

# Multivariate Analysis Using Co-Expression Network Modeling Identifies Specific Inflammation and Neurological Disease-Related Genetic Modules 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.

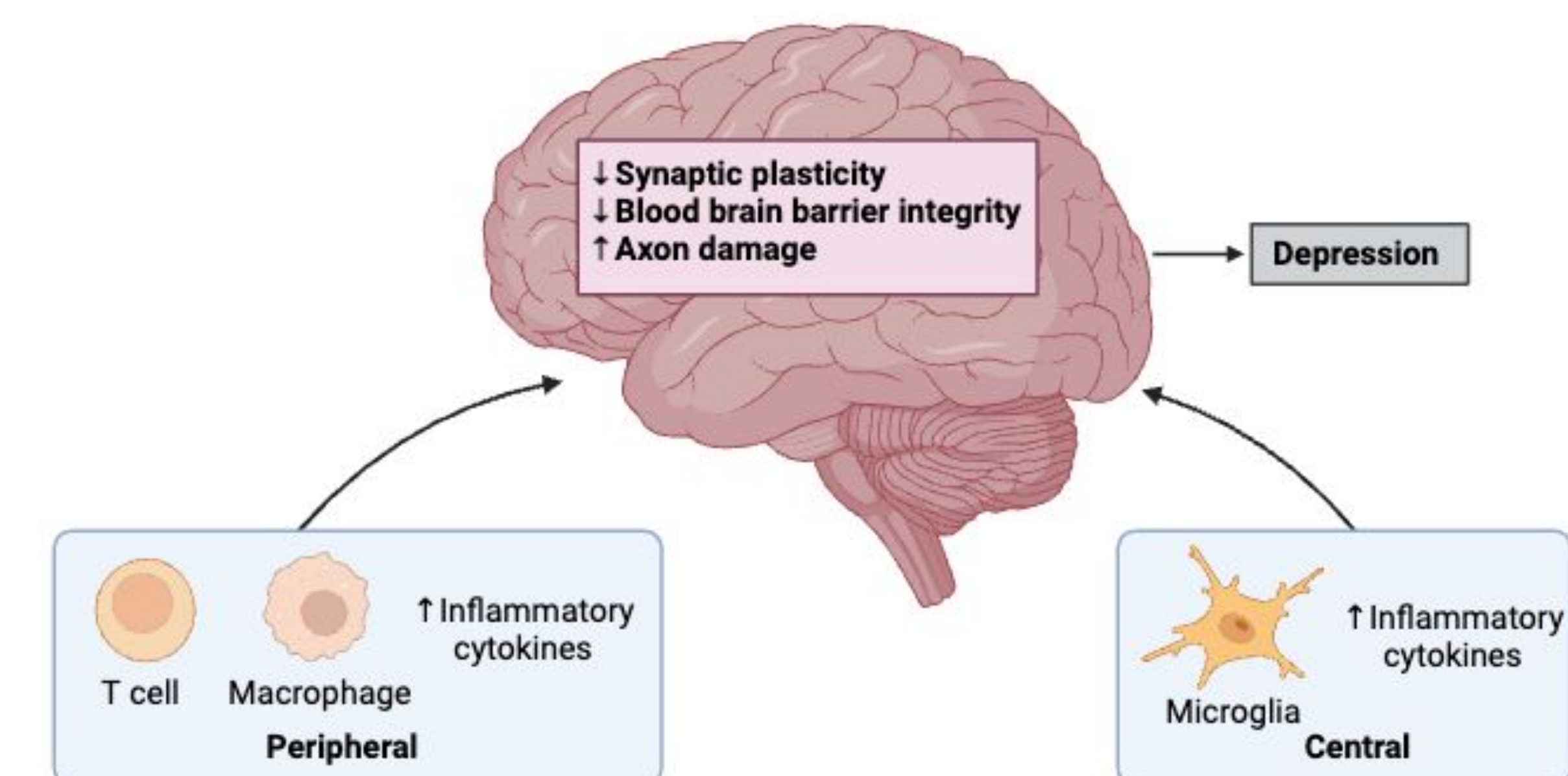


Figure 1. Mechanisms of Neuroinflammation [1]

