Acute stress enhances intestinal permeability to intact protein in Roman Low Avoidance rats, but not in Roman High Avoidance rats, by a cholinergic mechanism.


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**G1434**


Previously we have shown an enhanced intestinal macromolecular permeability after acute cold restraint stress in the stress-susceptible rat strain Wistar Kyoto, which occurred via a cholinergic mechanism (Gastroenterol. 108 Suppl: A911, 1995). Here we examined the effect of cold restraint stress in Roman High Avoidance (RHA) rats which have an active, mainly sympathetic stress coping style, and in Roman Low Avoidance (RLA) rats, which have a passive, mainly parasympathetic stress coping style. Rats were stressed by immobilization for 2 hours at 8°C followed by 2 hours recovery at room temperature in their home cage. Atropine i.p. (20mg/kg) was given to 50% of the rats prior to restraint, or 4 hours prior to sacrifice in controls.

Permeability of stripped segments of jejunal mucosa was measured in Ussing chambers and perfused in carbogenated Ringer's solutions of 37°C. Mean one hour HRP accumulations ± s.e.m. (in pmol/cm²) are given in the table. Significant differences from controls were tested by two-tailed t-test (p < 0.05).

| Stress | Control | Atropine | Acute stress
<table>
<thead>
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<tbody>
<tr>
<td>RHA</td>
<td>2.0 ± 0.6</td>
<td>2.0 ± 0.5</td>
<td>3.0 ± 0.6</td>
</tr>
<tr>
<td>n</td>
<td>5</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>RLA</td>
<td>0.9 ± 0.2</td>
<td>3.5 ± 0.9*</td>
<td>1.6 ± 0.3</td>
</tr>
<tr>
<td>n</td>
<td>5</td>
<td>6</td>
<td>6</td>
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</table>

Acute cold restraint stress caused a significant, more than 3-fold increase in HRP permeability in RHA rat jejunum, which could be blocked by prior injection of rats with atropine. This is consistent with the primarily sympathetic (vagal) stress response in RHA rats, and indicates the involvement of cholinergic activation in the observed permeability increase. In RLA rats, an induced increase in jejunal HRP permeability was not apparent. Injection of atropine in both RHA and RLA controls tended to decrease intestinal HRP permeability, which may indicate that in control rats of the Roman strain a minimal cholinergic tone is required to maintain intestinal barrier function, while in stressed animals atropine may prevent an increased cholinergic tone back to control levels. We conclude that effects of stress on intestinal barrier function may be dependent on individual stress coping strategies.

This research was supported in part by a grant from Nutricia, Zoetermeer, The Netherlands.

**G1435**


Recently we reported an increased trans- and para-cellular protein permeability in rat small intestine after acute (2 hours) cold restraint stress (Gastroenterol. 108 Suppl: A911, 1995). This is a rather strong stressor, as judged from the observed 225-250 ng/ml increment in plasma corticosterone levels (Neuroendocrinol. 65: 200-209, 1997; Am. J. Physiol. 267: G794-G799, 1995). In the present study we applied randomized 95 dB white noise pulses during 45 min per hour, 12 hours per day, duration 8 days, as a mild subchronic stressor to male Wistar rats (~250 g). At 8 days (day-8) before the noise experiments (day 0), 50% of the animals were cannulated in the vena cava allowing free movement, and blood samples were obtained at day -1, 0, 1, 2, 4, 7 and 9. The other 50% of the animals were sacrificed at day 9, segments of ileum were stripped from muscle layers and mounted in Ussing chambers and perfused in carbogenated Ringer’s solutions of 37°C. Horse RBCs (20%, Percoll, 40K, 10^5 M side) were added to the mucosal side, and serosal samples were taken at 60 and 120 minutes. Tissues were fixated for electronmicroscopical HRP staining and serosal appearance of HRP was detected enzymatically. In the cannulated noise-exposed animals, serum catecholamine and prolactine levels were unchanged, corticosterone levels were significantly enhanced from day 2 compared to controls (36 ± 11 vs 16 ± 5 ng/ml, p < 0.01, Mann-Whitney test), and remained at this level at day 7 and 9. Real HRP (40K, 10^5 M side) was significantly enhanced in noise exposed animals (n=12) compared to controls (n=13), resp. 2.3 ± 0.4 vs 1.0 ± 0.2, 60 - 2 - 0 minutes, and 5.9 ± 0.8 vs 3.3 ± 0.5 ± 60 - 2 - 0 minutes, p < 0.01. Electronmicrographs of tissues from stressed or control animals showed no traces of acellular HRP-containing endosomes in enterocytes revealed a significant increase in HRP-containing endosomes in enterocytes revealed a significant increase in

**endothome number (0.77 ± 0.16 vs 0.38 ± 0.15, per apical area of 4 ± 6 pm², p < 0.04). Moreover, there was a positive correlation between the number of HRP-filled endosomes and HRP flux in both control (n=8, p < 0.005) and stressed animals (n=65, p < 0.05), with similar slopes and y-axis offsets of the correlation lines, indicating that the increase in endocytosis was primarily due to increased endocytosis. We conclude that in addition to strong acute cold restraint stress, also mild subchronic noise stress may cause a diversion in intestinal barrier function by increased endocytosis of luminal antigens, although with no clear involvement of paracellular leak. The twofold increase in macromolecular permeability may lead to an increased antigenic load to the mucosal immune system, thus possibly stimulating sensitization to food antigens and inflammatory responses of the gut mucosa. This research was supported in part by a grant from Nutricia, Zoetermeer, The Netherlands.