

Sex differences in vascular burden and neurodegeneration: insights from patients with PSP-Richardson Syndrome

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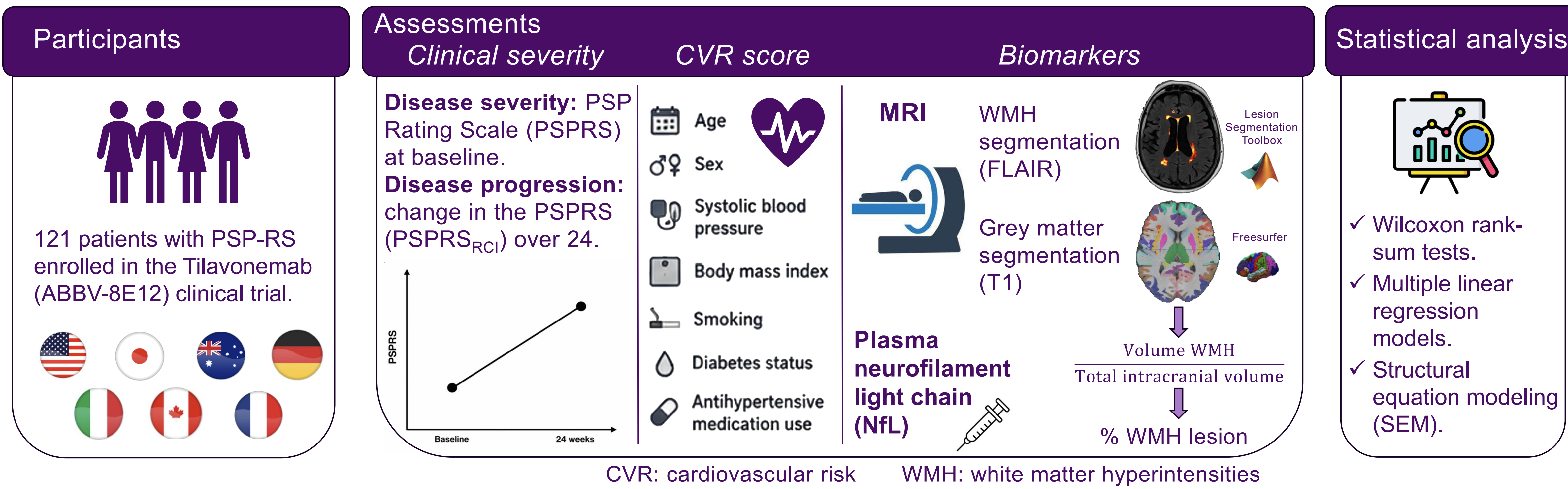
Key finding: *In Progressive Supranuclear Palsy-Richardson Syndrome, disease progression follows sex-specific biological pathways.*

INTRODUCTION

Background: Sex differences in vascular burden and neurodegeneration in the clinical progression of Progressive Supranuclear Palsy – Richardson Syndrome (PSP-RS) remain poorly understood¹. White matter damage may also contribute to disease progression².

Objective: To investigate sex differences in cardiovascular risk, white matter hyperintensities (WMH) and neurodegeneration and their associations with clinical progression in patients with PSP-RS.

METHODS



RESULTS

Table 1. Demographics, clinical characteristics and biomarkers for female and male patients.

