

Multivariate Analysis Using Co-Expression Network Modeling Identifies Specific Inflammation and Diffusion MRI Features in Major Depressive Disorder

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BACKGROUND

Major depressive disorder (MDD)

- MDD is the most prevalent psychiatric condition marked by persistent sadness and cognitive impairments.
- Only 50% of the MDD population respond to treatments derived from the monoamine hypothesis, implicating alternative pathophysiological underpinnings.
- Recent research indicates that neuroinflammatory processes play a significant role in its development. Crucially, there are notable sex differences in both the presentation and underlying neuroinflammatory mechanisms.

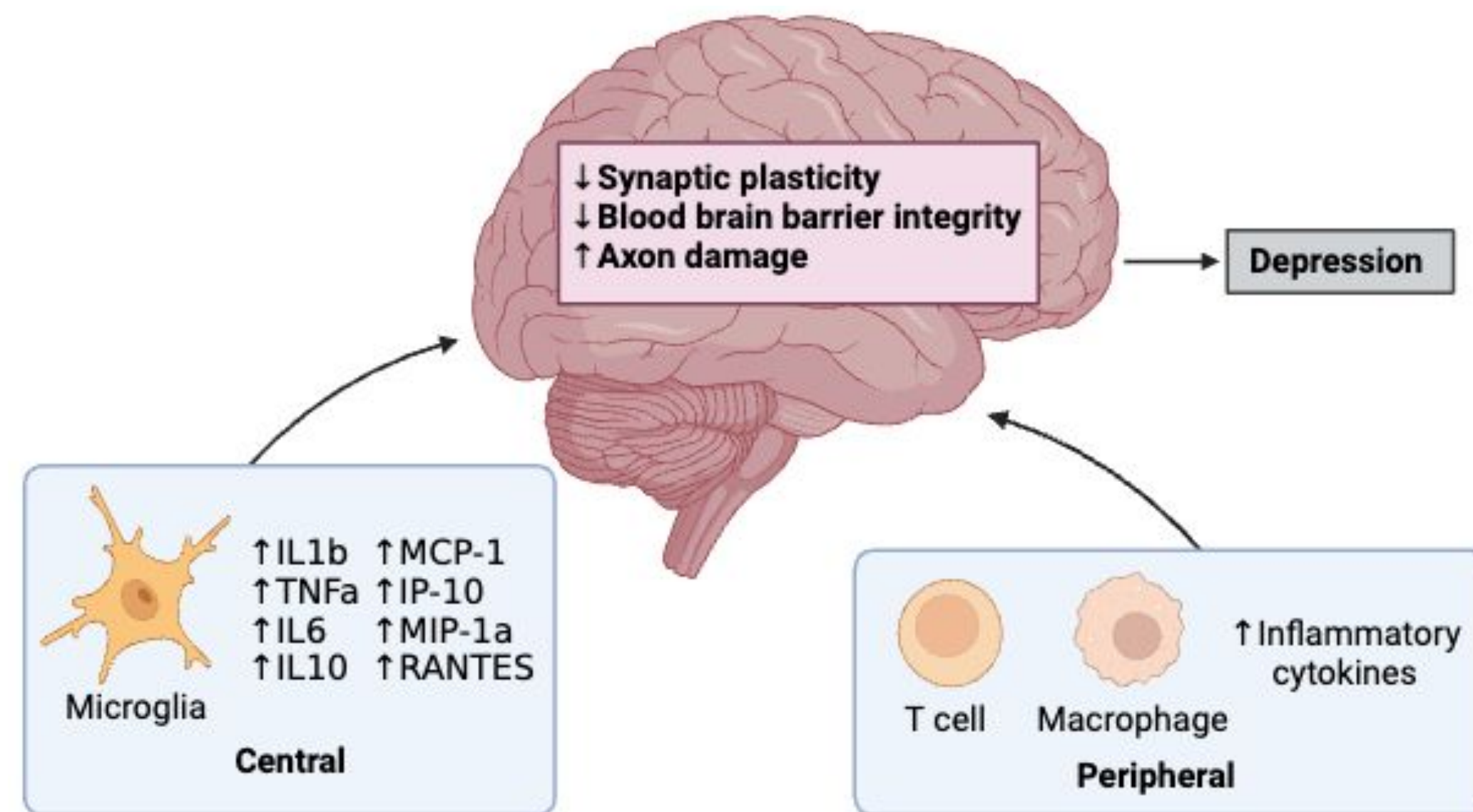


Figure 1. Mechanisms of Neuroinflammation [1]

Weighted Gene Co-expression Network Analysis (WGCNA)

- Bioinformatics tool used to identify modules or clusters of highly correlated genes across different biological conditions.
- Constructs a network where nodes represent genes and edges represent pairwise correlations between gene expression profiles.
- Unveils biological processes by associating modules with phenotypic traits, clinical outcomes, or experimental conditions.

