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**Title:** Identifying a Biological Signature of Vulnerability to Prenatal Maternal Stress: Implications for Infant Neurodevelopment.

**Background:** It is well known that maternal stress during pregnancy can incur adverse neurodevelopmental outcomes in the offspring. Such stress has been shown to increase gastrointestinal (GI) permeability, potentially via actions on the gut microbiota, leading to bacterial components entering circulation and inducing a low-grade inflammatory state. This in turn may lead to alterations in tryptophan metabolism along the kynurenine pathway which evidence suggests can impact negatively on neurodevelopment. This study aims to investigate whether stress during otherwise healthy pregnancies elicits a biological signature which can be used to infer enhanced liability to psychopathology in the offspring.

**Objective:** To assess circulating markers of GI permeability, immune activation and tryptophan degradation towards identification of a biological signature of vulnerability to prenatal maternal stress.

**Design/Methods:** A healthy cohort (N = 105) of nulliparous female participants with singleton pregnancies derived from the Screening for Pregnancy Endpoints (SCOPE) study were utilised in the analysis. Self-reported assessments of stress using validated questionnaires were used to stratify this cohort into equally matched high and low stress groups. Plasma samples were collected during the first (15 weeks) and second (20 weeks) trimesters of pregnancy. Markers of GI permeability (Intestinal Fatty Acid Binding Protein (IFABP); Lipopolysaccharide Binding Protein (LBP); Soluble CD14), pro-inflammatory cytokines (IFNγ; TNFα; IL-6; IL-18) and chemokines (IL8; IP-10; MCP-1; MIF; SDF-1α) were assessed by Enzyme-linked Immunosorbent Assay (ELISA), while plasma tryptophan and kynurenine concentrations were determined using High Performance Liquid Chromatography (HPLC).

**Results:** Preliminary results suggest that circulating markers of GI permeability are influenced by high levels of prenatal maternal stress. Whether such influences translate to a pro-inflammatory response that remodels the direction of tryptophan metabolism is currently under investigation.

**Conclusion:** Our findings demonstrate the potential for markers of GI permeability to inform suitable intervention strategies aimed at counteracting the effects of prenatal maternal stress either via stress reduction techniques or microbiota targeted nutritional approaches.