbance in DLB.



CONCLUSION

Several neurodegenerative diseases, particularly PSP, display smaller brainstem nuclei volumes. Smaller volumes of several of these nuclei were associated with lower cognitive scores in PSP, and less sleep disturbance in DLB. Larger volumes of all nuclei were associated with decreased mortality in all disease groups.

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