

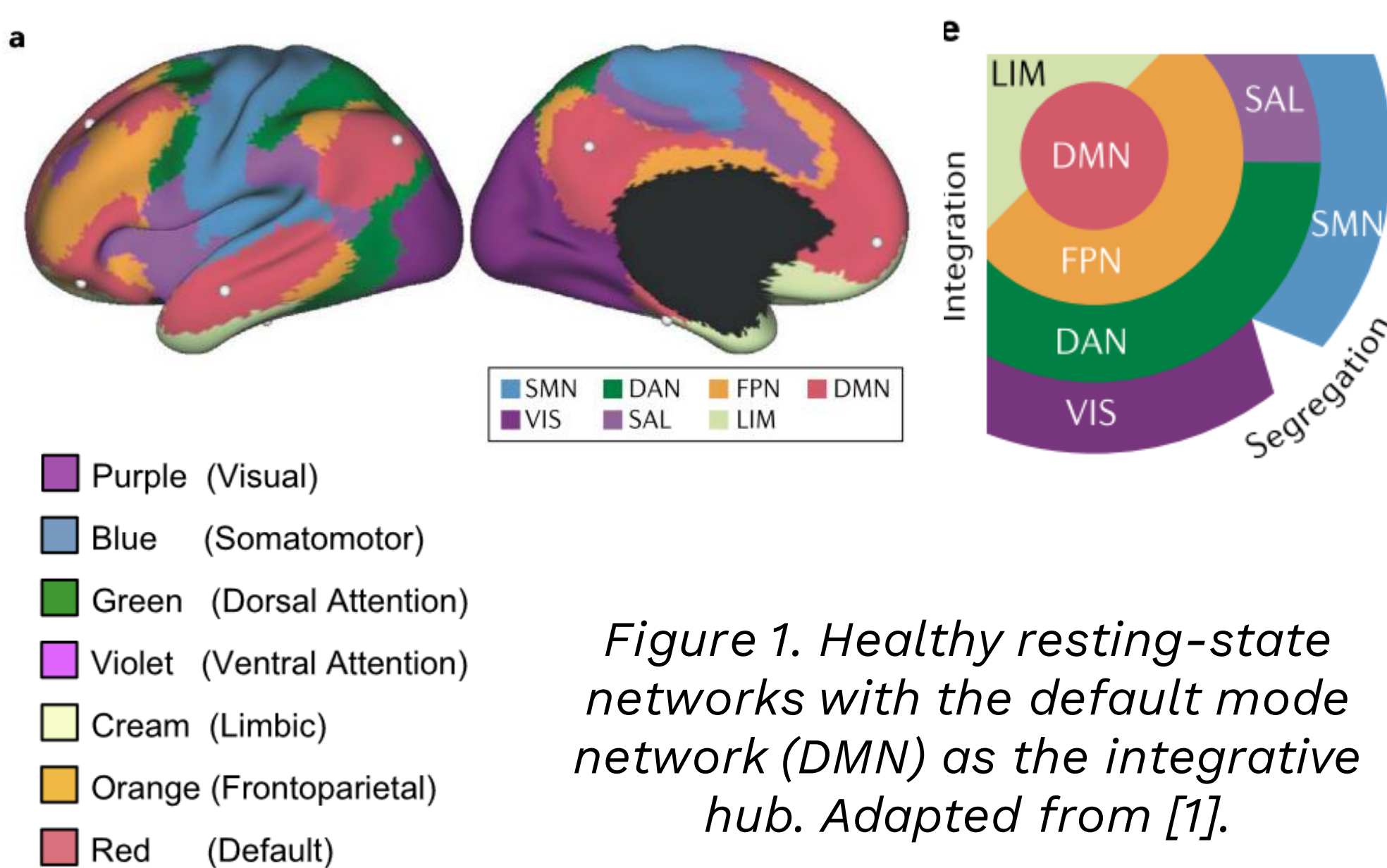
Metabolic Imaging Of The Default Mode Network In Neurodegenerative Disorders Provides A Novel Network-based Framework

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INTRODUCTION

Neurodegenerative disorders are characterized by the appearance of abnormal brain networks, whose increased expression may interfere with normal default mode network (DMN) – the dominant resting-state functional topography in the brains of awake healthy subjects [1], Figure 1.

Here, we wanted to determine whether topographic similarity between disease-specific metabolic networks [2] and the DMN provides a network-based framework for classifying common neurodegenerative disorders.