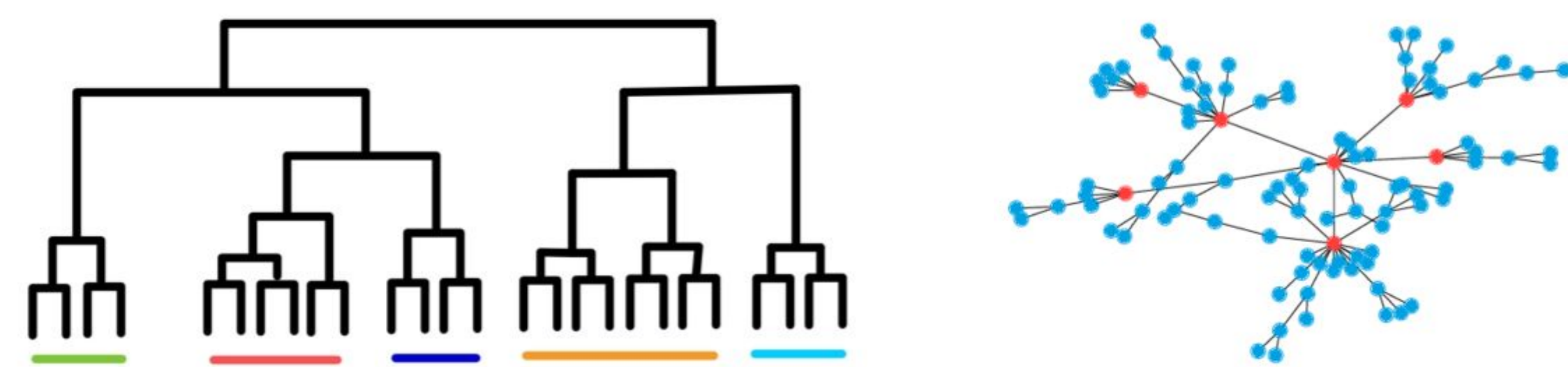


Figure 2. Hierarchical clustering for scale free networks [2-3]

OBJECTIVES

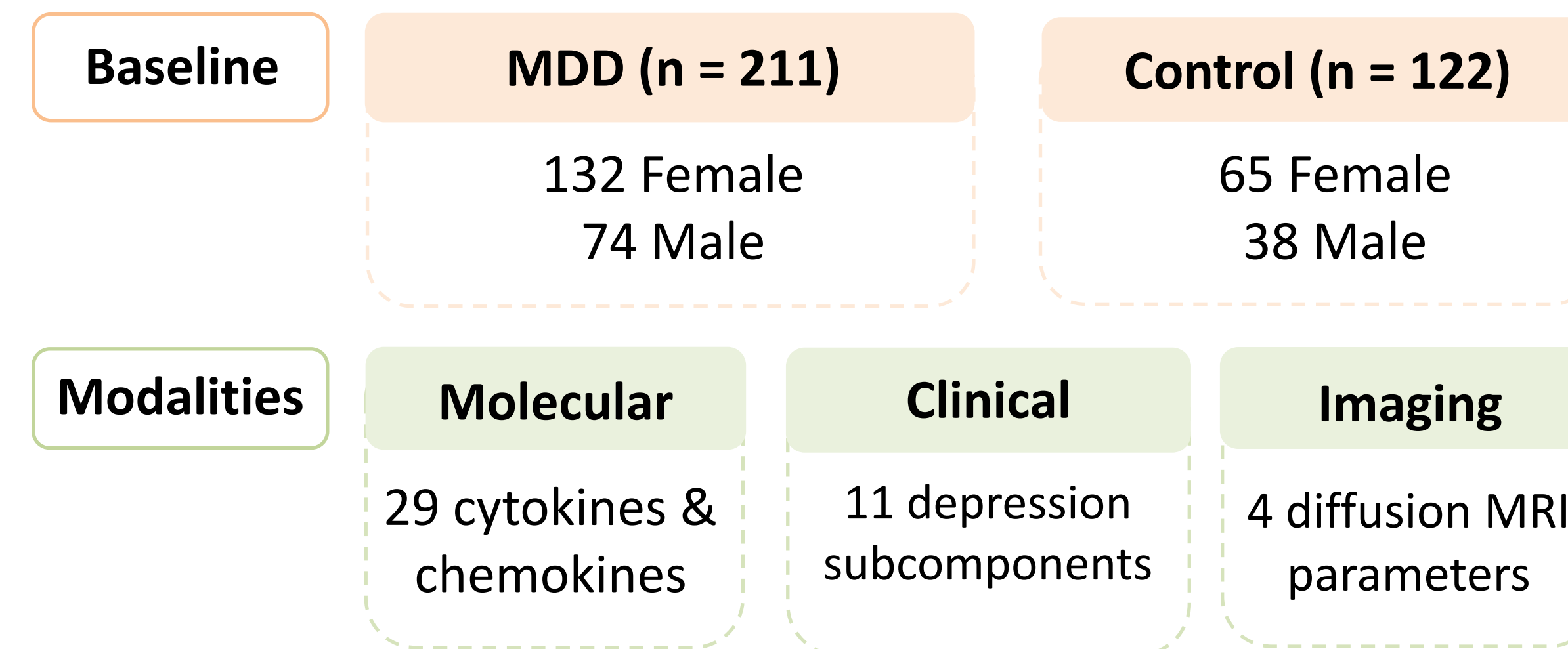
- Identify sex-dependent modules of co-expressed genes associated with inflammatory biomarkers in MDD patients and healthy controls, elucidating shared and distinct networks underlying inflammation in depression.
- Assess the correlation between inflammatory gene expression modules, clinical variables, and neuroimaging markers to elucidate the clinical relevance of immune dysregulation in MDD.

