A NOVEL ANIMAL MODEL OF GASTROPARESIS

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Background: Gastroparesis, or delayed gastric emptying, occurs in 24.2 per 100,000 adults. Although the prevalence is unknown in the pediatric population, the cost of hospital care for children with gastroparesis has risen dramatically over the last decade. Gastroparesis is observed in a broad range of undernourished states including small for gestational age neonates, children with acute and profound weight loss, and adolescents with anorexia nervosa. Undernutrition creates a cycle of physiologic disturbances, including delayed gastric emptying, that make catch-up growth difficult. Animal models are needed to further elucidate causes of and potential therapies for malnutrition-associated gastroparesis. We aimed to characterize a novel model of gastroparesis induced by early postnatal malnutrition.

Materials/Methods: Malnutrition was induced by timed maternal separation (TmSep) of pups from lactating dams for 12 hours per day. Control mouse pups nursed uninterrupted. On day-of-life 15, a gastric gavage of fluorescein isothiocyanate-conjugated dextran was administered, and the gastrointestinal tract was harvested 30 minutes later. Percent gastric emptying was determined by quantifying fluorescence throughout the gastrointestinal tract. H&E-stained sections were imaged on an Eclipse 90i microscope, and thickness of muscularis propria and mucosa was measured by a blinded observer using NIS Elements (Nikon).

Results: Compared to control pups, malnourished mice were moderately underweight, mean 4.45 ± 0.1 g versus 6.96 ± 0.2 g ($p < 0.0001$). On gross examination, stomachs of TmSep mice were strikingly distended compared to control mice. Gastric emptying was impaired in TmSep versus controls (87.3% versus 97.0%, $p=0.023$). The gastric smooth muscle layer was thinner in TmSep mice versus controls, mean 16.9 ± 5.3 μm versus 30.4 ± 8.8 μm ($p=0.03$).

Conclusions: We present a novel model of malnutrition-associated gastroparesis induced by timed separation of mouse pups from lactating dams. We further highlight thinning of the gastric smooth muscle layer as a potential etiology that warrants further investigation, although we cannot yet rule out potential contributions from an altered enteric nervous system, gut microbiota, or neuro-hormonal signaling pathways. Defining the underlying pathophysiology may create opportunities for new therapeutic interventions for gastroparesis in children.