

Background

- Growing research is showing the links between gut microbiota and either risk or resilience to anxiety and depression disorders⁽¹⁻³⁾
 - Stress can influence the composition of gut microbiota which influences the central nervous systems response to future stressors^(2,4)
 - Substance abuse, including alcohol use, can influence the diversity of microorganisms in the gut^(5,6)
 - Deviations in microbiota have been shown to directly influence immune development and inflammatory responses to potentially affect mental health outcomes⁽⁷⁻¹¹⁾
- C-Reactive Protein (CRP) is a biomarker for inflammation and tissue injury that has been linked to depression, anxiety disorders and PTSD⁽¹²⁻¹⁸⁾
- CRP is released in response to elevations of pro-inflammatory cytokines which have been explored as potential biomarkers for anxiety disorders, depression PTSD and substance abuse^(5,12,14,19-24)
- There are still many gaps in our understanding of how the microorganisms relate to stress, substance abuse, genetics and mental health, and we seek to test these relationships in a non-clinical population (see **Figure 1**)
- Understanding the relationships between biomarkers and vulnerability to psychiatric disorders will help to determine direct future research in assessing causal direction between all of these factors that can promote mental well-being, and even help re-think how we treat mental health disorders.

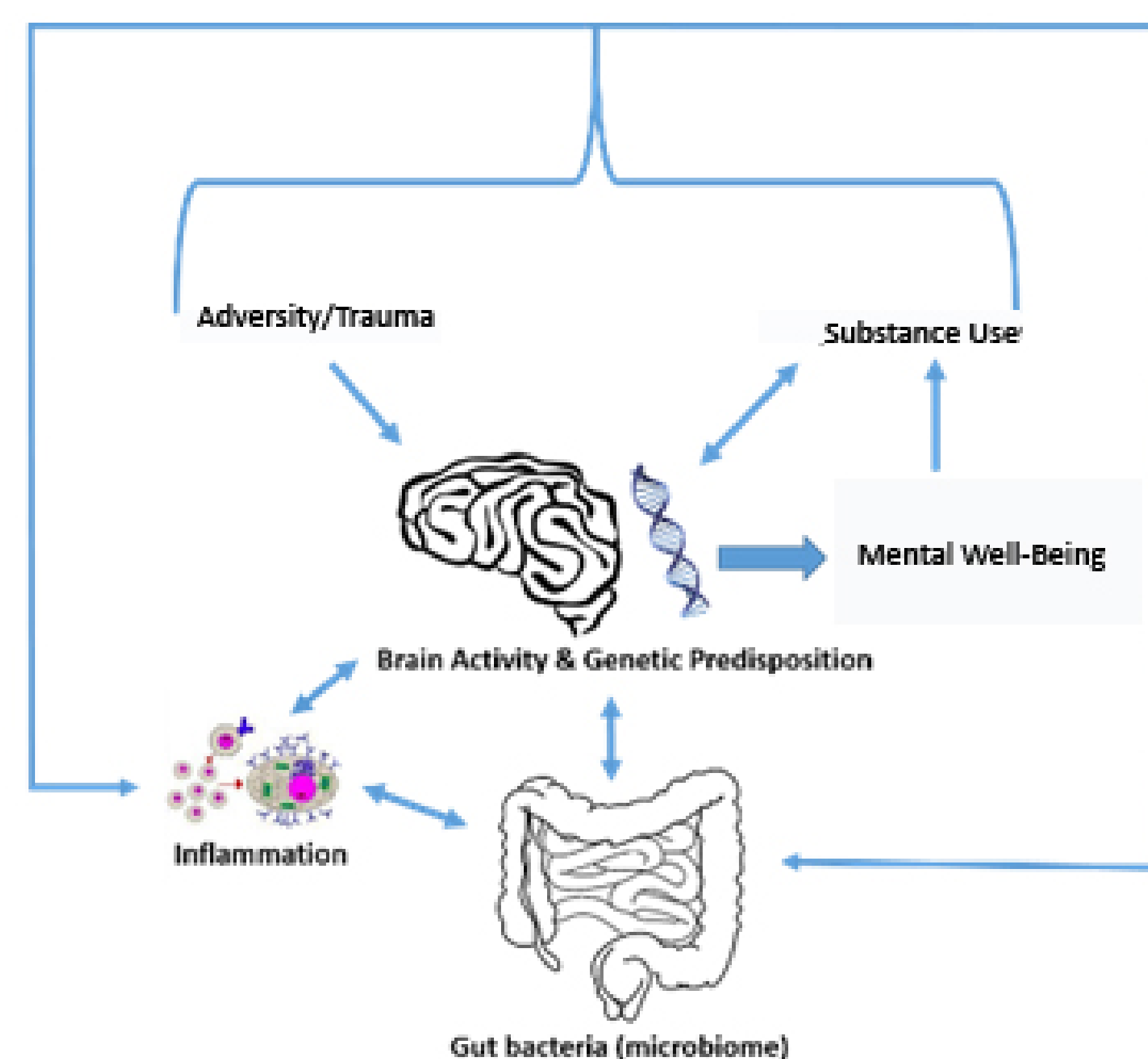


Figure 1: Hypothesized relationships to be tested by current study potentially determining mental well-being.