REFERENCES

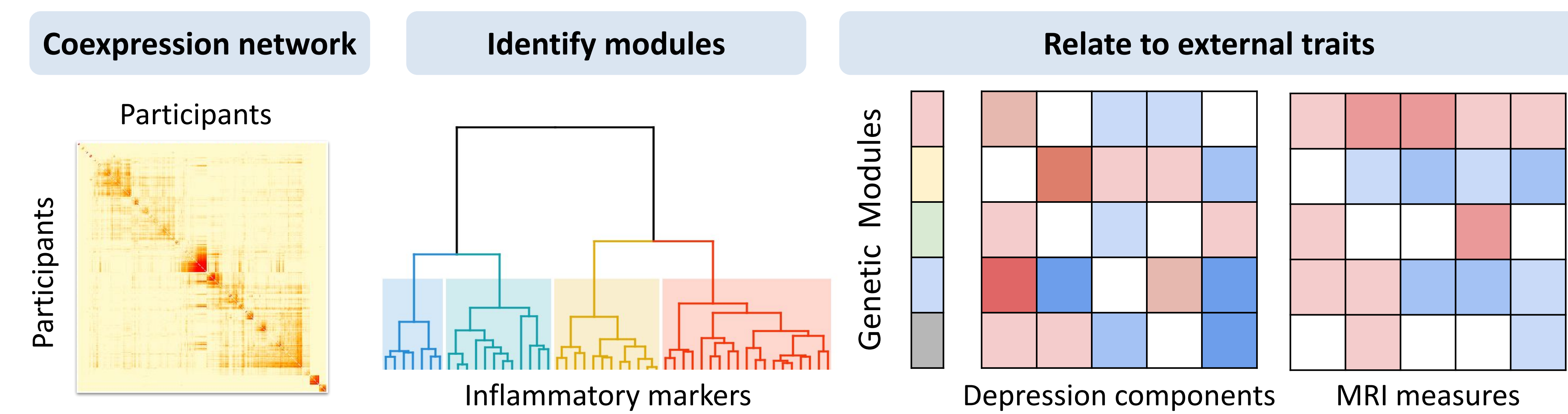
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PIPELINE

Canadian Biomarker Integration Network in Depression (CANBIND-1)



Weighted Gene Co-expression Network Analysis (WGCNA)