METHODS

Subjects ($n = 1,207$):

- 239 Parkinson disease (PD), 58 Parkinson disease dementia (PDD), 13 REM sleep behaviour disorder (RBD)
- 213 dementia due to Alzheimer disease (AD), 79 MCI due to Alzheimer disease (MCI-AD)
- 161 dementia with Lewy bodies (DLB), 28 MCI due to Lewy bodies (MCI-LB)
- 124 multiple system atrophy (MSA)
- 114 progressive supranuclear palsy (PSP)
- 109 behavioural variant frontotemporal dementia (bvFTD)
- 69 corticobasal syndrome (CBS)
- 499 normal controls (NC)

Image analysis:

Expressions of validated disease-related metabolic patterns and the normal DMN [3] were computed with the TPR algorithm and similarity assessed with the Dice-Sørensen coefficient (DSC) and voxel-wise correlations.

RESULTS

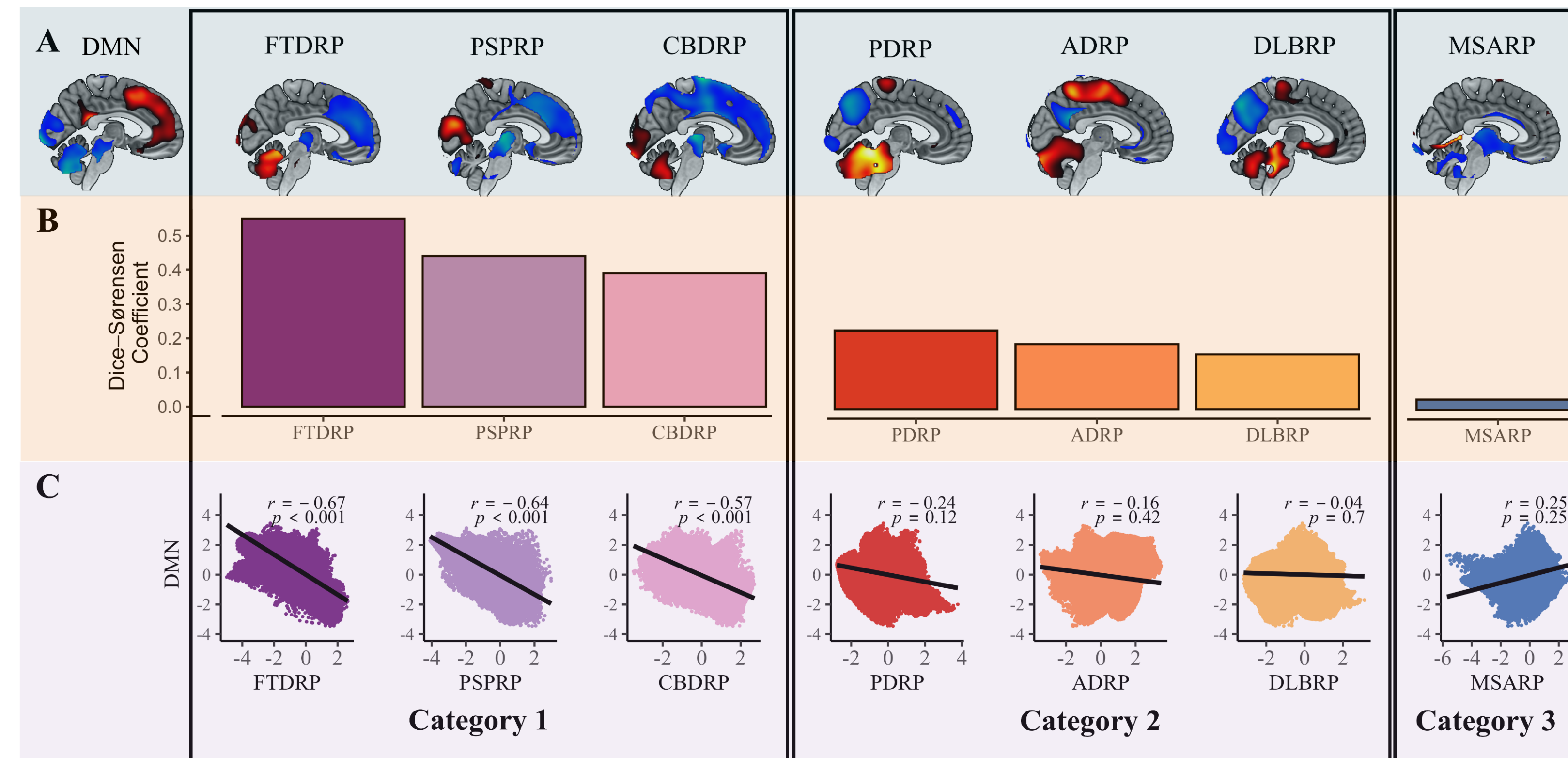


Figure 2. Topographical relationships of disease-related metabolic networks and the normal default mode network (DMN). (A) Visualization of DMN (left) and individual disease networks displayed by category. (B) Dice-Sørensen similarity coefficients. (C) Voxel-wise correlation plots.

