Granulocyte-colony Stimulating Factor Alters the Proteomic Landscape of the Nucleus Accumbens

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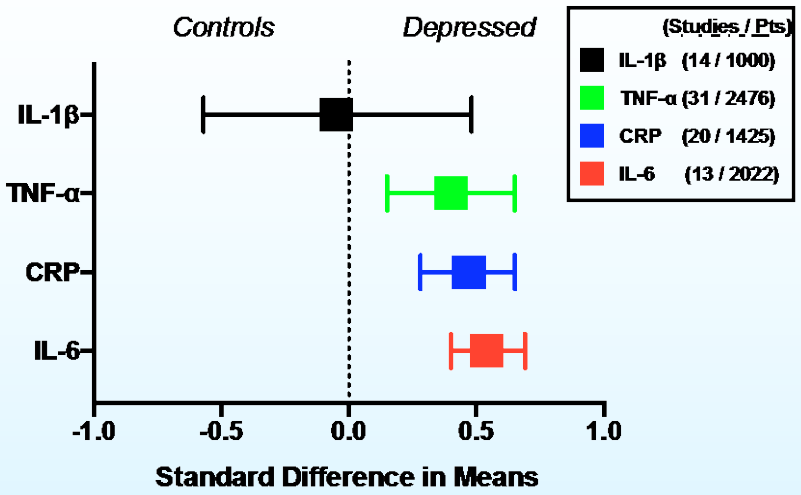
What is the role of inflammation in mental illness?

Meta-analysis of Cytokines in Depression

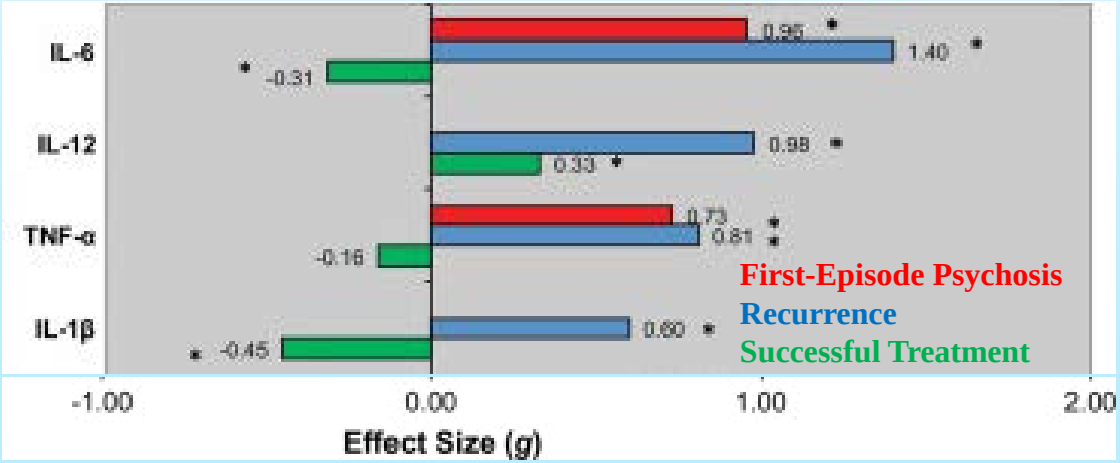


(Haapkoski et al *Brain Behav Immun* 2014)

Dysregulation of cytokines or other markers of immune function are seen in many psychiatric illnesses:

- **Autism Spectrum Disorder**
- **PTSD**
- **Bipolar Disorder**
- **Alzheimer's**
- **Others**

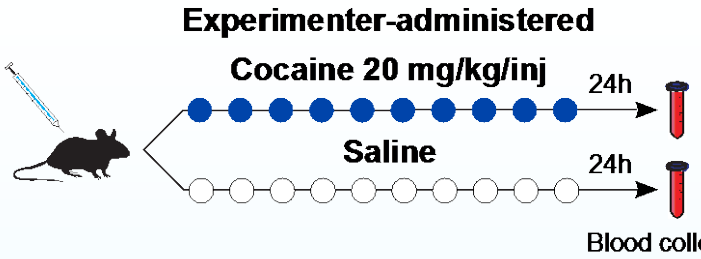
Meta-analysis of Cytokines in Schizophrenia and Treatment