RESULTS

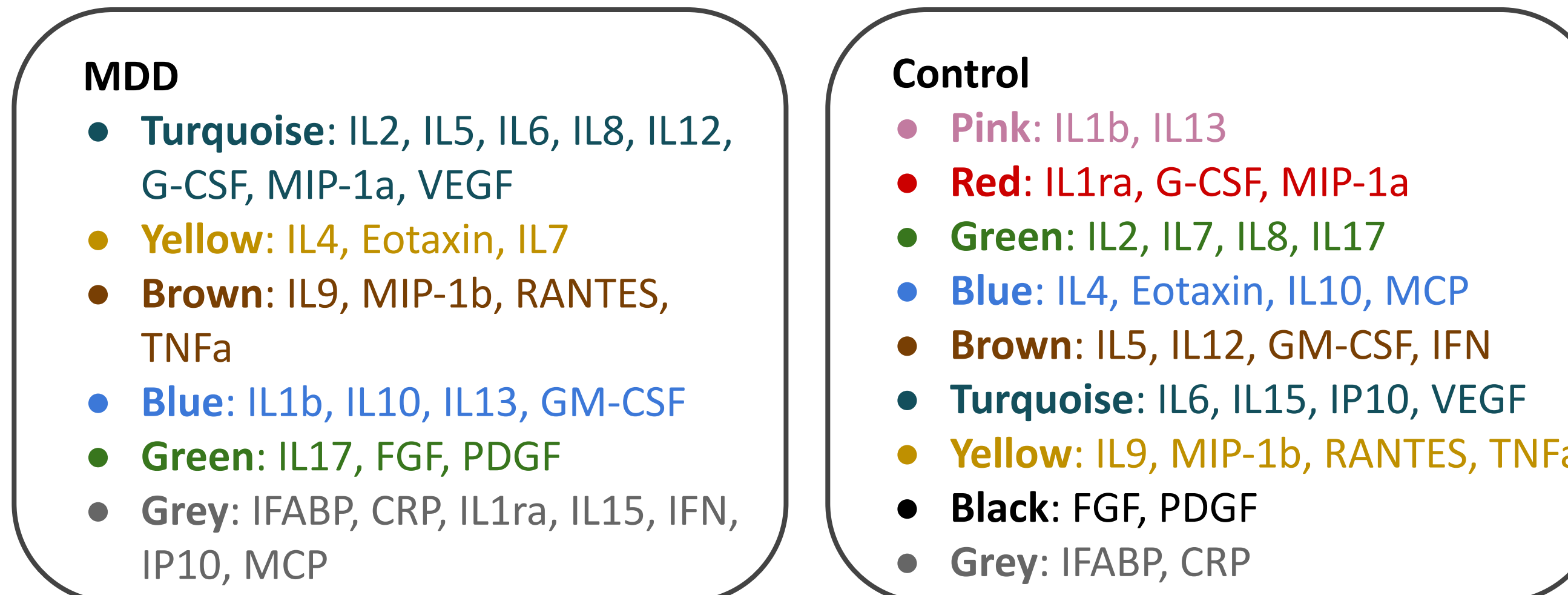


Figure 3. Inflammatory modules detected by WGCNA in MDD and control subjects.