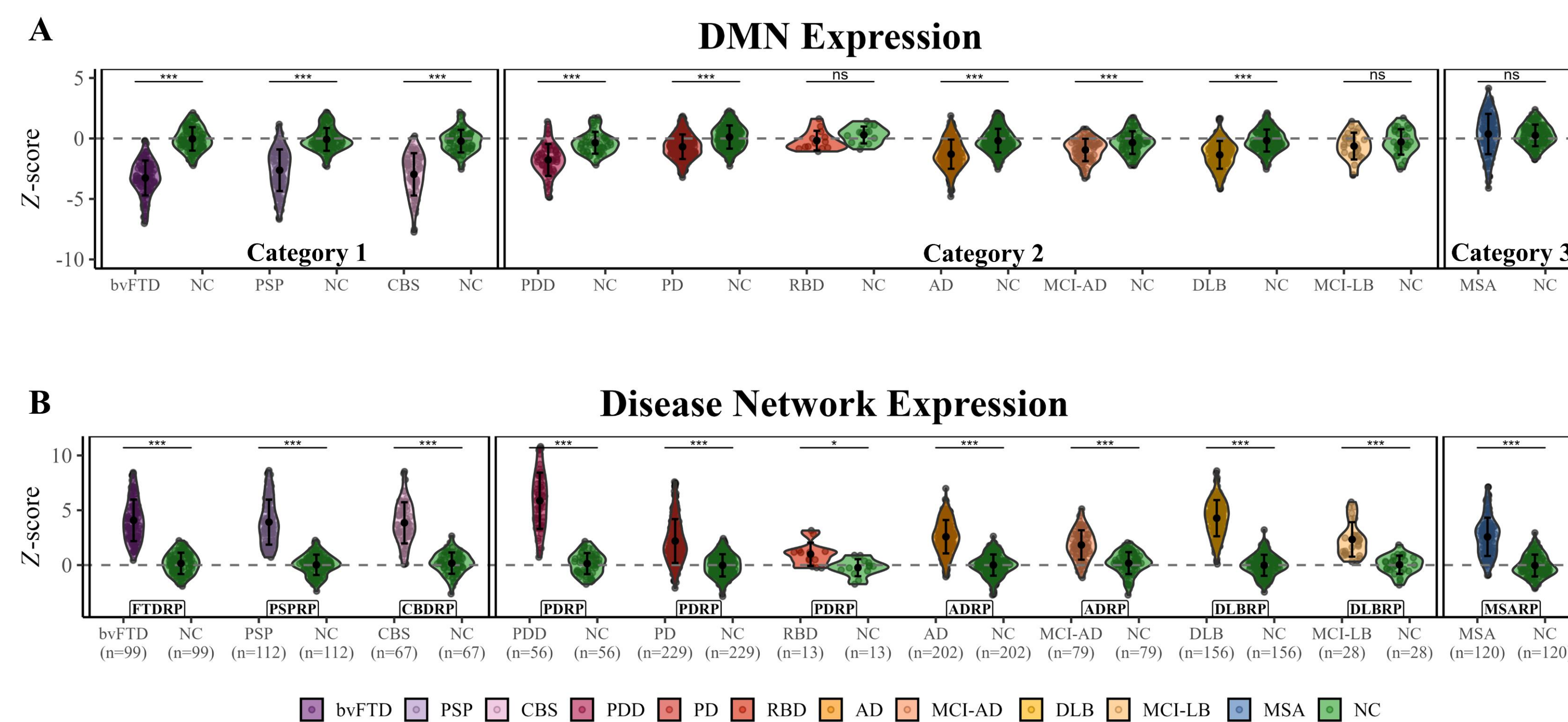


Figure 3. Expression levels for the default mode network (DMN) and for the disease-related metabolic networks in patients and matched healthy subjects. *** $p < 0.0001$, * $p < 0.05$, ns – non-significant.

