Small and large MRI-visible perivascular spaces in the basal ganglia of Parkinson's disease patients

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INTRODUCTION

Perivascular spaces (PVS) are fluid-filled spaces surrounding the cerebral vasculature[1]. There is evidence to suggest that pathologically dilated PVS that become visible on MRI may be indicative of hypertensive arteriopathy and glymphatic clearance dysfunction[2,3]. Additionally, dilated PVS burden in the basal ganglia region (BG-PVS) have been implicated as potential indicators for the progression of motor disability[4,5], and cognitive decline[6–8] in PD. Evidence suggests that there are pathophysiological differences between **large (> 3mm diameter) and small (≤ 3mm) PVS**,[9,10] although not specifically demonstrated in PD. The purpose of this study is to examine associations between quantitative measures of BG-PVS, and motor and non-motor features assessed using the **Movement Disorder Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS)** Parts I-IV[11]. Below is a brief overview of each Part:

Part I	Part II
Daily Non-Motor Symptoms Cognitive Impairment Fatigue Depressed Mood	**Daily Motor Symptoms** Speech Chewing & Swallowing Hygiene
Part III	**Part IV**
Motor Examination Gait Postural Stability Resting Tremor	**Motor Complications** Dyskinesias Dystonia Motor Fluctuations

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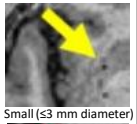
METHODS

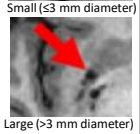
Study participants were 139 PD patients from the Ontario Neurodegenerative Disease Research Initiative (ONDRI)[12]. PD motor and non-motor symptom severity was assessed using the MDS-UPDRS Parts I-IV. Cognition was assessed using the Montreal Cognitive Assessment tool (MoCA).[13] Using the ONDRI neuroimaging quantification method, 3T brain MRI was used to quantify periventricular and deep white matter hyperintensities (p/dWMH), lacunes, and dilated PVS.[14] BG-PVS were delineated and used to classify study participants into two groups: small BG-PVS (≤ 3mm diameter) and large BG-PVS (> 3mm diameter).

Statistical Analysis:

Partial Spearman's correlation and negative binomial regression models adjusted for multiple comparisons using Bejamini-Hochberg false discovery rate (FDR). All analyses accounted for age, sex, education, HbA1C, cholesterol, systolic BP, smoking, lacunes, and head-size adjusted WMH.



Small (≤3 mm diameter)



Large (>3 mm diameter)

RESULTS

Small BG-PVS (≤3 mm in diameter)

FDR-adjusted negative binomial regression revealed an association with small BG-PVS counts and the MDS-UPDRS Part I ($p < 0.01$, 95% confidence interval: 0.005, 0.023) and Part II ($p < 0.01$, 95% C.I.: 0.004, 0.023).

Large BG-PVS (>3 mm in diameter)

Similar analysis as above, revealed an association with large BG-PVS counts and the MDS-UPDRS Part III ($p < 0.0001$, 95% C.I.: 0.012, 0.027) and Part IV ($p < 0.001$, 95% C.I.: 0.015, 0.05).

Additional Findings

Partial Spearman's correlation showed that small BG-PVS were correlated with pWMH (rho=0.26, p=0.015)

DISCUSSION

These results suggest that small BG-PVS in PD patients may impact the motor and non-motor aspects of daily living such as fatigue and speech whereas large BG-PVS may impact the motor symptoms and complications from PD such as gait and dyskinesias.

The precise etiology of small BG-PVS, specifically in PD, may not be in line with current theories that have been proposed of hypertensive arteriopathy. Some insight can be drawn from the correlation between small BG-PVS and pWMH. This finding suggests that global cerebral small vessel disease severity, indicated by pWMH, and smaller dilated PVS in the striatum may share similar etiology. In contrast, large BG-PVS may be more clinically relevant to PD neurodegenerative processes occurring in the striatum, which is congruent with the current study's association with large BG-PVS and motor symptoms/complications, and the lack of correlation with other small vessel disease markers.

CONCLUSION

The main finding of this study was that there is a differential association between large and small BG-PVS in PD patients. Specifically, a higher burden of small BG-PVS negatively impacts motor and non-motor aspects of experiences in daily living, whereas large BG-PVS are more likely to impact the motor symptoms and complications from PD. These findings were independent of the basic demographic variables and vascular risk factors that are commonly associated with PVS and other imaging markers of cerebral small vessel disease.

References

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