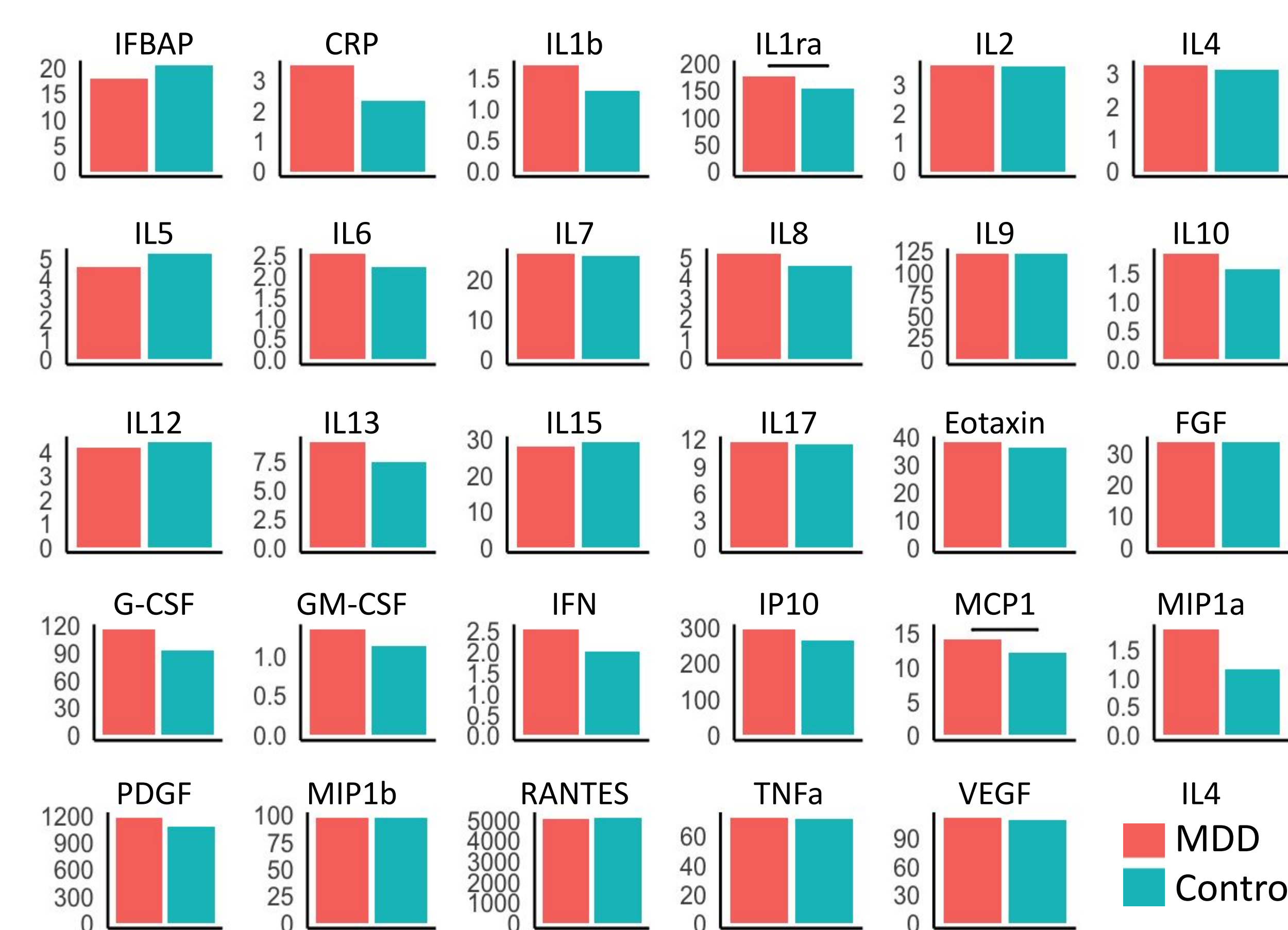
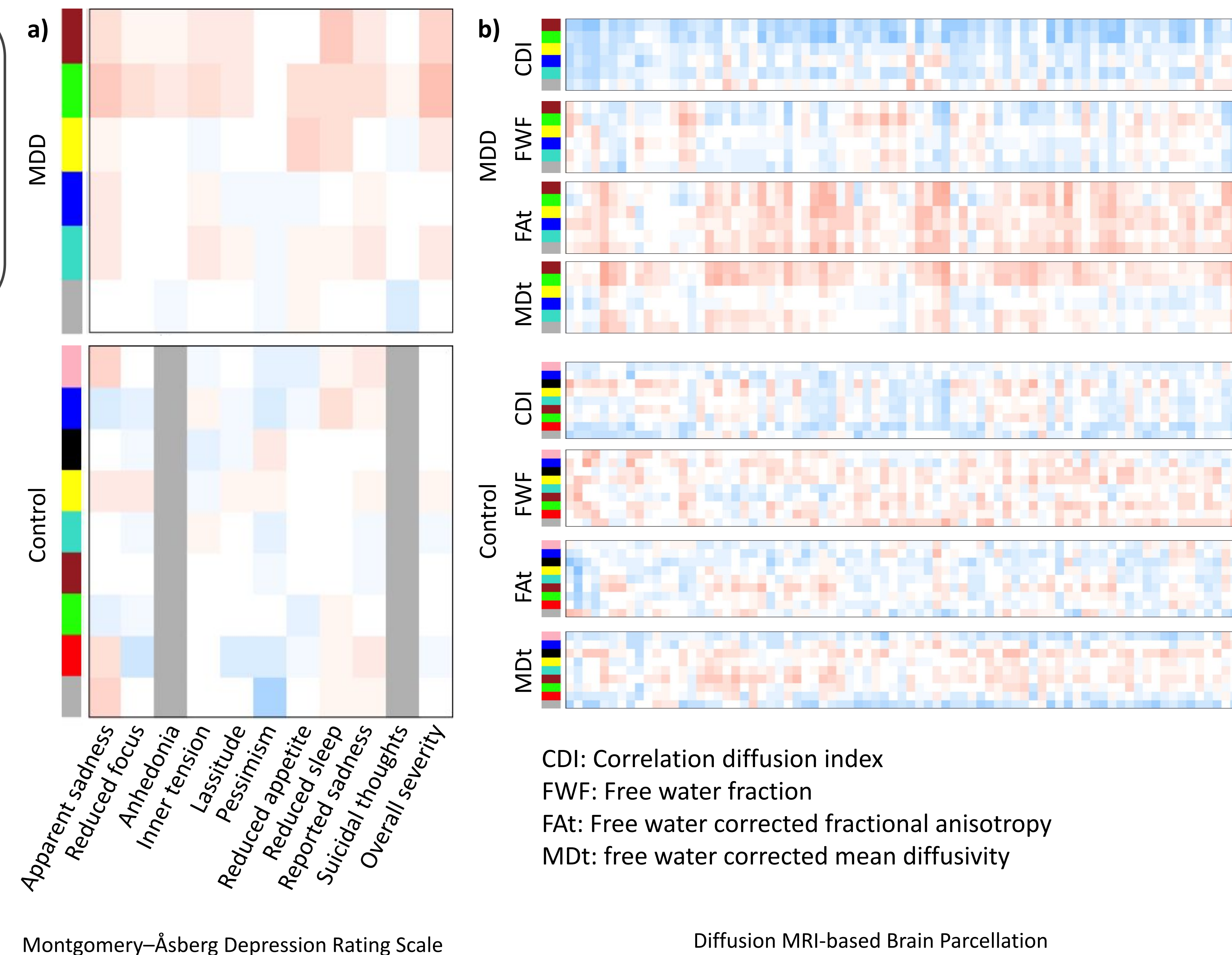


Figure 4. Average inflammatory marker levels (mg/L) in MDD and control subjects. Horizontal bar depicts $p < 0.05$.