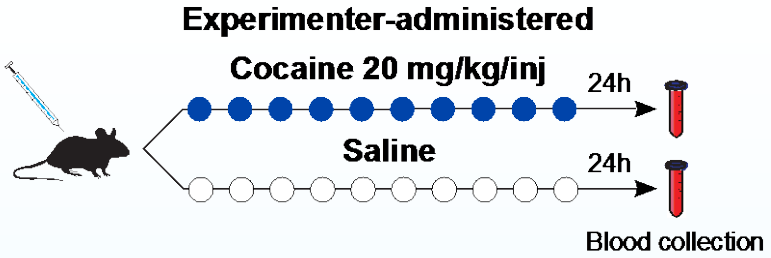


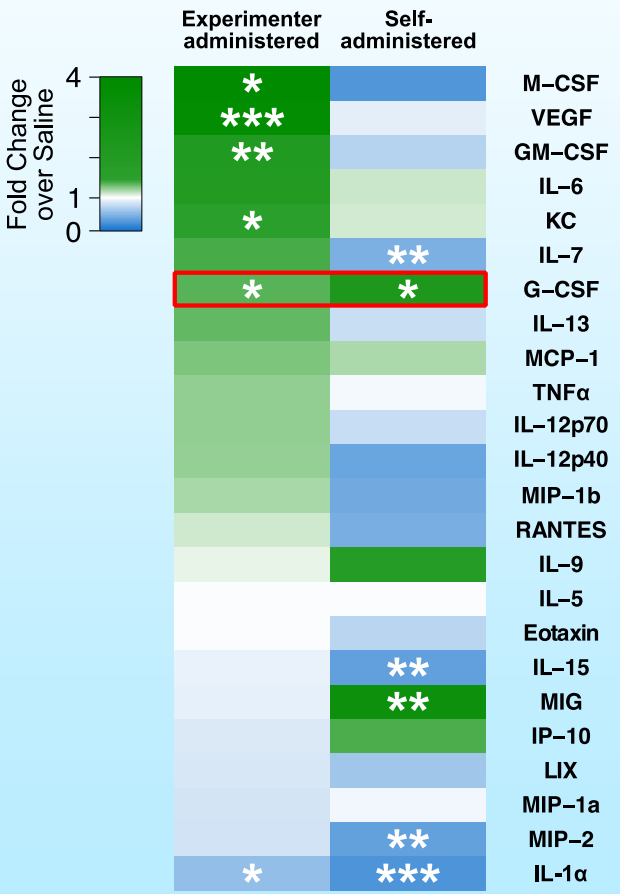
(Miller et al. *Biol Psychiatry* 2011)

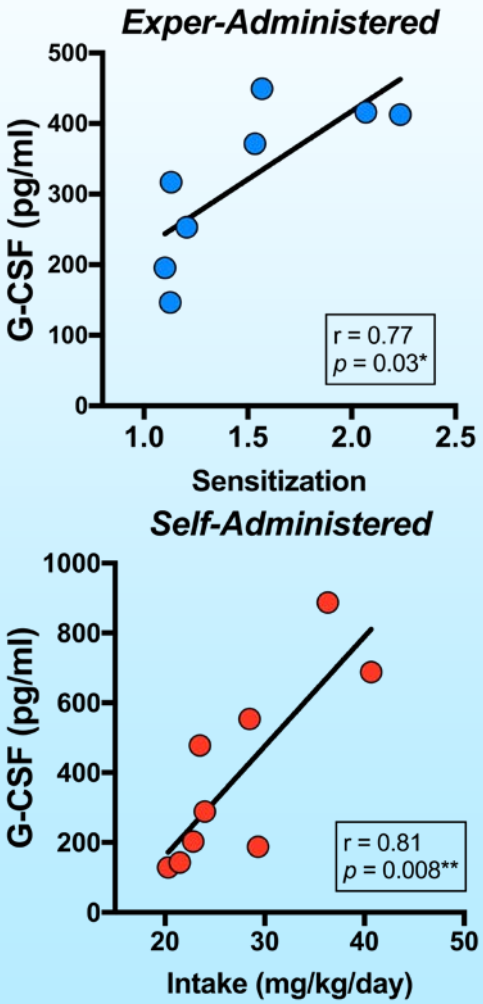
How does this affect disease progression, and can it be harnessed as a possible therapeutic strategy?

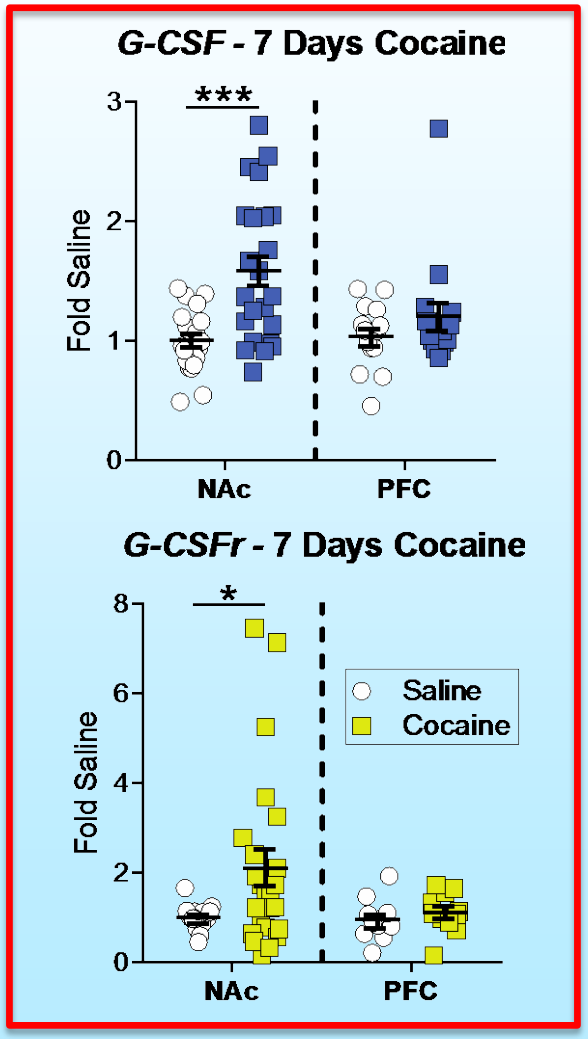
Multiplex Analysis of Serum Cytokines After Cocaine



