

Patients with Chronic Traumatic Brain Injury Show Persistent Proteomic Alterations Associated with PTSD and Aggression Symptoms

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BACKGROUND

- Traumatic brain injury (TBI) is a risk factor for neurodegenerative¹ and psychiatric² disorders
- Compared to civilians, military personnel have an increased risk of repetitive (r)TBI exposure and experience distinct injury mechanisms³
- Biomarkers for acute TBI have been established but remain underexplored for chronic (c)rTBI⁴
- We conducted proteomic profiling⁵ of controls, crTBI, and severe (s)TBI patients to identify persistent molecular alterations associated with chronic injury

METHODS

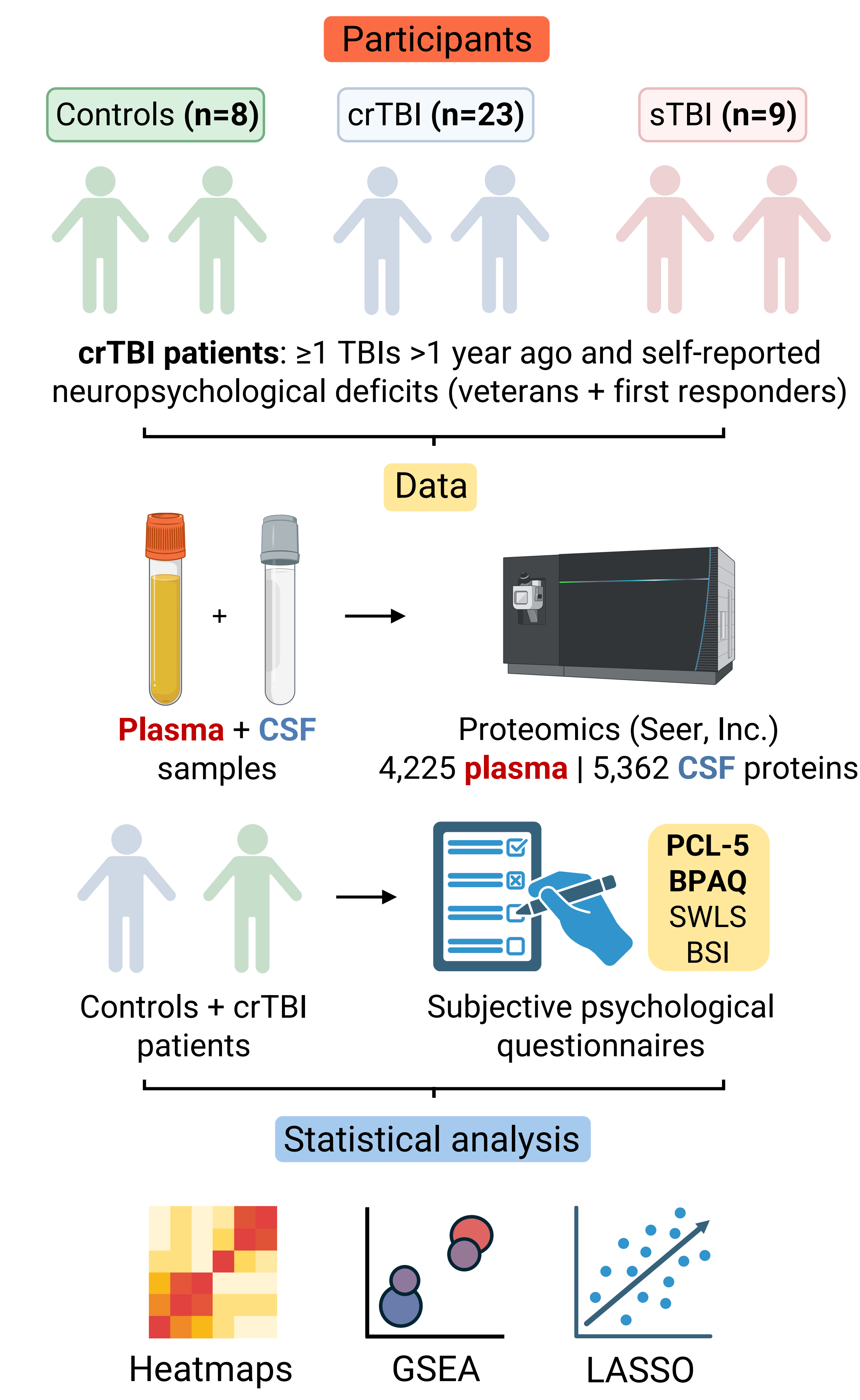


Fig. 1. Overview of study design. Plasma and CSF samples from controls, crTBI, and sTBI patients were subjected to proteomic (Seer, Inc.) profiling. Controls and crTBI patients responded to subjective neuropsychological questionnaires. Statistical analysis and visualization were conducted using R.