### 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.

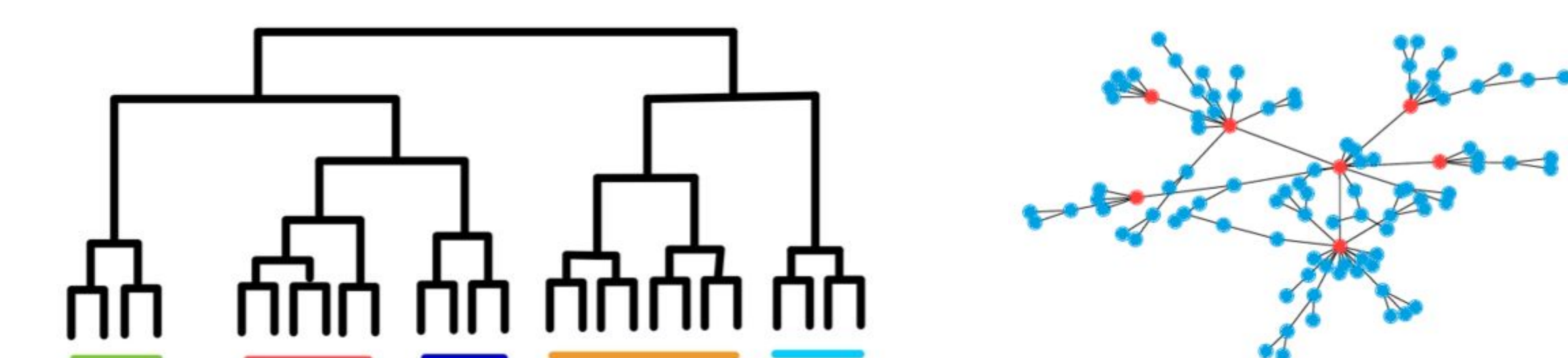


Figure 2. Hierarchical clustering for scale free networks [2-3]