Montgomery-Åsberg Depression Rating Scale

Diffusion MRI-based Brain Parcellation

Figure 5. Module-Trait correlations for depression (a) and MRI (b). Red: $r^2 > 0$. White: $r^2 = 0$. Blue: $r^2 < 0$. Grey: missing values.

DISCUSSION

- WGCNA-derived brown and green inflammatory modules revealed positive correlations with the traits of depression, fractional anisotropy, and mean diffusivity in MDD.
- The simultaneous reduction of fractional anisotropy with mean diffusivity in MDD suggests the presence of cytotoxic edema and neurodegeneration.
- Moreover, MDD inflammatory modules are negatively correlated with correlation diffusion index in white matter tracts, implying decreased white matter integrity.

ACKNOWLEDGEMENTS

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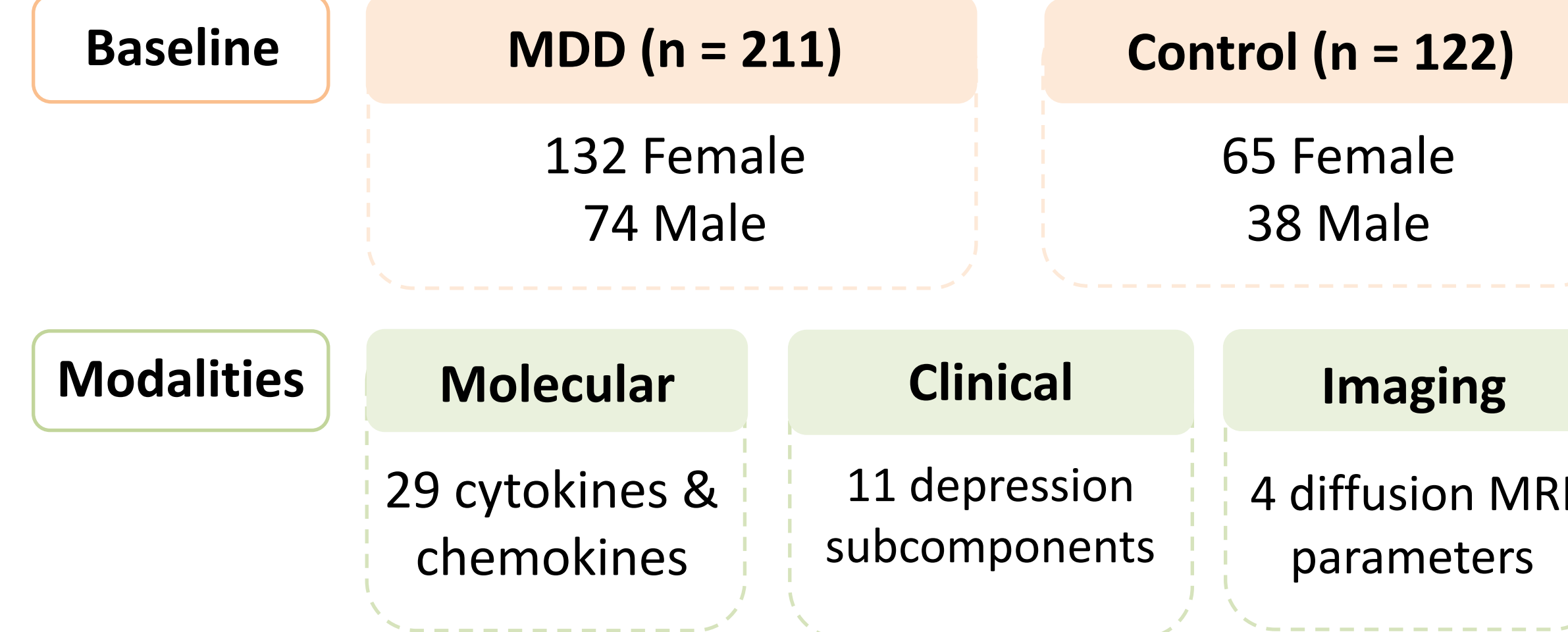
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- Identify sex-dependent modules of co-expressed genes associated with inflammatory biomarkers in MDD patients and healthy controls, elucidating shared and distinct networks underlying inflammation in depression.
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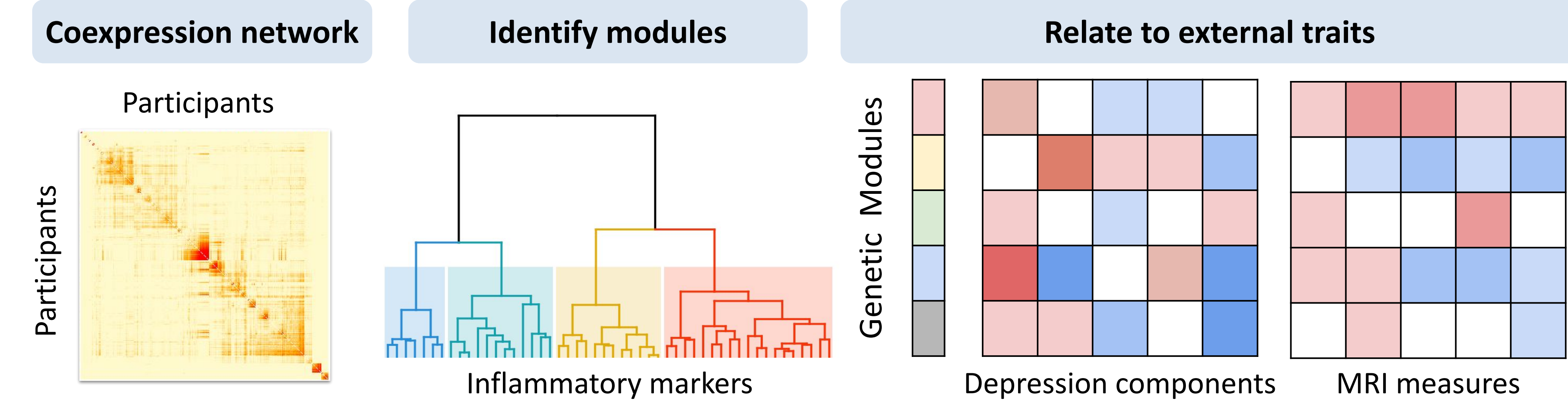