RESULTS

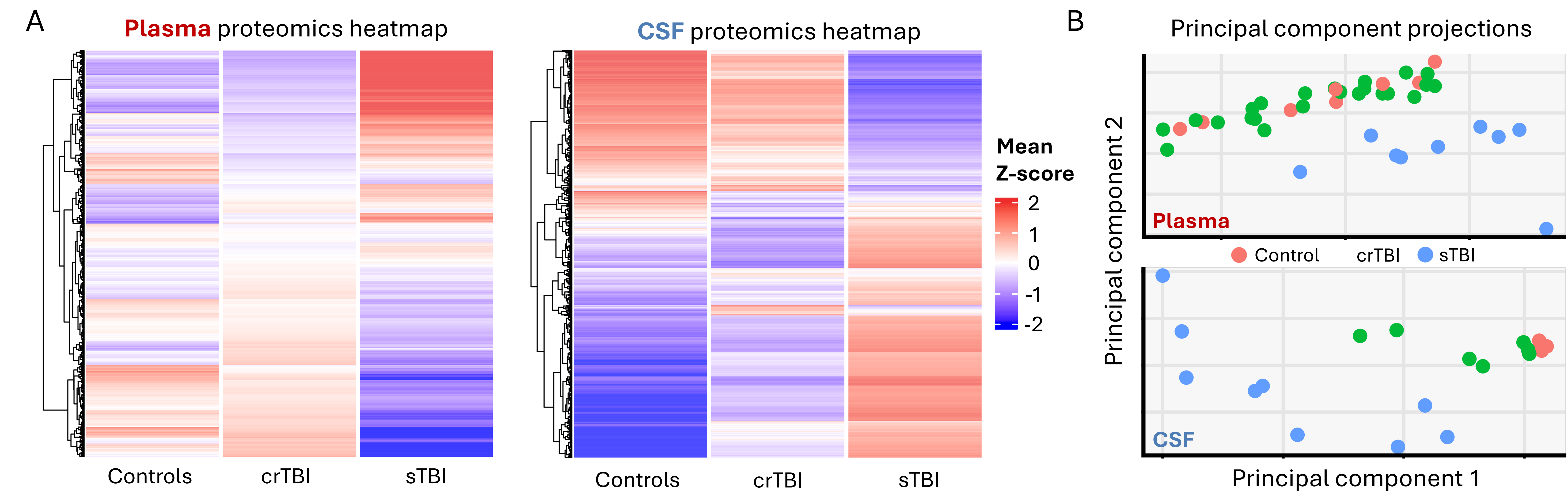


Fig. 2. Comparison of proteomic profiles across groups. a Heatmaps of plasma and CSF proteins show differences between controls and crTBI patients with more pronounced alterations in sTBI patients. b Principal component analysis shows slight proteomic profile separation between controls and crTBI patients in CSF.