Purpose

- To investigate a direct association between behavior profiles such as anxiety and depression, the composition of the gut microbiota, basal levels of CRP and cytokines, cortisol and genetic predisposition in a general population (e.g. **Figures 2 and 3**)
- To seek to better understand the role of biomarkers in vulnerability and resilience to psychiatric disorders such as depression, PTSD and substance dependence.

Specifically we aim to determine if:

- The composition of gut microbiota is related to inflammation markers in the blood, i.e. increased basal inflammation expressing a linear relationship with decreased biodiversity.
- Chronic changes in cortisol levels are related to gut microbiota; specifically, if increased cortisol levels are associated with decreased biodiversity of gut microorganisms.
- Increased anxiety and depression profiles are correlated with higher basal levels of pro- inflammation markers (cytokines and CRP), decreased levels of anti-inflammation markers (cytokines), and reduced gut microbiota diversity.
- Substance use behaviors mediate the relationship between basal inflammation markers and/or decreased gut microbiota diversity with anxiety/depression.
- Genetic variants (IL4, 6, 10, IL-1 β , IFN- γ , TNF- α , glucocorticoid receptor, SERT, and CRP genes) and/or early-life experiences can be used to predict relationships between baseline inflammation levels and anxiety/depression in a non-clinical population.

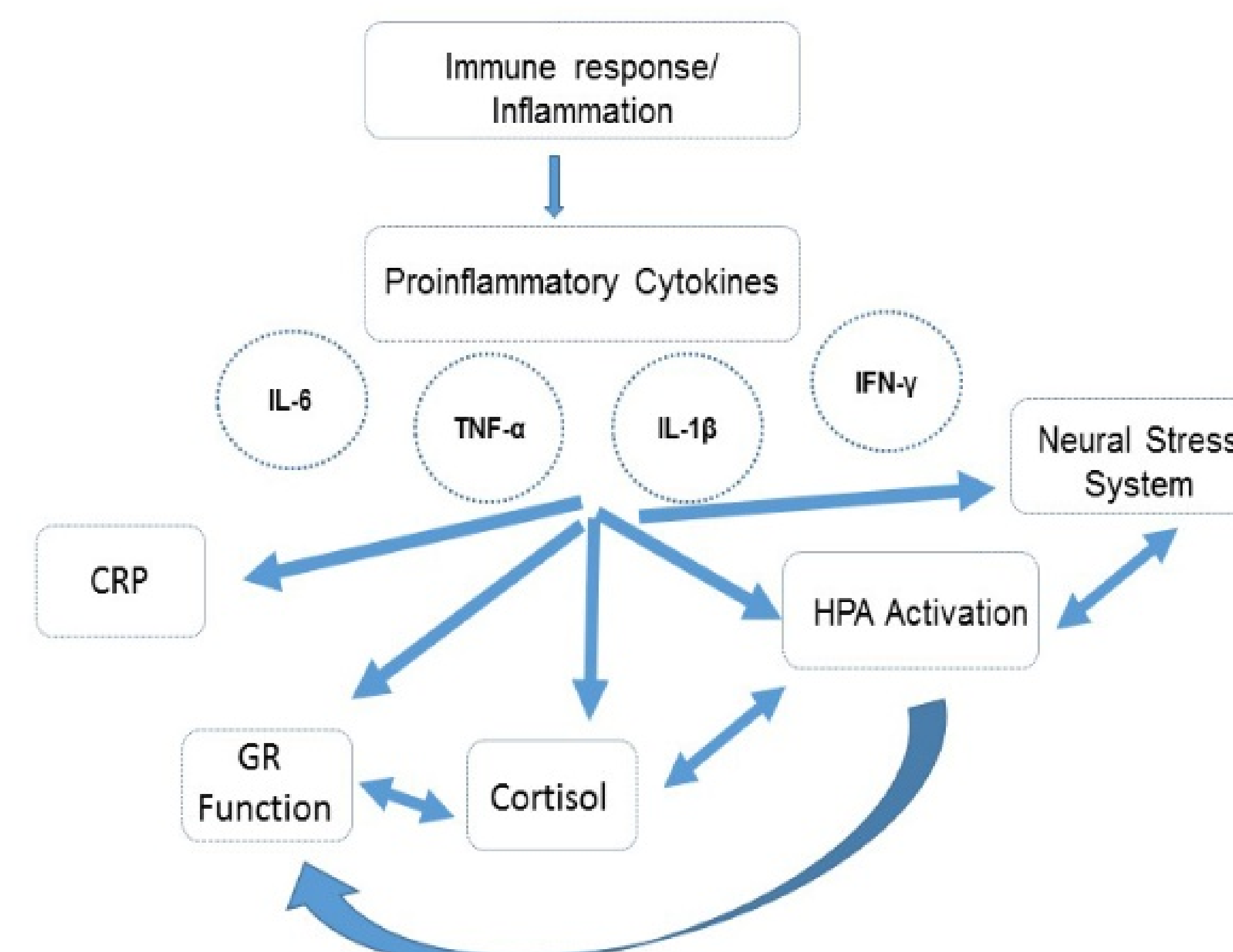


Figure 2: Proposed relationship between immune response and mental health⁽²⁵⁻²⁶⁾