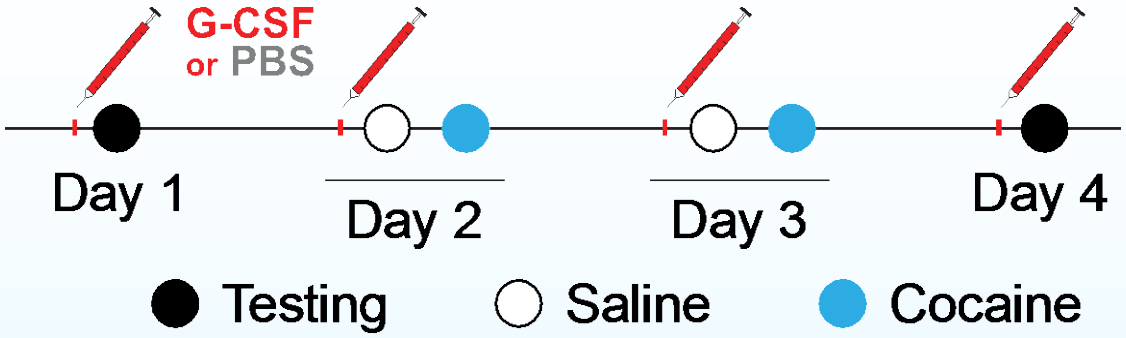


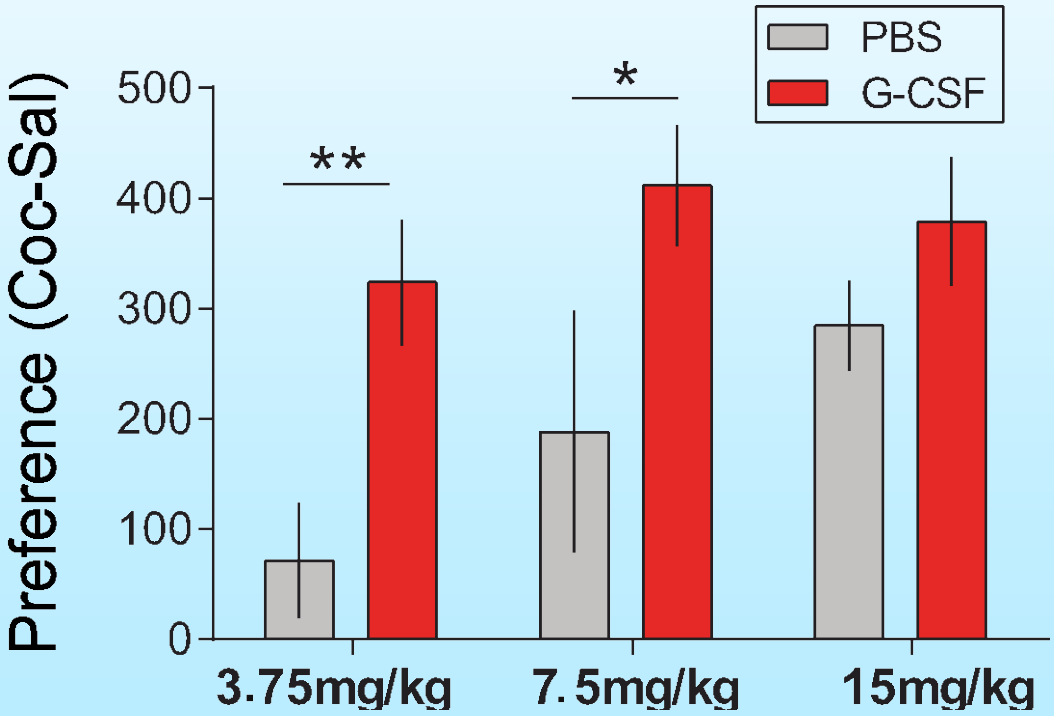






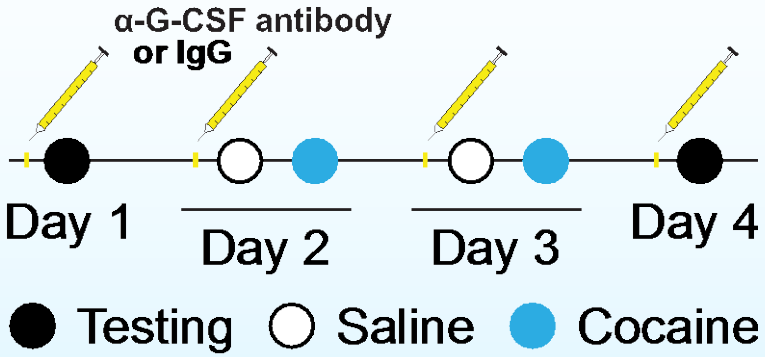
Effect of G-CSF on behavioral response to cocaine – Conditioned Place Preference