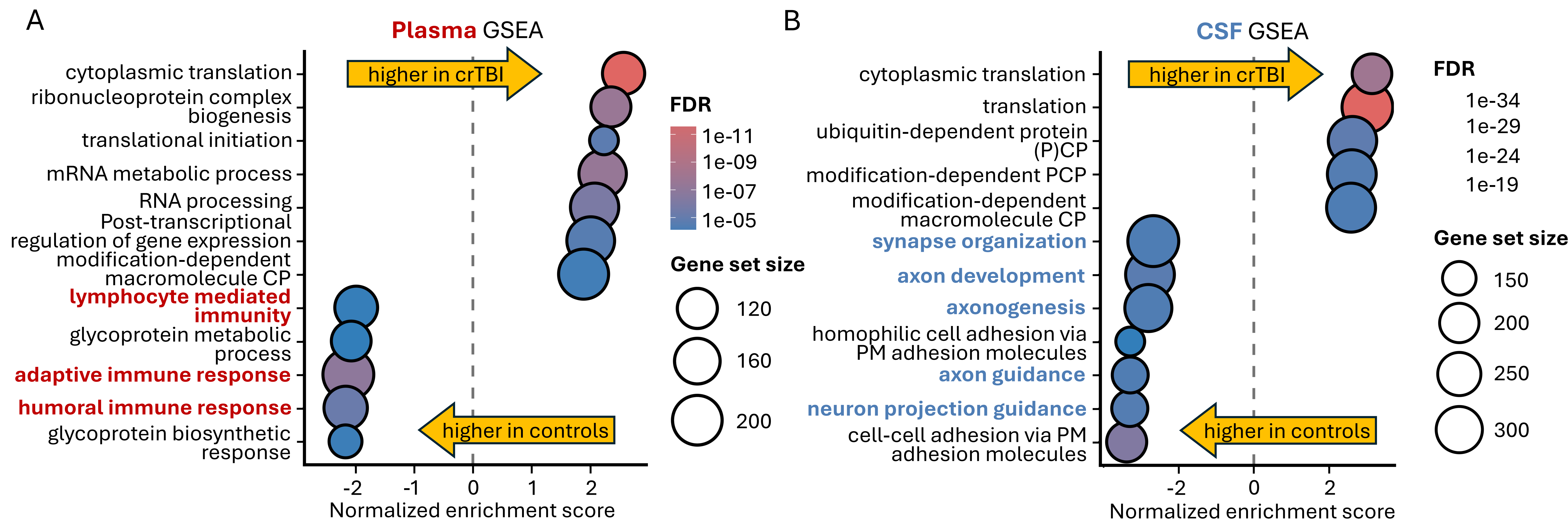


Fig. 3. Gene set enrichment analysis (GSEA). a GSEA of plasma proteins reveals downregulation of immune pathways in crTBI patients. b GSEA of CSF proteins reveals downregulation of neuronal pathways in crTBI patients. CP, catabolic process; PM, plasma membrane.

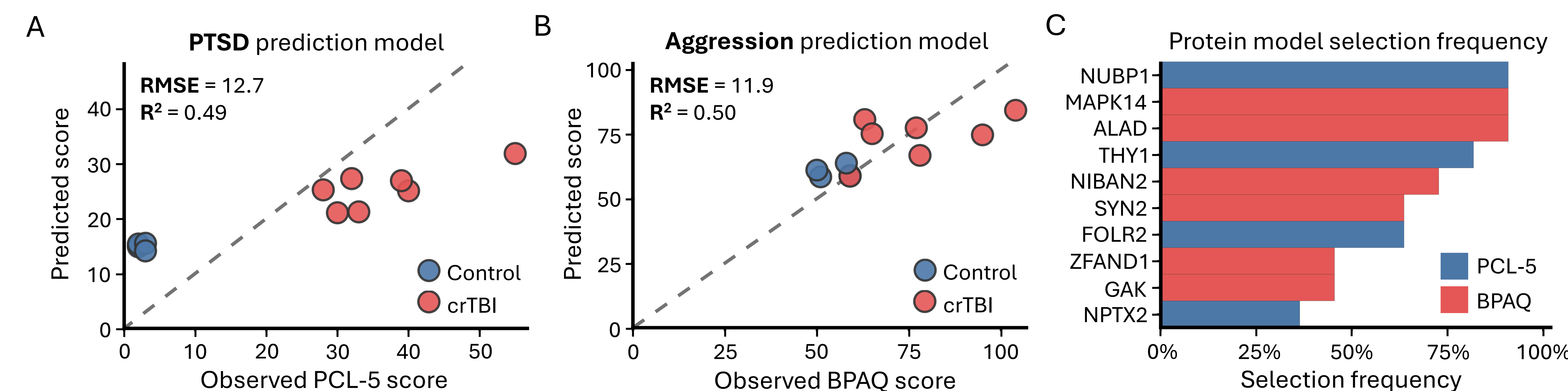


Fig. 4. CSF proteins predict subjective measurements of post-traumatic stress disorder (PTSD) and aggression symptoms. a, b CSF proteins predict subjective assessment of (a) PTSD and (b) aggression symptoms. c Bar plot shows the proteins most often selected by the LASSO model for both regressions.

CONCLUSIONS

- As expected, sTBI patients exhibited dramatic proteomic differences compared to controls and crTBI patients
- Subtler proteomic changes persisted between crTBI patients and controls**
- This suggests that acute TBI-induced proteomic changes resolve with time but important differences remain
- crTBI patients exhibited **downregulation of immune pathways** in plasma and **neuronal pathways** in CSF compared to controls
- CSF proteins predict subjective assessment** of PTSD and aggression symptom severity

LIMITATIONS

- Low sample size** restrains generalizability of findings
- Proteomics assays captured only a subset of the plasma and CSF proteome
- Psychological questionnaires provided subjective measurements of symptom severity
- Findings are associative** and should not be interpreted as causal

REFERENCES & DISCLOSURES

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