## OBJECTIVES

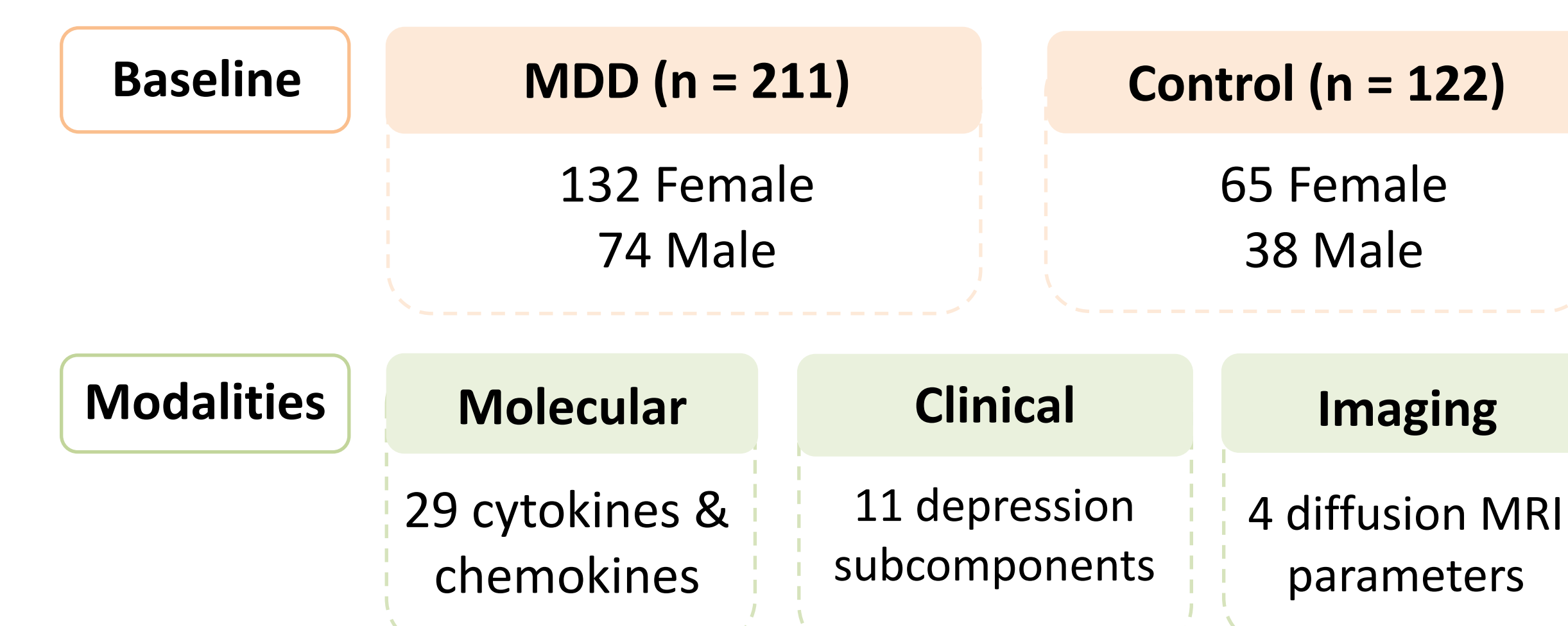
- Identify sex-dependent modules of co-expressed genes associated with inflammatory biomarkers in MDD patients and healthy controls, elucidating shared and distinct networks underlying inflammation in depression.
- Assess the correlation between inflammatory gene expression modules, clinical variables,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

## REFERENCES

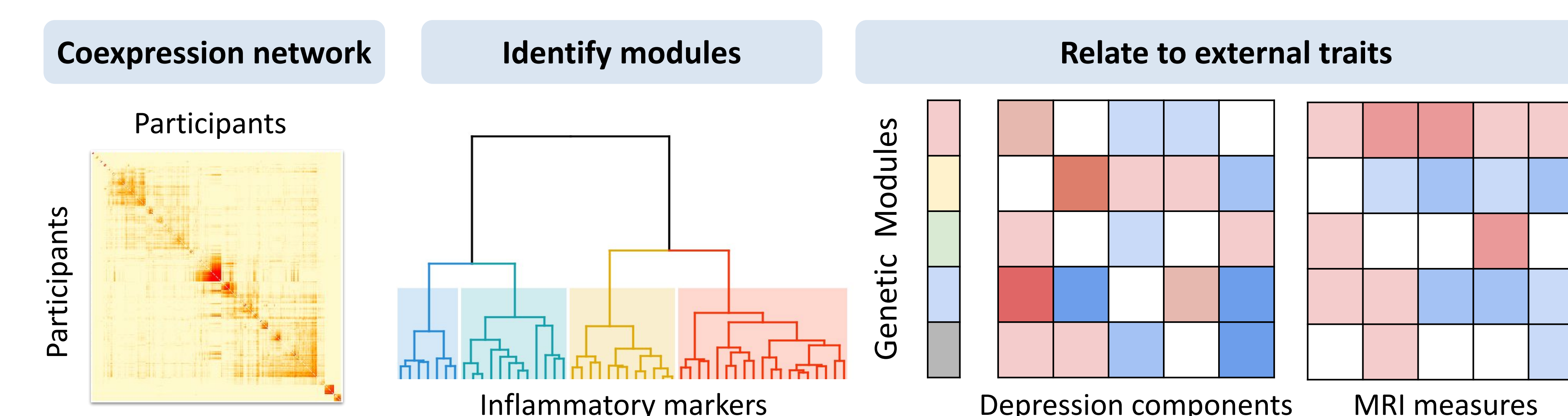
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- Kim, C. How to find the optimal number of clusters with R? Medium (2022). <https://medium.com/@chyun55555/how-to-find-the-optimal-number-of-clusters-with-r-dbf849883888>
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## PIPELINE

