

Stress Induced Changes in SAMP1 Mice: A Murine Model of Crohn's Disease

Harsha Sanaka, ¹ Adrian Gomez-Nguyen, ² Fabio Cominelli ²
Hawken School, ¹ Digestive Health Research Institute, Case Western Reserve
University, Ohio ²

BACKGROUND

- Inflammatory bowel disease (IBD) is a set of chronic inflammatory conditions of the gastrointestinal (GI) tract, including Crohn's disease (CD) and ulcerative colitis, that affects approximately 1.6 million individuals in the United States alone.
- Studies have shown that psychological stress is a significant risk factor for symptomatic flares of IBD, indicating the existence of a brain-gut axis.
- The SAMP1/YitFc (SAMP) mouse model is an ideal candidate for exploring the mechanisms of the brain-gut axis because it develops spontaneous CD-like ileitis in a predictable time course.
- SAMP mice have previously been shown to generate colonic tertiary lymphoid organs (TLO), composed primarily of CD4⁺ T cells, B cells, dendritic cell clusters, and stromal cells, after restraint stress (RS).
- Dextran sodium sulfate (DSS) is often used to induce colitis that mimics clinical and histological features of IBD in mice.
- We hypothesize that stress and DSS induce an inflammatory flare up in SAMP mice. Therefore, our aim was to assess the effect of stress and DSS-induced colonic insult on the GI tract and mesenteric lymph nodes (MLN) of SAMP mice.

METHODS

- Forty SAMP mice were split into an experimental group (stressed) and a control group (unstressed).
- RS was performed on the mice where they were placed in a 50 mL conical tube for 3 hours a day over the course of 56 days (8 weeks).
- Mice were further divided and subsequently treated with 3% DSS via drinking water for 7 days, followed by a recovery period of 14 days.
- On days 8 and 21 of the DSS trial, colonoscopies were performed on the mice up to the splenic flexure.
- Inflammation was evaluated by a colonoscopy score.
- Intestinal tissue was fixed in Bouin's solution for histology and hematoxylin and eosin (H&E) stain, from which inflammatory score was calculated.
- MLN composition was assessed with fluorescence-activated cell sorting (FACS).
- Stool was homogenized in PBS to quantify IgA levels via ELISA.
- To assess the differences between the groups, parametric one-way analysis of variance (ANOVA), Mann-Whitney, and Kruskal-Wallis tests were performed.
- A p-value of <0.05 was considered significant.

RESULTS

- Interestingly, stressed mice had healthier colons compared to unstressed mice following DSS administration.
- Colonoscopy scores were significantly lower in stressed mice (Figures 1, 3).
- On histology, total inflammatory scores were lower in the colon of the stressed mice with DSS with no significant differences seen in the ileum (Figure 1).
- Stress resulted in decreased levels of IgA; however, this reduction was seen only following DSS (Figure 2).