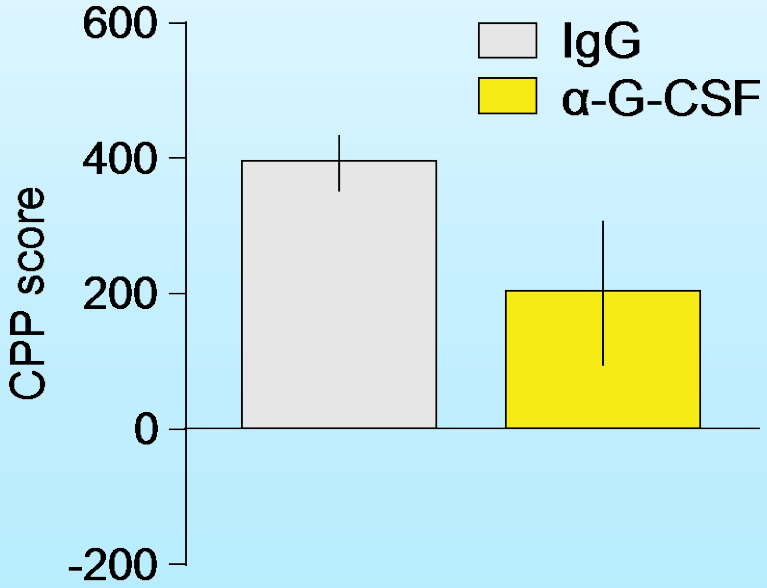




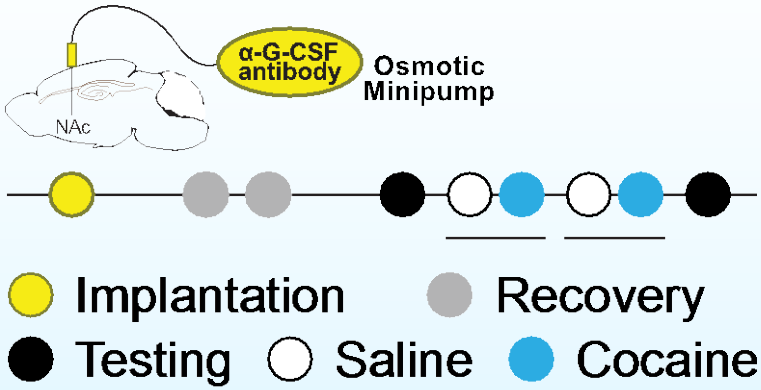
Effect of G-CSF on behavioral response to cocaine – Conditioned Place Preference