PIPELINE

Canadian Biomarker Integration Network in Depression (CANBIND-1)



Weighted Gene Co-expression Network Analysis (WGCNA)



RESULTS

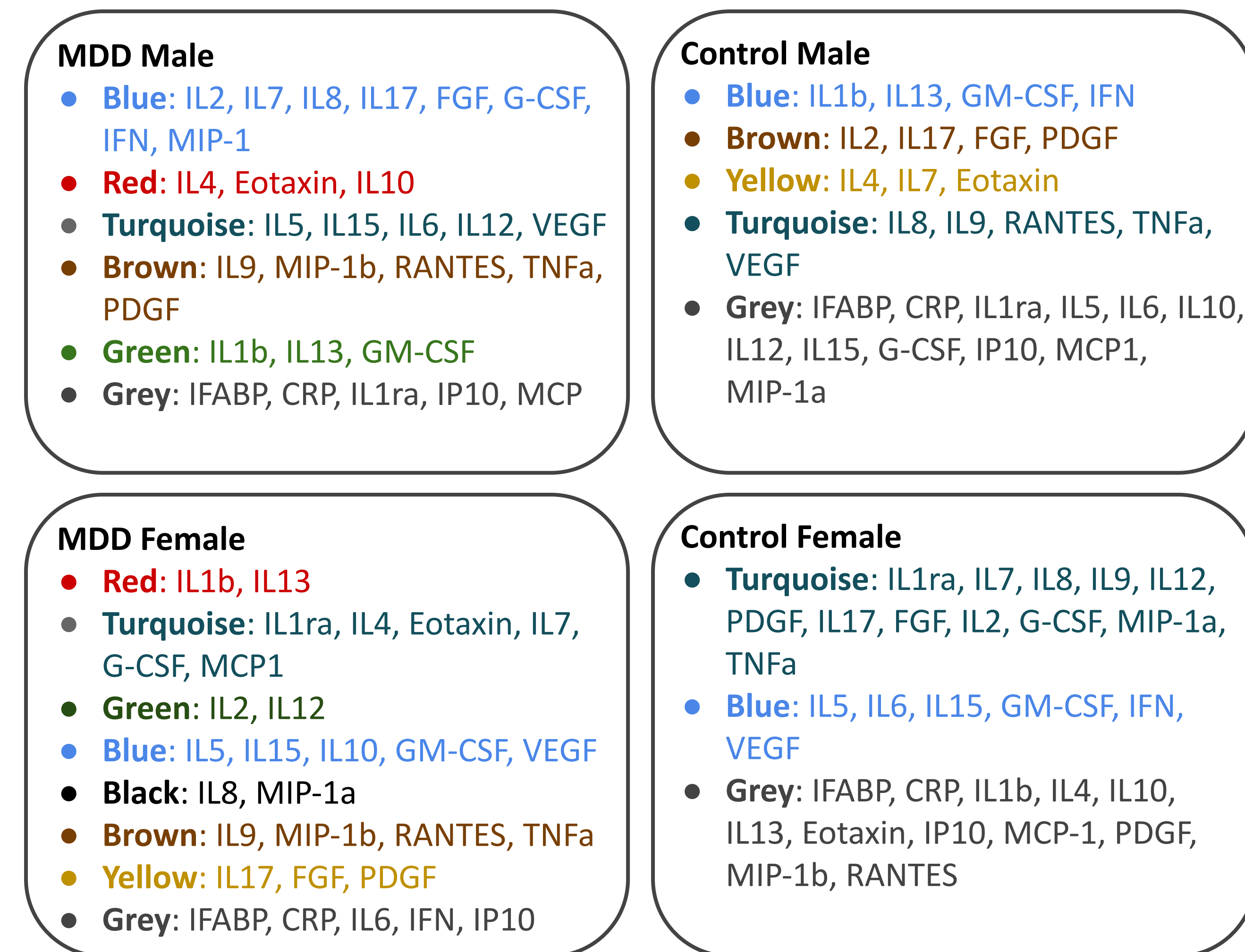