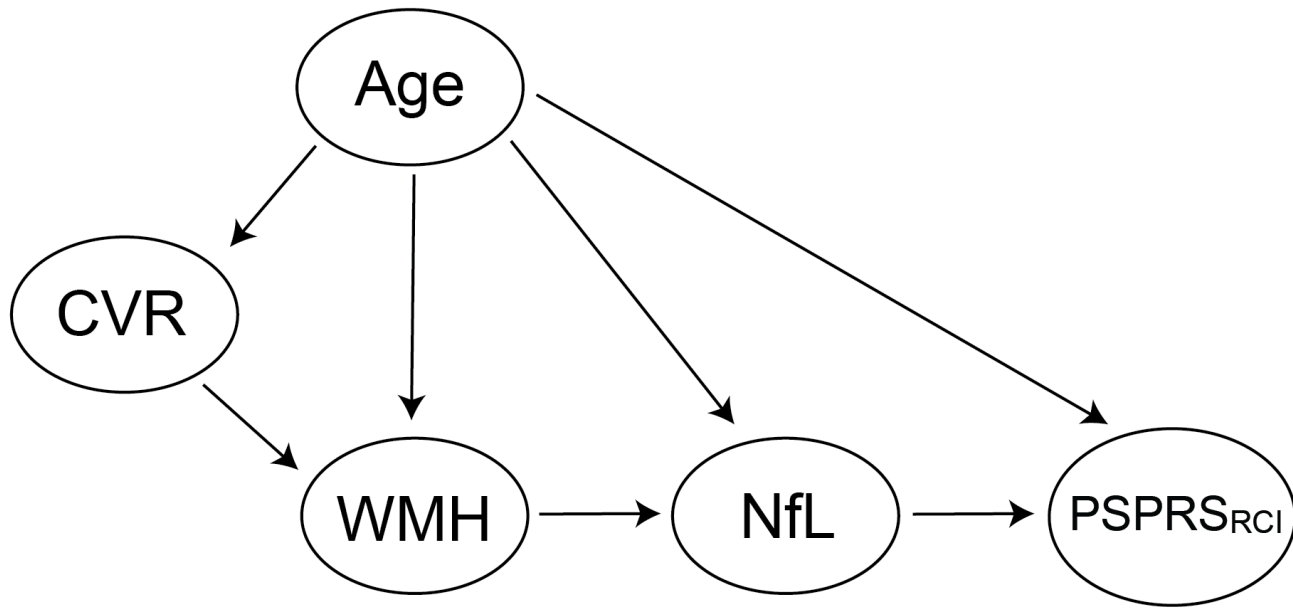
Variable	Females (n = 49)	Males (n = 72)	p-value
Age (years)	67.2 ± 6.3	69.7 ± 7.2	0.05 ^a
Disease duration (years)	2.9 ± 1.9	3.2 ± 1.8	0.14 ^a
PSPRS _{Baseline}	35.5 ± 10.6	31.5 ± 10.7	0.03 ^{b,c}
PSPRS _{Week 24}	39.0 ± 12.6	34.8 ± 13.5	0.13 ^{b,c}
PSPRS _{RCI}	0.5 ± 1.6	0.5 ± 1.4	0.73 ^{b,c}
CVR score	16.7 ± 4.5	18.1 ± 3.7	0.05 ^a
WMH burden (% lesion)	0.4 ± 0.5	0.6 ± 0.6	0.37 ^{b,d}
Plasma NfL (log, pg/mL)	3.3 ± 0.5	3.1 ± 0.5	0.21 ^{b,c}

Values are expressed as mean ± standard deviation. ^aWilcoxon rank-sum tests. ^bMultiple linear regression models with robust (sandwich) standard errors. ^cModels were adjusted for age and disease duration. ^dModels were adjusted for age, disease duration, and scanner type.

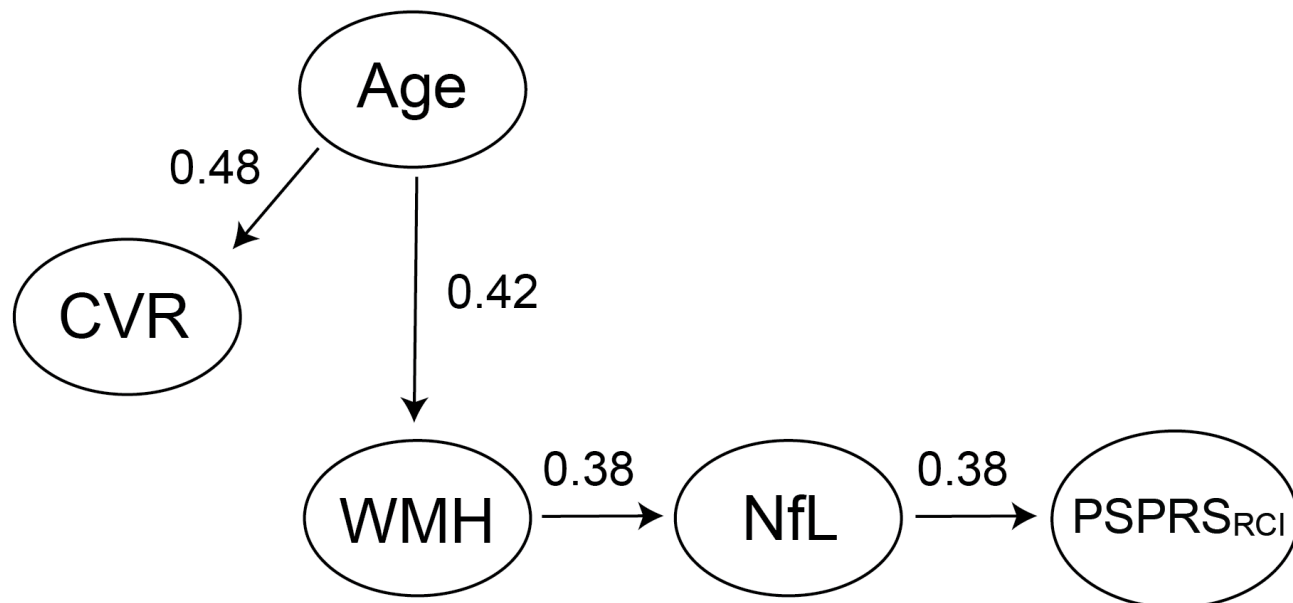
References: (1) Tepedino MF, et al. The contribution of white matter changes to clinical phenotype in progressive supranuclear palsy. J Neurol. 2024 Oct;271(10):6866-6875. (2) Piattella MC, et al. Neuroimaging evidence of gray and white matter damage and clinical correlates in progressive supranuclear palsy. J Neurol. 2015 Aug;262(8):1850-8.