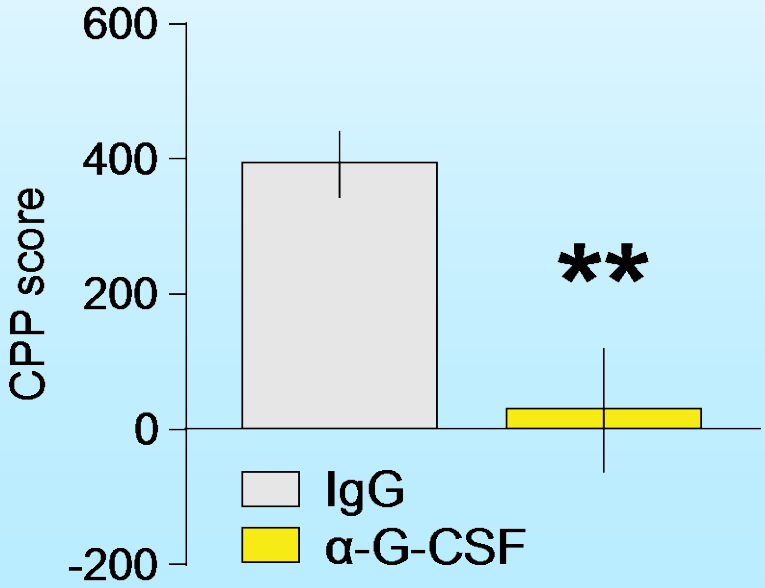
CPP with i.p. antibody



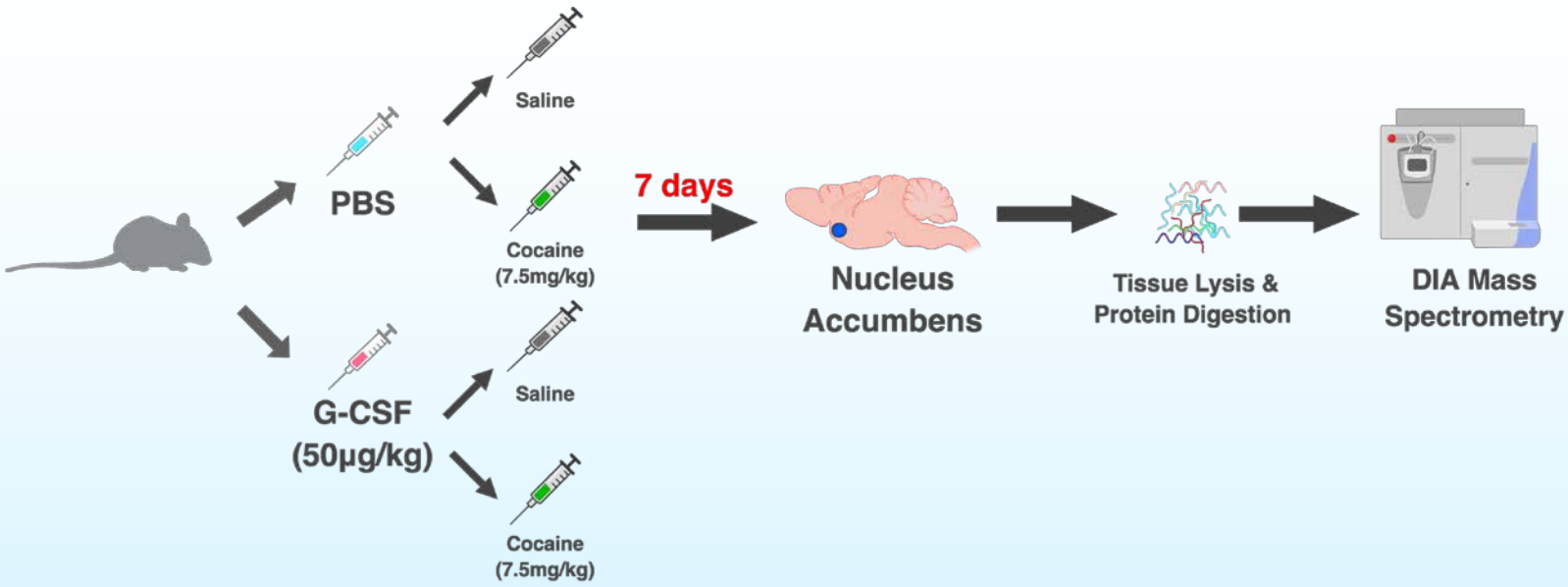


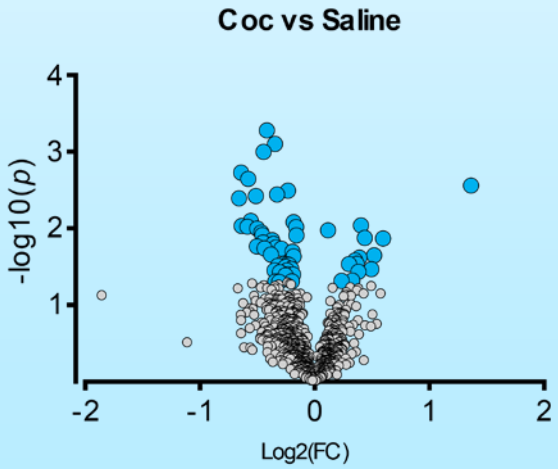
CPP with antibody in NAc

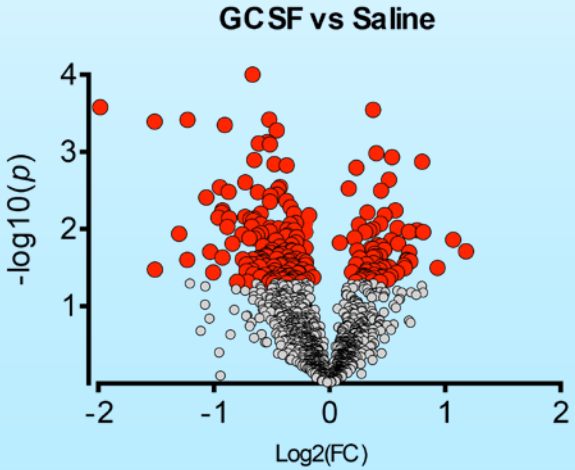


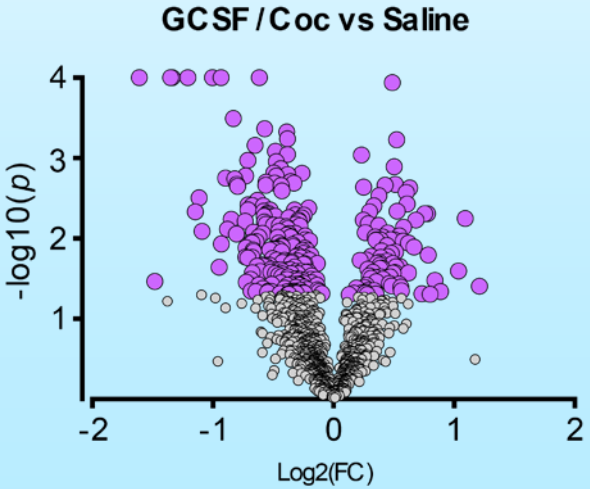


