Prenatal alcohol exposure (PAE) results in a constellation of negative consequences clinically known as fetal alcohol spectrum disorders (FASD), which include disorders of mood, behavior, and cognition. The hypothalamus and amygdala influence the stress response of the hypothalamic-pituitary-adrenal (HPA) axis. Glucocorticoids (CORT) released into circulation following HPA activation exert negative feedback by activating glucocorticoid receptors (GR) that inhibit further HPA activation and CORT release. Stress-induced production of corticotropin-releasing hormone (CRH) in the brain initiates HPA activation, a process also associated with the activation of astrocytes and production of proinflammatory cytokines such as interleukin-1β (IL-1β). We hypothesize that PAE alters brain astrocyte and cytokine actions in response to acute stress in adulthood.

Dexamethasone (DEX), a synthetic GR agonist, was administered to mimic glucocorticoid negative feedback in response to stress. 1.5-hr prior to 30-min restraint stress, subcutaneous vehicle (DMSO; 1:100 in sterile phosphate buffered saline, (PBS), pH 7.4) or DEX (25 μg in DMSO:PBS) was given to 3–5-month-old female C57BL/6 mouse offspring that underwent prenatal control exposure (saccharine; SAC) or PAE (10% EtOH). Tail vein blood collection occurred immediately after stress. The hypothalamus and amygdala were collected 24-hr or 3-hr after stress. Messenger RNA (mRNA) expression levels of CRH, IL-1β, and glial-fibrillary-acidic-protein (GFAP; for astrocyte activation) and NR3C1 (GR gene) were assessed by RT-qPCR. Glucocorticoid levels were assayed by quantification of blood plasma CORT via enzyme-linked immunosorbent assay (ELISA).

In both SAC and PAE, stress increased circulating CORT levels. DEX pretreatment blunted CORT levels in both SAC and PAE. At 3 hours, the PAE-stressed hypothalamus revealed blunted CRH mRNA expression. At 24 hours, the PAE-stressed hypothalamus revealed elevations in GFAP mRNA expression levels. The results of this study indicate that the peripheral GR response is functional, and that astrocytes may play a role in the dysregulation of the PAE brain-stress response.