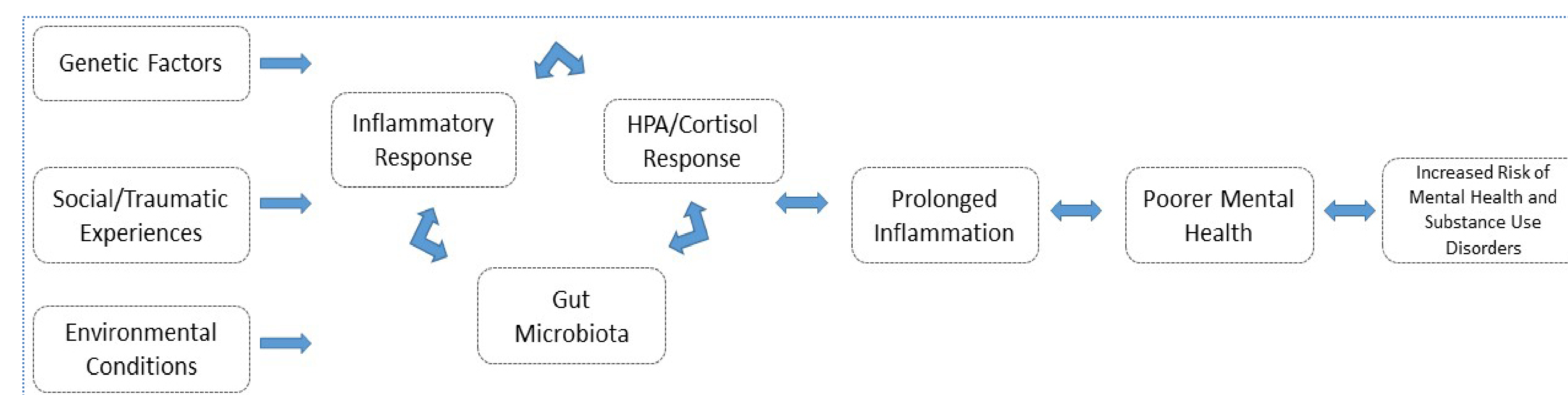


Figure 3: Proposed pathway of relationships to be tested. Directionality is hypothesized⁽²⁷⁾

Approach

- Participants will be recruited from the campus USD, as well as within the city of Vermillion and surrounding towns by use of posted advertisements.
- Prior to testing, participants will be asked about exclusion criteria, including use of blood thinners or injectable glucocorticoids, recent surgery or illness, pregnancy or mastectomy as these can influence inflammation markers or interfere with blood collection safety.
- Participants will be consented to the procedure and will be asked to complete a series of assessments including:
 - demographics, medications, diet, exercise, mental and physical health diagnoses and general health.
 - depression, anxiety, PTSD, substance use, and overall health.
 - self-care behavior, and previous and current trauma
- Participants will have hair and blood samples collected, and be given instructions for the return of the stool sample
- Hair will be analyzed for cortisol, blood samples for CRP and cytokine content and SNP's, and stool for microbiota.
- Data will be compiled and regression analysis will be employed to examine potential relationships between immune function, psychological health and substance use.

Next Steps

- Continue actively recruiting participants to the project
- Continue with data collection and sample storage
- Following collection of samples from 80 participants begin analyzing biological samples

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