### Canadian Biomarker Integration Network in Depression (CANBIND-1)



### Weighted Gene Co-expression Network Analysis (WGCNA)



## RESULTS

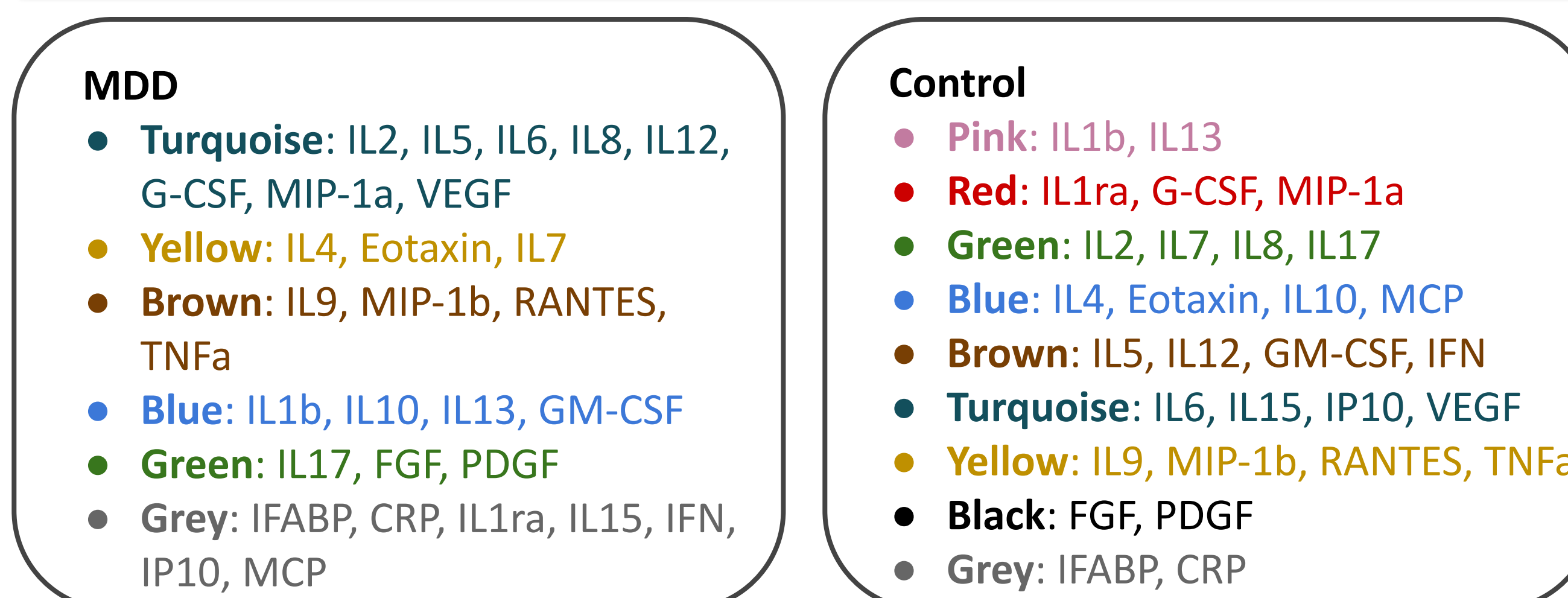


Figure 3. Inflammatory modules detected by WGCNA in MDD and control subjects.