*Based on research using data from AbbVie that has been made available through Vivli, Inc. Vivli has not contributed to or approved, and is not responsible for the contents of this publication.

A. Directed acyclic graph



B. Significant paths from the SEM in female patients



C. Significant paths from the SEM in male patients

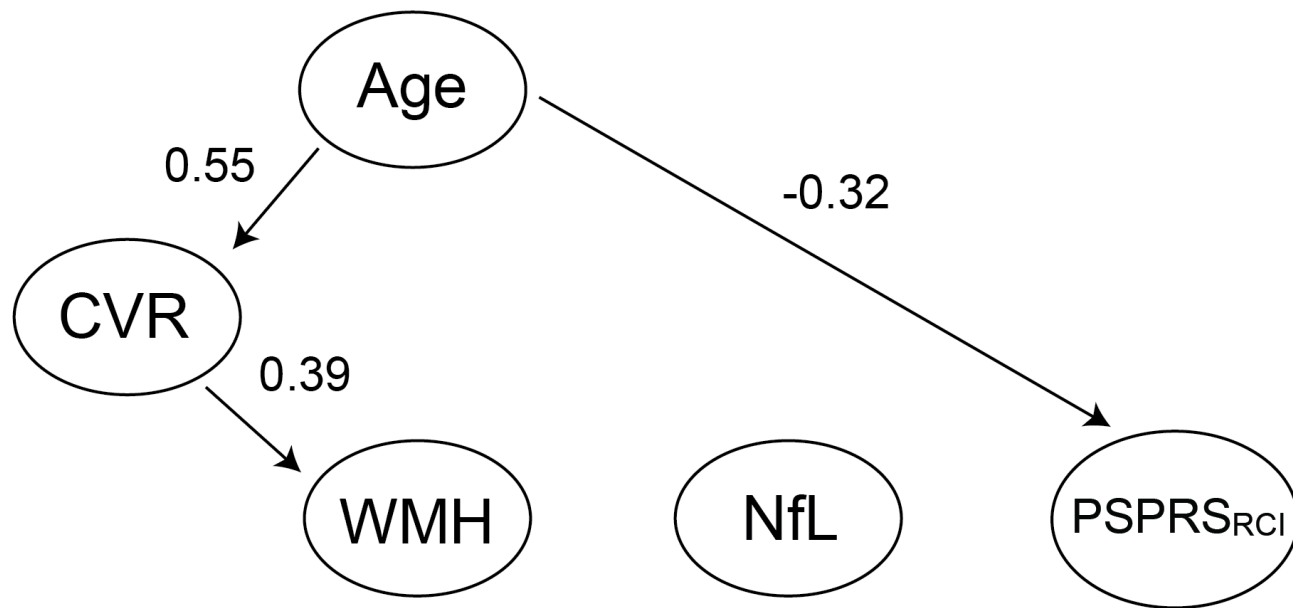


Figure 1. Structural equation modeling (SEM) framework and sex-specific significant pathways. (A) Hypothesized directed acyclic graph (DAG) representing the proposed relationships between variables. The SEM showed excellent model fit in both males and females. Significant pathways ($p < 0.05$) identified in female (B) and male (C) patients. Values on the arrows represent standardized path coefficients (β).

CONCLUSIONS

- Similar clinical progression between males and females, but different biological mechanisms underneath.
- Females: older age was associated with higher CVR and greater WMH burden. WMH relates to neurodegeneration (NfL), which in turn is associated with disease progression, suggesting a potential CVR-WMH–NfL–progression pathway.
- Males: older age was associated with higher CVR. WMH is linked to CVR, but not to neurodegeneration or progression. Disease progression appears primarily driven by age rather than vascular or NfL-related mechanisms.
- Sex differences should be considered in mechanistic models of PSP-RS and in the development of therapeutic strategies.

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