

| PublisherInfo | |
|----------------------|------------------|
| PublisherName | : BioMed Central |
| PublisherLocation | : London |
| PublisherImprintName | : BioMed Central |

Selective jejunal manipulation initiates a proinflammatory molecular response within the gastric and colonic muscularis

| ArticleInfo | |
|-----------------------|---|
| ArticleID | : 1371 |
| ArticleDOI | : 10.1186/cc1330 |
| ArticleCitationID | : P266 |
| ArticleSequenceNumber | : 259 |
| ArticleCategory | : Meeting abstract |
| ArticleFirstPage | : 1 |
| ArticleLastPage | : 2 |
| ArticleHistory | : RegistrationDate : 2001-1-15 Received : 2001-1-15 OnlineDate : 2001-3-2 |
| ArticleCopyright | : The Author(s)2001 |
| ArticleGrants | : |
| ArticleContext | : 1305455S1S1 |

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Introduction

Postsurgical ileus significantly increases morbidity and mortality. We have shown that intestinal manipulation initiates an intense molecular and cellular inflammatory response within the jejunal muscularis that causes ileus. The objective of this study was to investigate the molecular inflammatory responses in the stomach and colon initiated by selective small bowel manipulation and its functional significance.

Methods

The small intestine of ACI rats was gently manipulated and the animals were sacrificed between 0 and 24 h. RT-PCR of mRNA samples and electrophoretic mobility shift assay (EMSA) of protein extracts from the isolated gastric, jejunal and colonic muscularis were performed. *In vitro* mechanical recordings using an organ chamber as well as *in vivo* transit measurements were performed.

Results

EMSA for Stat3, the cytosolic messenger for IL-6 which promotes leukocyte infiltration showed a 4.8-fold increase in transcription factor activation in the jejunal bowel muscularis compared to a 3.8-fold increase in the gastric muscularis and an even higher 8.8-fold activation for Stat3 in the colonic muscularis. RT-PCR demonstrated a rapid 7.6-fold upregulation of IL-6 mRNA within the jejunal muscularis, which remained elevated for 12 h after surgery. In stomach and colon, a significant 4.0-fold and 5.8-fold upregulation of IL-6 mRNA was also seen when comparing isolated muscularis extracts from controls and animals 3 hrs after the manipulation ($P < 0.05$, $n = 5$). Similarly an upregulation of TNF- α shared a 4.8-, 2.1- and 3.4-fold upregulation in the muscularis of small bowel, stomach and colon respectively. The jejunal manipulation initiated the recruitment of neutrophils into the unmanipulated colonic muscularis ($46.0 \pm 4.3/\text{field}$) reflecting a cellular inflammatory response as in the jejunal muscularis ($63.2 \pm 5.1/\text{field}$). Functionally we could observe a significant suppression of gastric and colonic smooth muscle motility *in vitro* as well as *in vivo*.

Conclusion

We conclude that manipulation of the small bowel leads to a "field effect phenomenon" in the unmanipulated gastric and colonic muscularis. We hypothesize that the proinflammatory milieu within the stomach and colon plays an additional important role in gastrointestinal postoperative ileus.