Figure 1

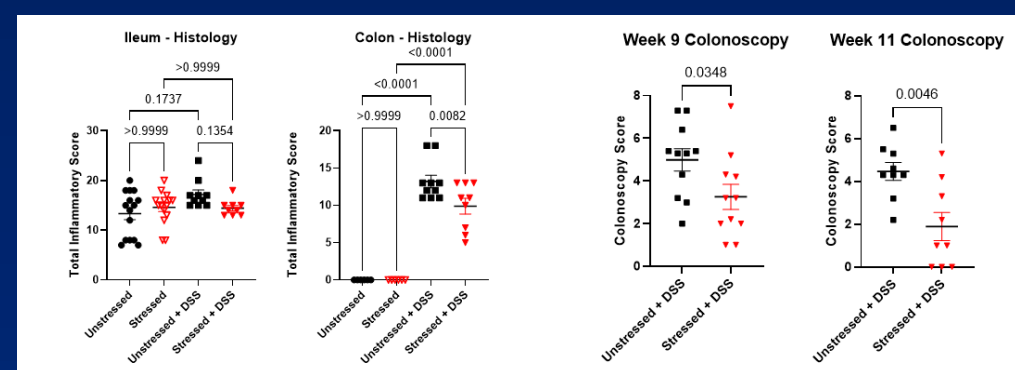


Figure 2

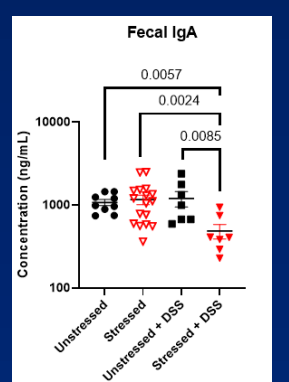
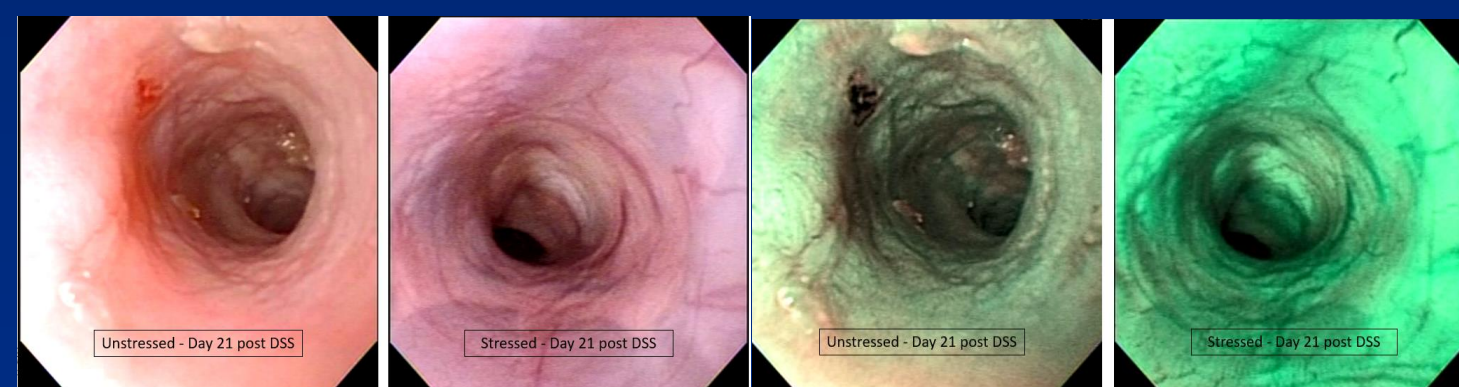


Figure 3



- The inflammatory cell profile of the MLN was largely unchanged by stress, but addition of DSS was associated with lower levels of CD3⁺CD4⁺ T cells and higher levels of CD3⁺CD8⁺ T cells and dendritic cells (Figures 4 and 5).

Figure 4

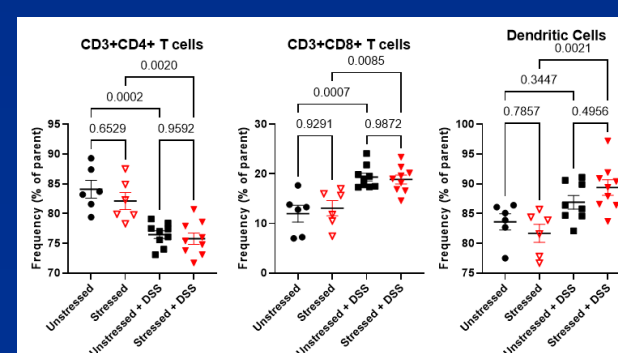
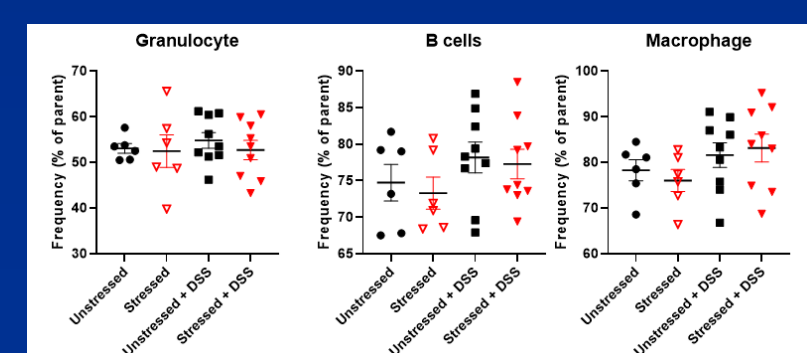


Figure 5



DISCUSSION

- The protective effect of stress against DSS in SAMP mice is an interesting result, especially given the lack of changes to MLN cell profile and reduction in stool IgA levels.
- Increased binding of IgA to bacteria might explain the decrease in IgA levels seen with DSS.
- Future work is aimed at elucidating the pathways involved in the protective role of TLOs against inflammation in SAMP mice.