- Category 1 (bvFTD, PSP, and CBS): disease networks overlap with DMN (Figure 2B), giving rise to highly significant inverse correlations between the respective topographies (Figure 2C) and between the corresponding subject scores (Figure 3, 4).
- Category 2 (PD, DLB, and AD): disease networks have limited topographic overlap with DMN (Figure 2B) and reductions in DMN subject scores are small compared to contemporaneous increases in pathological network expression in the same patients (Figure 3, 4). Accordingly, correlations between the pathological and healthy networks were weak and failed to reach significance (Figure 2C).
- Category 3 (MSA): pathological networks can develop without consistent DMN involvement.

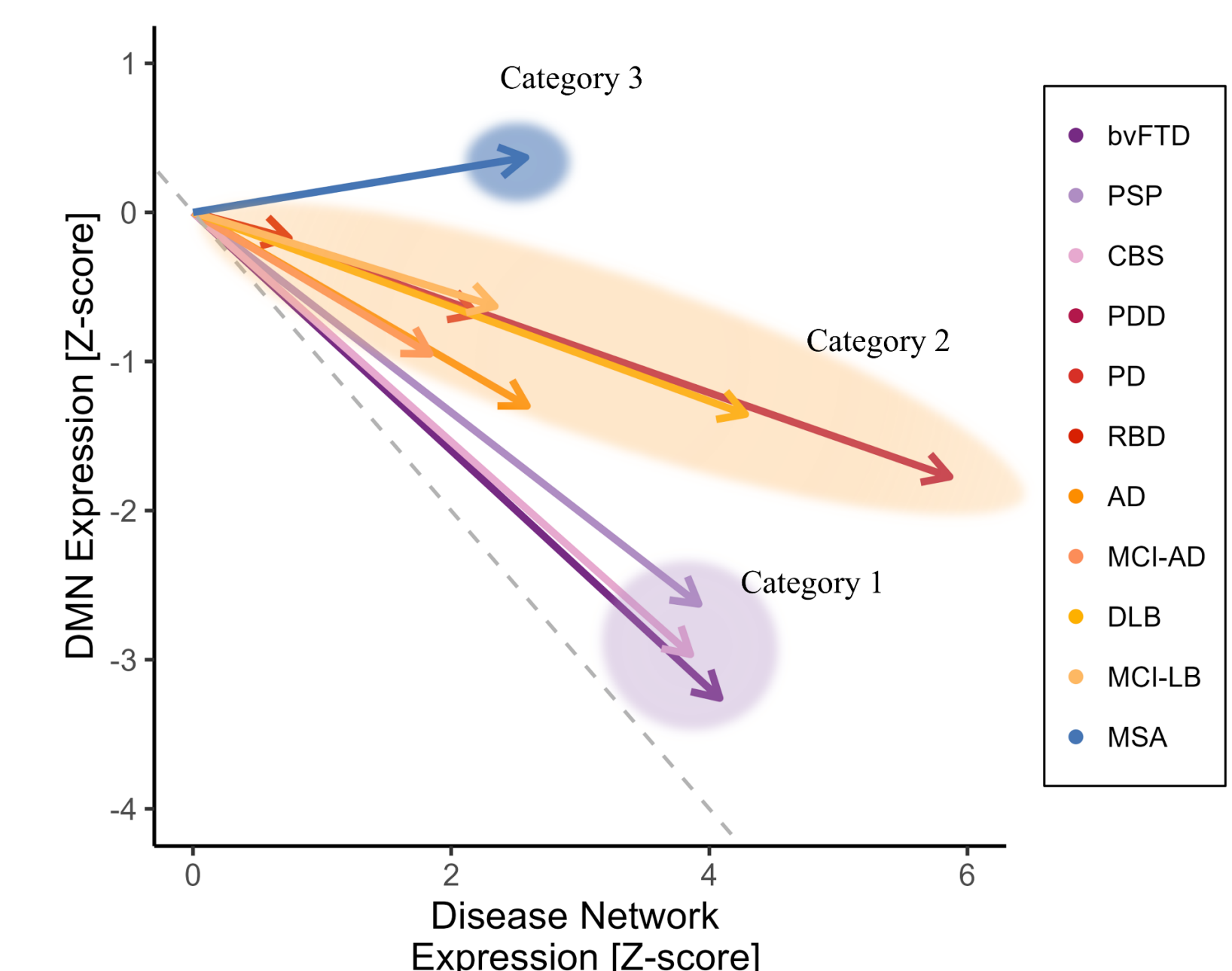


Figure 4. Relationships between expression levels for disease-related networks and normal DMN in the patient groups. For each group, mean expression values for the normal DMN and the associated disease-specific pattern are represented by an arrowhead.

CONCLUSIONS

- Novel network-based stratification may improve diagnosis, staging, and trial design by linking disease-network progression to DMN integrity.

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