

## Mechanism of Interdigestive Contractions of GI Tract

Toku Takahashi

Department of Surgery, Medical College of Wisconsin, Milwaukee, Wisconsin

Migrating motor complex (MMC) is well characterized by the appearance of gastrointestinal (GI) contractions in the interdigestive state. Duodenal motilin plays an important role to initiate MMC. Gastric-MMC (G-MMC) and intestinal MMC (I-MMC) are controlled by different mechanisms, because vagal blockade abolishes G-MMC, but not I-MMC. 5-HT<sub>3</sub> antagonists attenuate G-MMC, but not I-MMC.

We raised the following questions. *Is released motilin cause or effect of gastric phase III? How is I-MMC regulated? How does motilin interact with 5-HT to mediate MMC?*

Five strain gauge transducers were implanted on the stomach and intestine in dogs. To investigate the correlation between luminal 5-HT and phase III contractions, gastric and duodenal juice was collected during MMC cycle. 5-HT concentration in the gastric and duodenal juice was measured by HPLC. To investigate whether luminal 5-HT initiates MMC, 5-HT ( $10^{-8}$ - $10^{-6}$  M) was administered into the duodenum 20 min after gastric phase III. To investigate the involvement of 5-HT<sub>3</sub> or 5-HT<sub>4</sub> receptors in mediating G-MMC and I-MMC, 5-HT<sub>3</sub> antagonists (ondansetron) or 5-HT<sub>4</sub> antagonists (GR 125,487) were intravenously infused for 120 min.

Luminal administration of 5-HT ( $10^{-6}$  M) initiated duodenal phase II followed by G-MMC and I-MMC with a concomitant increase of plasma motilin release. Duodenal 5-HT concentration was significantly increased during phase II ( $59 \pm 9$  ng/ml) and phase III ( $251 \pm 21$  ng/ml), compared to that of phase I ( $29 \pm 5$  ng/ml). On the other hand, 5-HT content in the stomach was not significantly changed throughout MMC cycle. Intravenous infusion of motilin ( $0.3 \mu\text{g/kg/hr}$ ) increased luminal 5-HT content and induced G-MMC and I-MMC. 5-HT<sub>4</sub> antagonists significantly inhibited both of G-MMC and I-MMC, while 5-HT<sub>3</sub> antagonists inhibited only G-MMC. We propose that MMC cycle is mediated via the interaction between motilin and 5-HT by the positive feedback mechanism.