

Integrative GRN-Inspired Analysis Uncovers Multi-domain Links In Behavioral And Psychological Symptoms Of Dementia

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- BPSD (Behavioral And Psychological Symptoms Of Dementia) symptoms cluster into a highly interconnected network rather than independent clinical domains.
- Metabolic markers occupy strategic positions between systemic physiology and neuropsychiatric manifestations.
- Targeting biological bridge nodes may offer new opportunities for precision management of BPSD.

INTRODUCTION

Behavioral and psychological symptoms of dementia (BPSD) are among the most challenging manifestations of dementia and are associated with reduced quality of life, increased caregiver burden, and higher healthcare utilization. Although individual symptoms and biomarkers have been extensively studied, BPSD likely arise from complex interactions among neuropsychiatric, metabolic, and immune processes.

Traditional analytic approaches often examine these factors separately and may fail to capture their broader organizational structure. We therefore applied a gene regulatory network (GRN)-inspired framework to integrate clinical, cognitive, and biological variables into a multidimensional network, with the goal of identifying central hubs and biological bridge factors associated with BPSD severity.

METHODS

Study Design

- Cross-sectional analysis of patients with dementia.
- Comprehensive clinical phenotyping was performed.

Clinical & Biological Variables

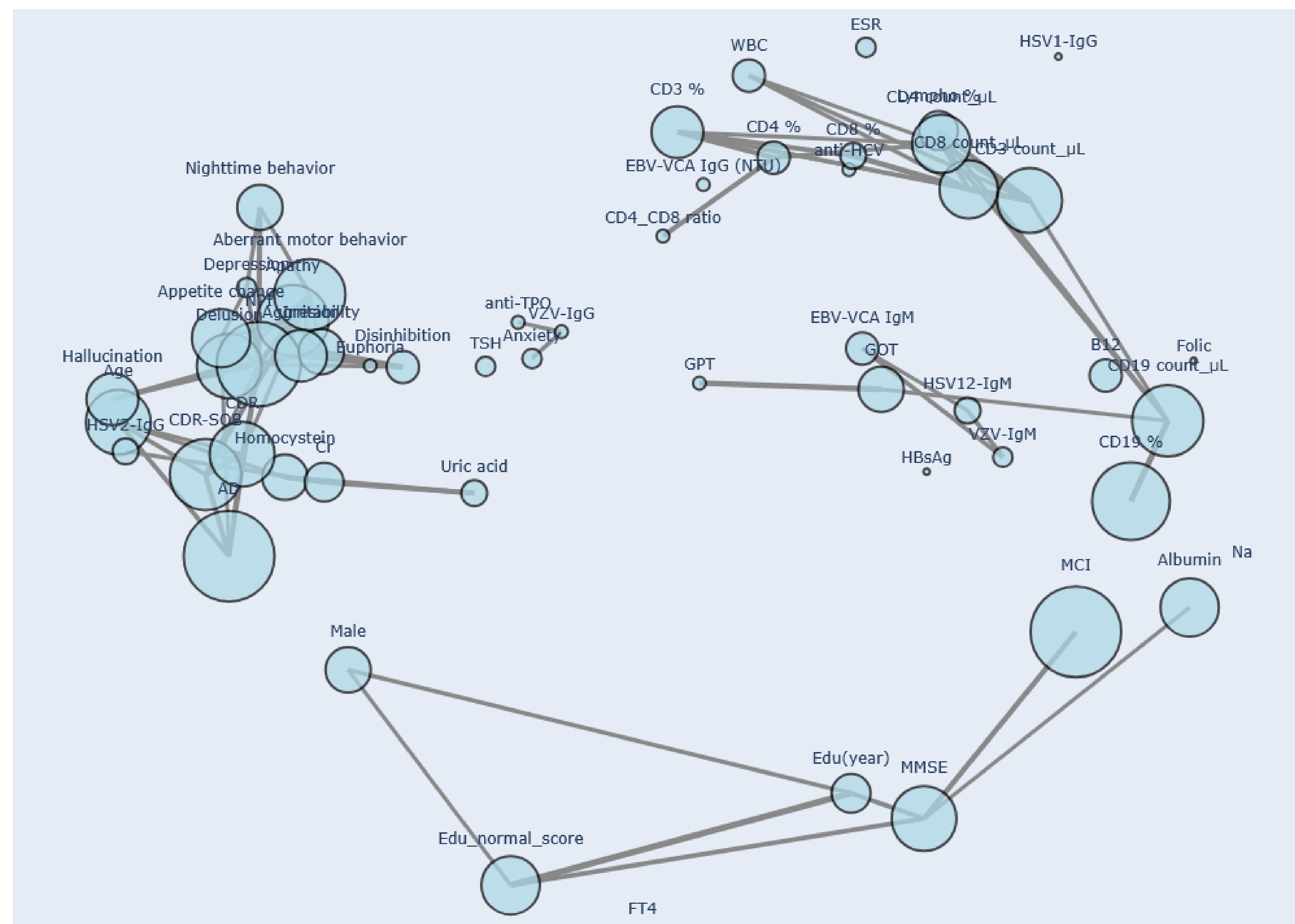
- Neuropsychiatric symptoms assessed using 12 NPI domains.
- Cognitive severity evaluated by MMSE, CDR, and CDR-SOB.

- Peripheral biomarkers: lymphocyte subsets, T cell function, and metabolic parameters

Network Analysis

- Partial correlations were calculated to estimate relationships while controlling for confounders.
- Variables were represented as nodes and associations as edges.
- A force-directed network layout was used to identify clusters, hubs, and bridge factors.

RESULTS



1. PTSD symptoms form a compact neuropsychiatric cluster

Agitation, delusion, hallucination, depression, anxiety, and related NPI domains are densely grouped, suggesting that BPSD domains are networked rather than isolated features.

2. Peripheral biological markers organize into distinct network neighborhoods

Immune markers such as CD3/CD4/CD8/CD19 cluster separately from the cognitive–nutritional axis involving MMSE, education, MCI, and albumin.

3. Homocysteine and uric acid sit near the interface of symptom and biological domains

Their positions suggest potential bridge roles between systemic metabolic status and the neuropsychiatric symptom network, without implying causality.

DISCUSSION / CONCLUSIONS

- The network architecture suggests that BPSD should be viewed within a broader biological context rather than solely as behavioral manifestations.
- Homocysteine and uric acid emerged as candidate bridge factors connecting neuropsychiatric symptoms with systemic physiology.
- While causality cannot be inferred, their network positions highlight potential pathways through which biological health and behavioral burden may intersect.
- Network-based approaches may provide a useful framework for precision-oriented dementia research.

REFERENCES

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