Figure 3. Inflammatory modules detected by WGCNA.



Figure 4. Average marker levels (mg/L) in MDD (left) and control (right).

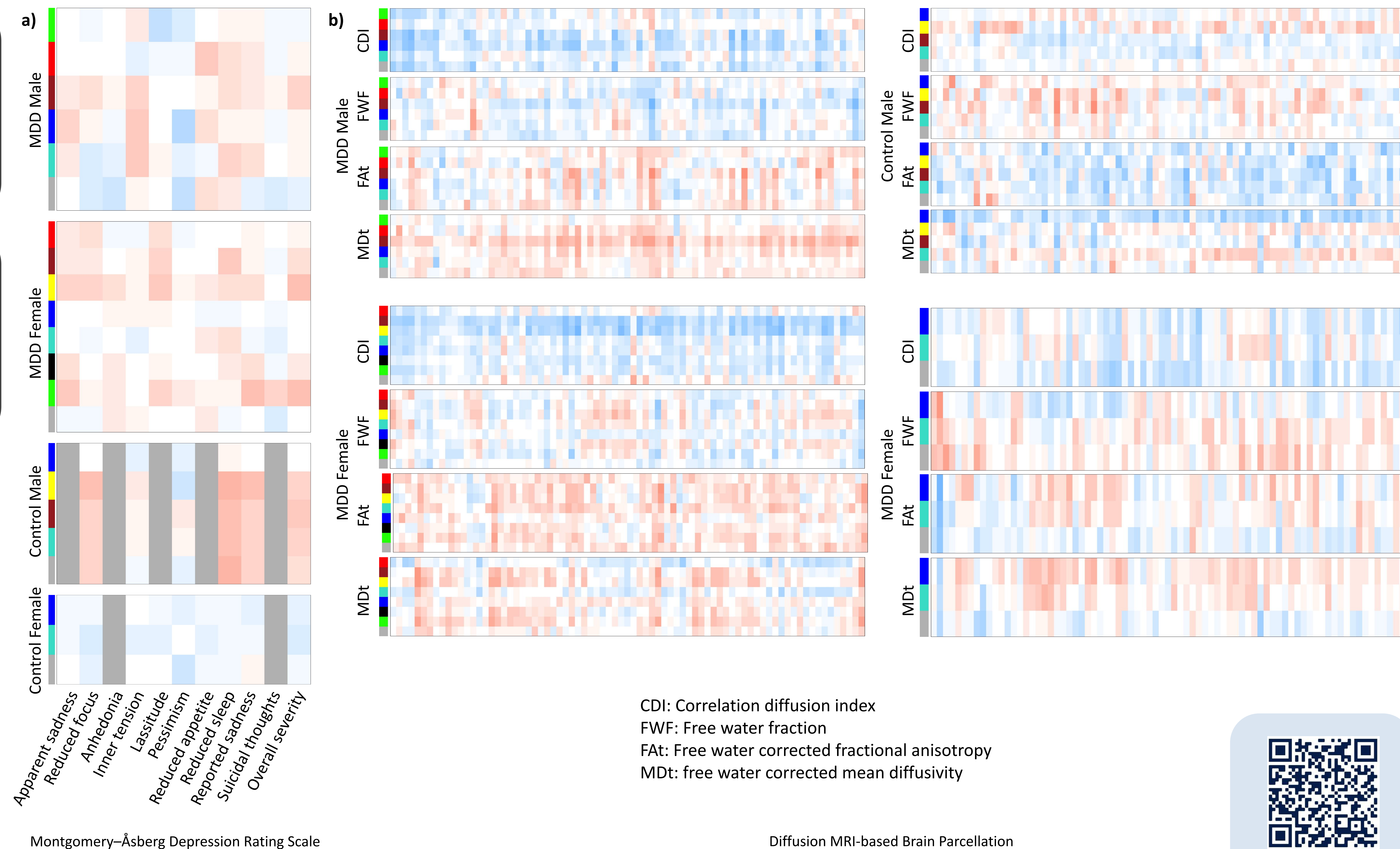


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