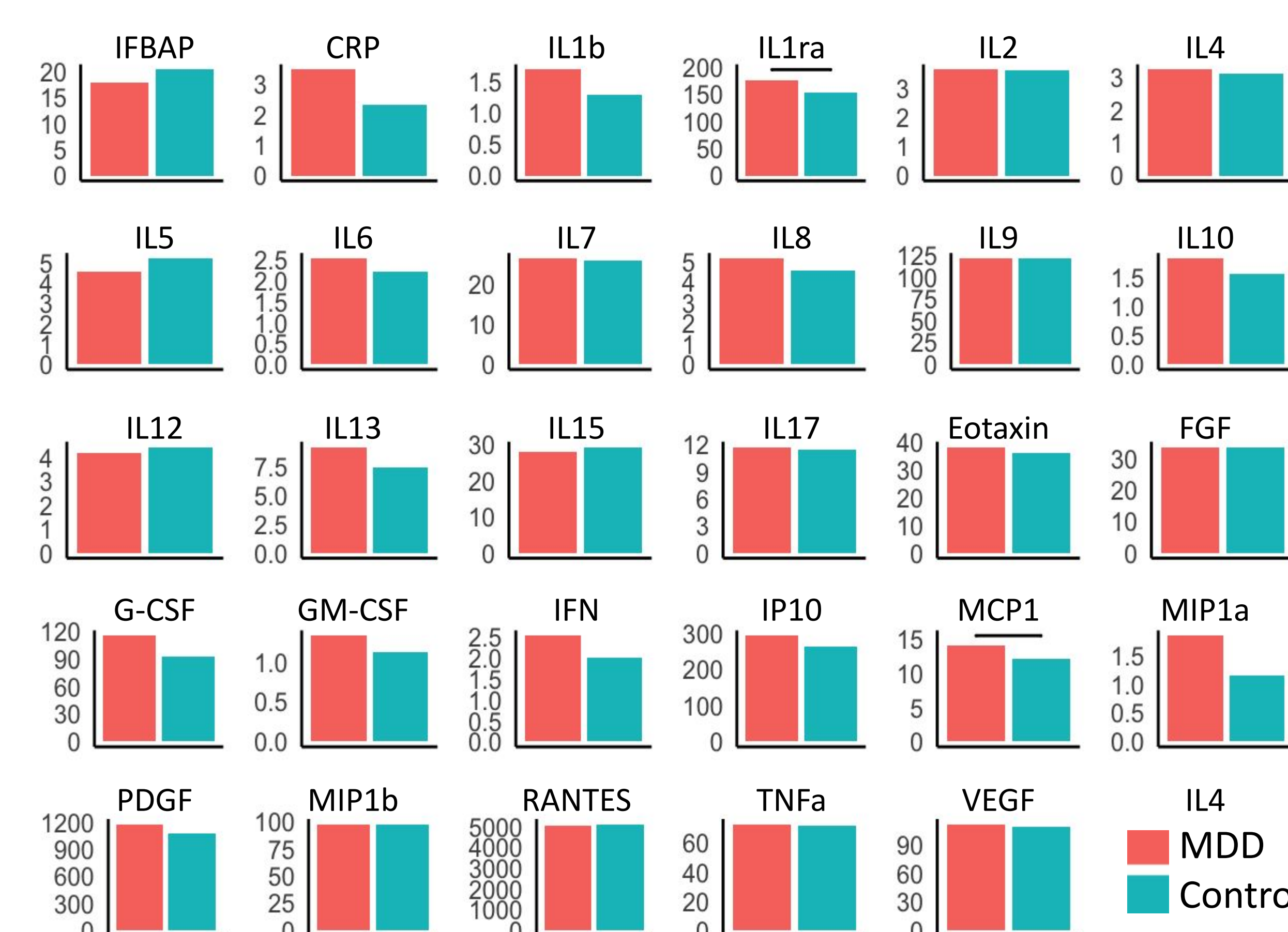
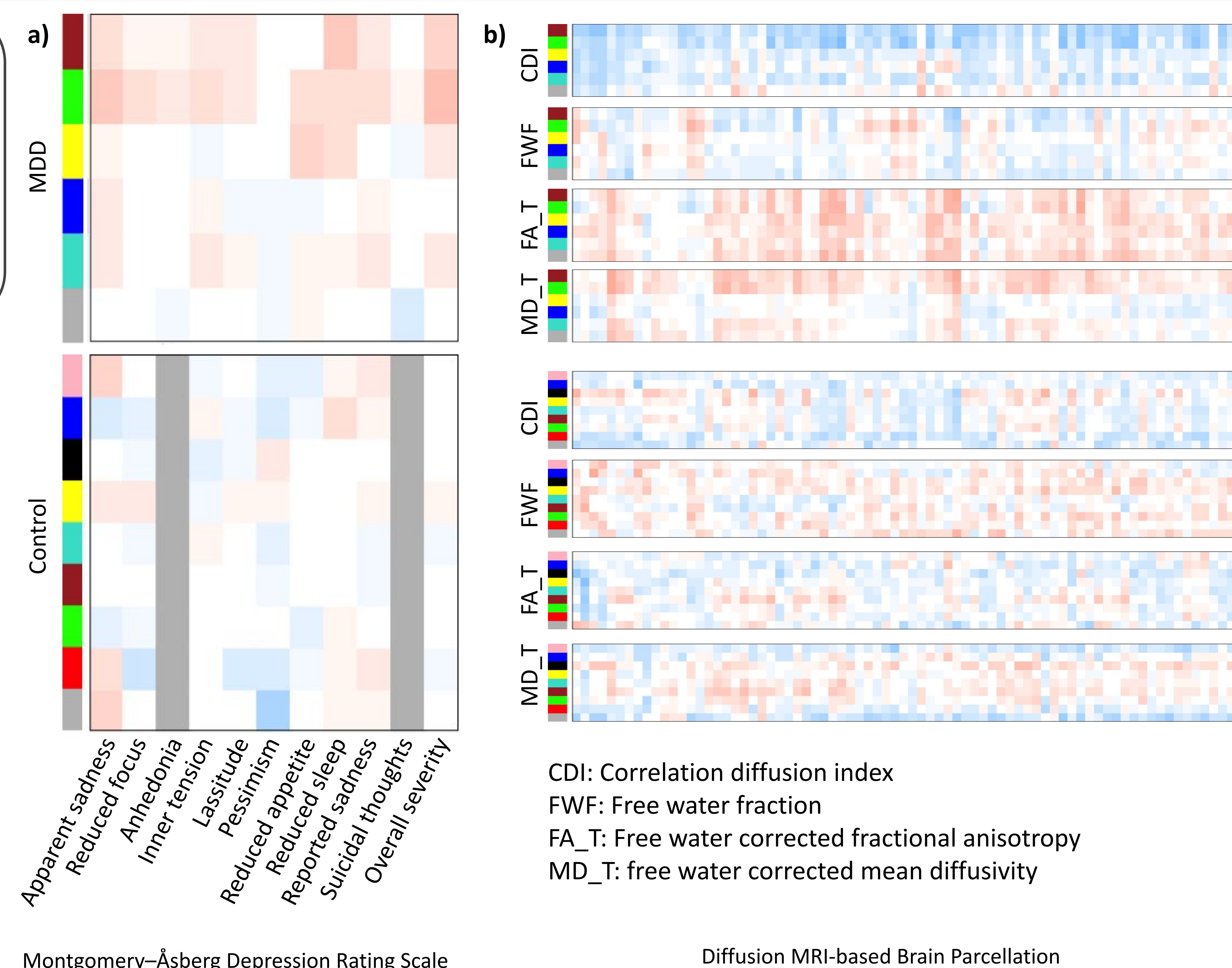


Figure 4. Average inflammatory marker levels (mg/L) in MDD and control subjects. Horizontal bar depicts  $p < 0.05$ .



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.
- A negative correlation of inflammatory modules in MDD with correlation diffusion index in white matter tracts implies decreased white matter integrity.
- Future results will subset the effects of microglial-specific inflammatory markers in the central nervous system.

## ACKNOWLEDGEMENTS

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