Discovery proteomics analysis of G-CSF effects

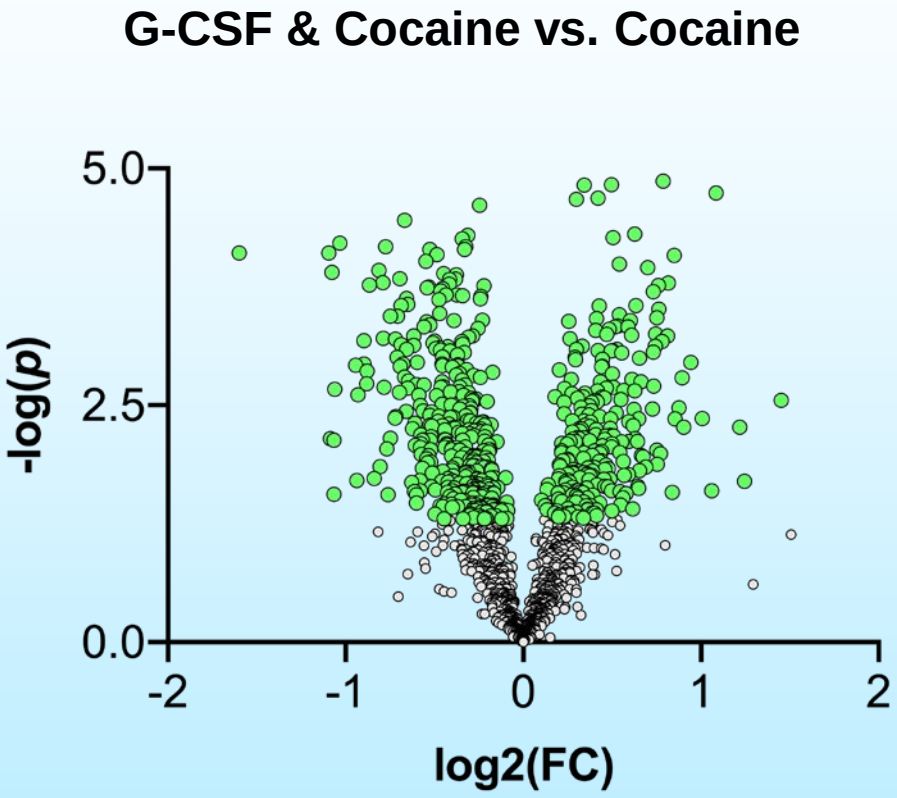




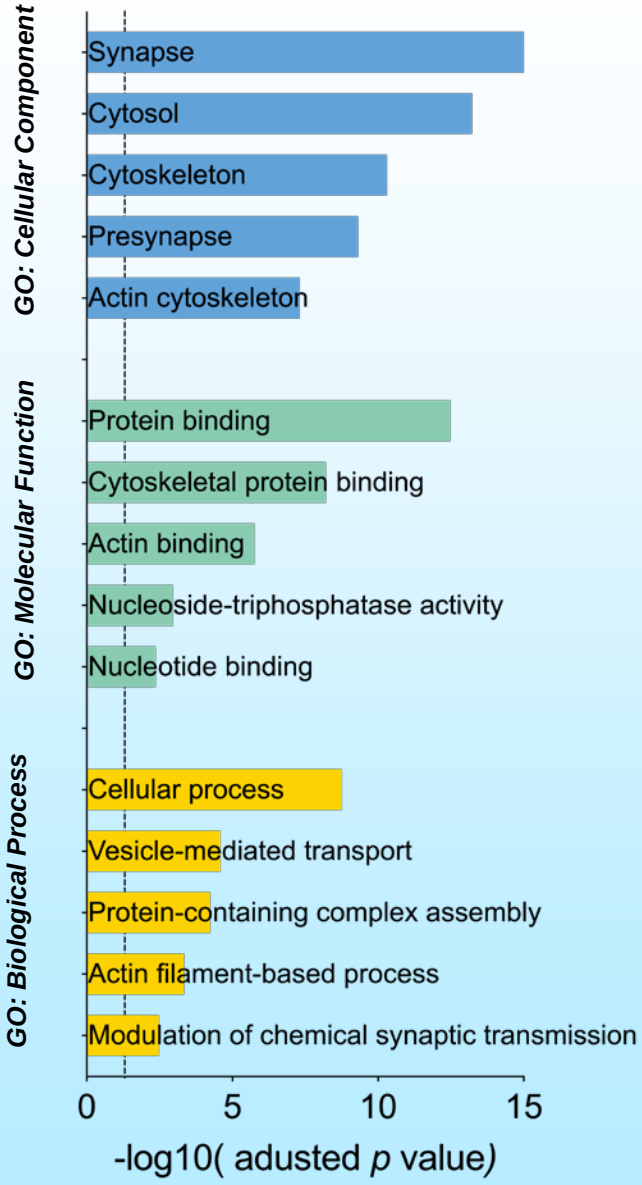




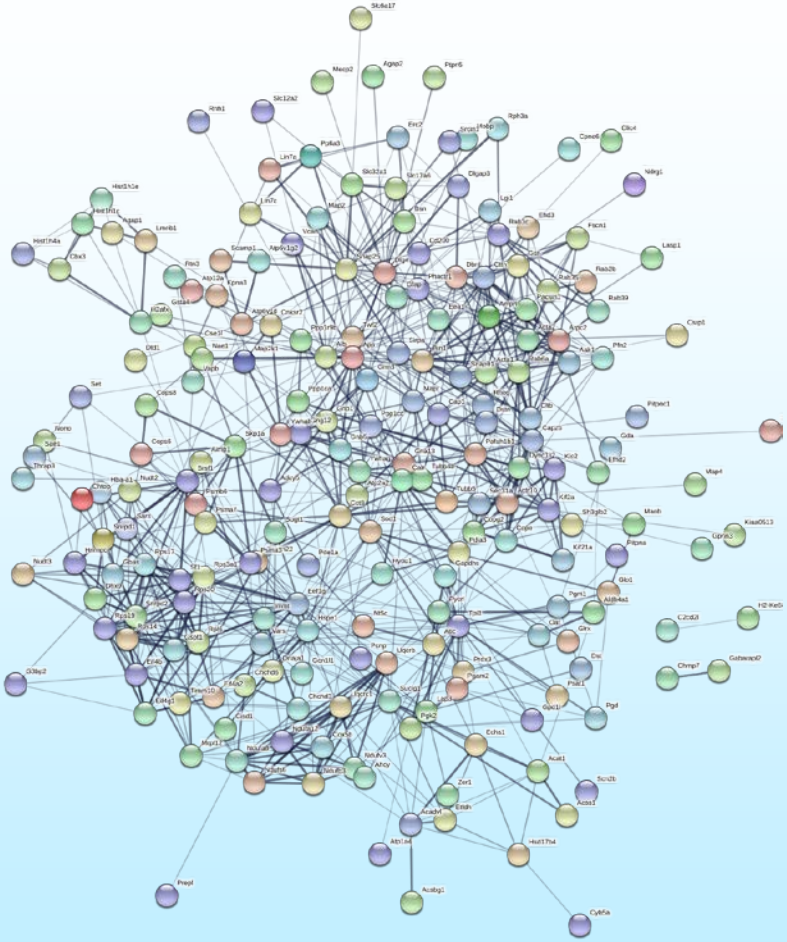
Examination of the interaction of G-CSF and Cocaine

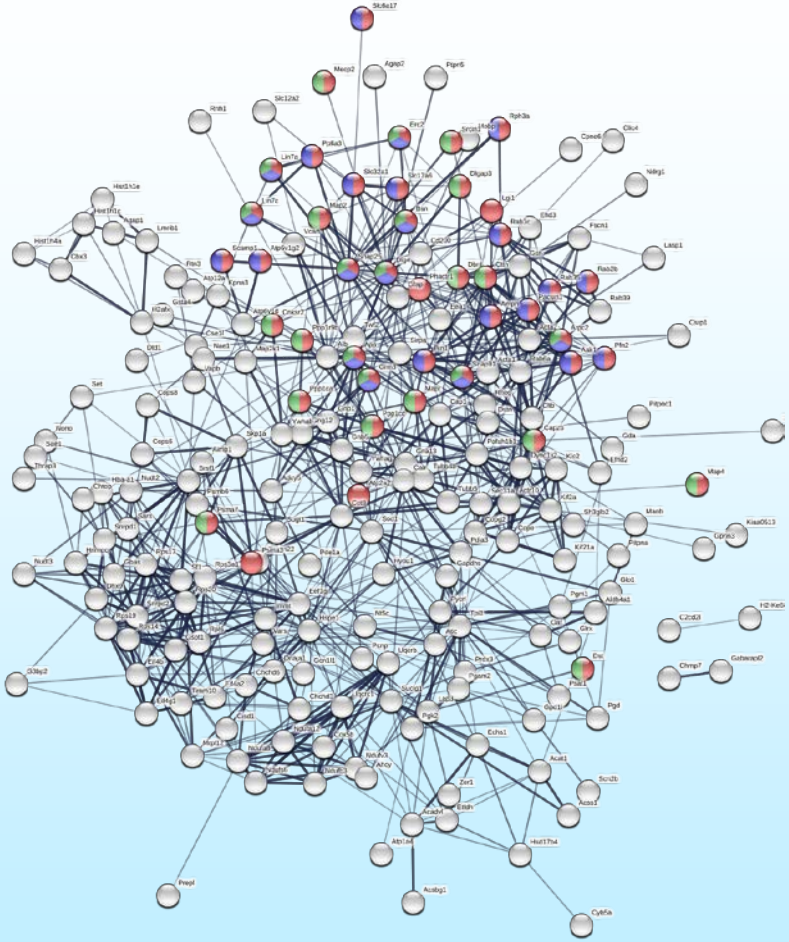


354 Decreased & 245 Increased



STRING protein-protein interaction analysis

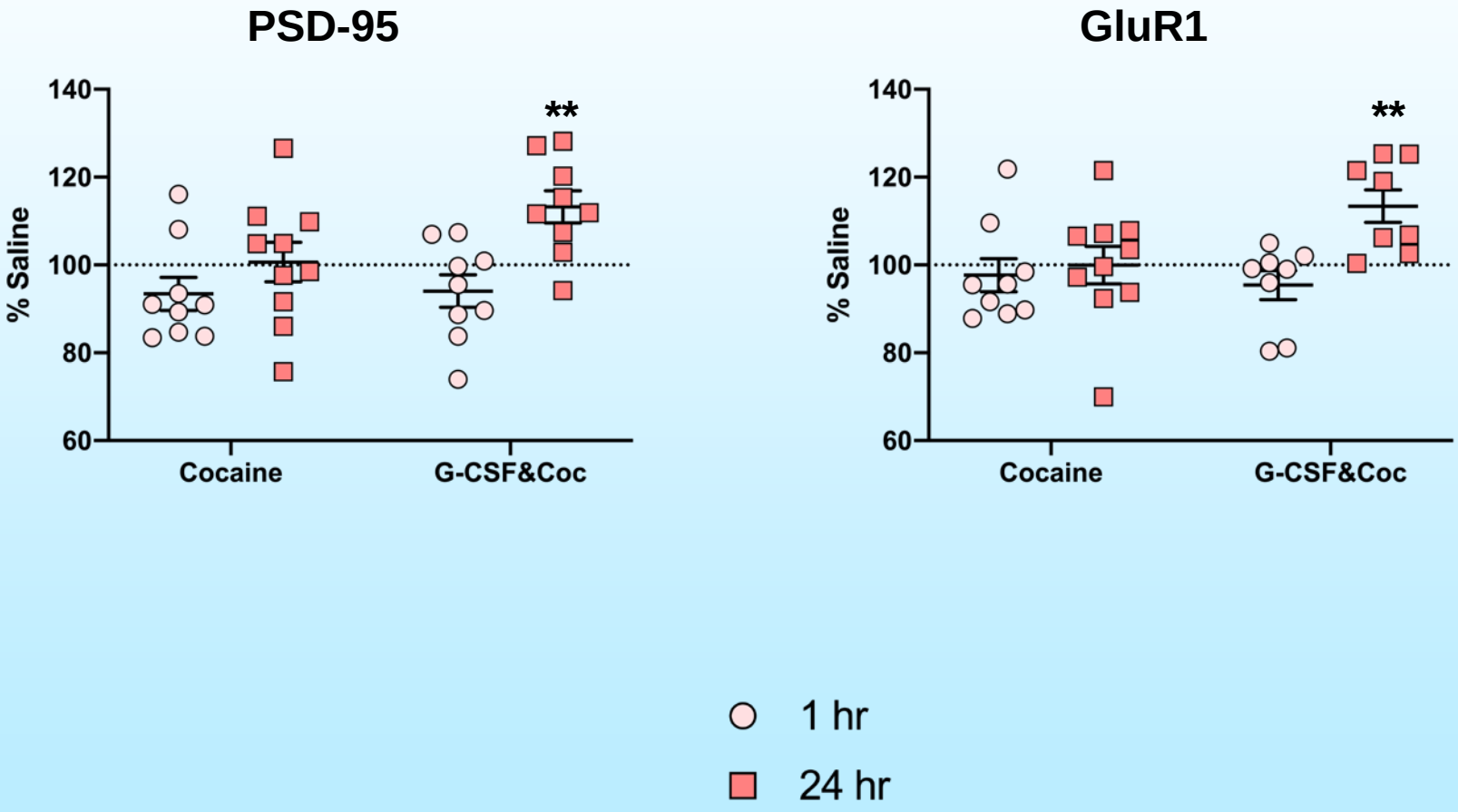




# of edges: 830
(Predicted: 491)
***p* < 1 x 10^{-16}**

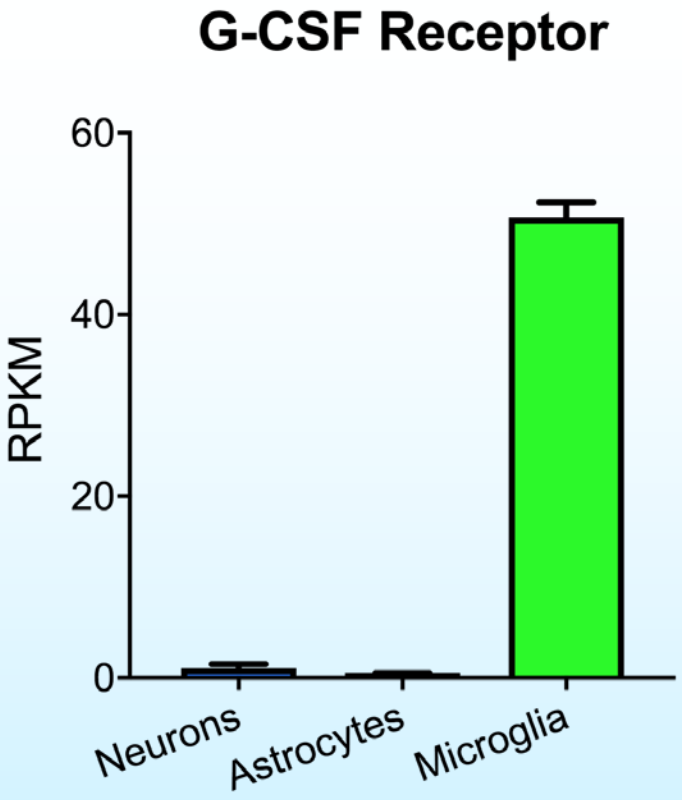
Synapse (46 proteins): ***p*** = 3.32 x 10^{-15}
Presynapse (27 proteins): ***p*** = 2.12 x 10^{-11}
Postsynapse (25 proteins): ***p*** = 1.83 x 10^{-8}

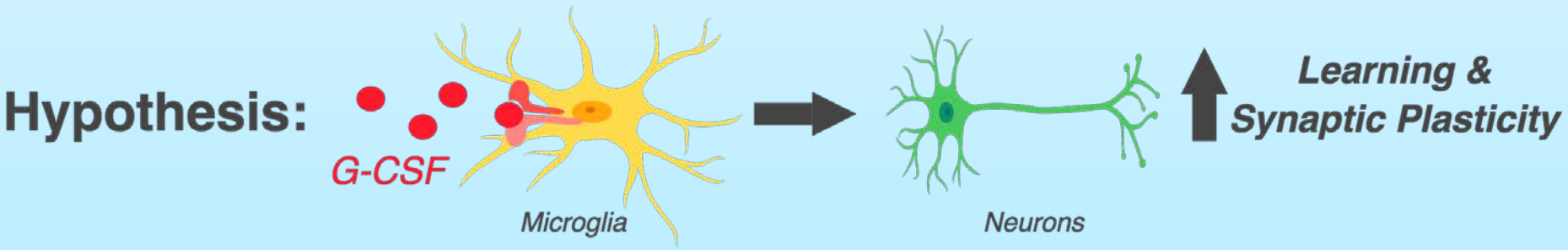
Western blot validation of proteomic targets



G-CSF is a potent neuroimmune modulator

- Enhances reward seeking
  - Cocaine & Natural
- Boosts cognitive flexibility
- Enhances DA release and neuronal activation
- Alters synaptic structure





Future Directions

- Analysis of G-CSF effects on drug extinction and seeking tasks
  - **Correlation of proteomic changes with behavioral response**
    - (This is partially done but not shown for lack of time)

- **Detailed proteomic characterization of synaptic fractions**
  - **Isolated synaptosomes/PSDs**
  - **Biotinylated cell-surface markers**

- **Investigation of cell-specific effects of G-CSF ± Cocaine**
  - **Microglia / MSNs**

- Circuit manipulation and imaging to determine pathways affecting G-CSF behavioral response

Thank You!

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