Learning about human physiology from animals

Eating Like a Pig

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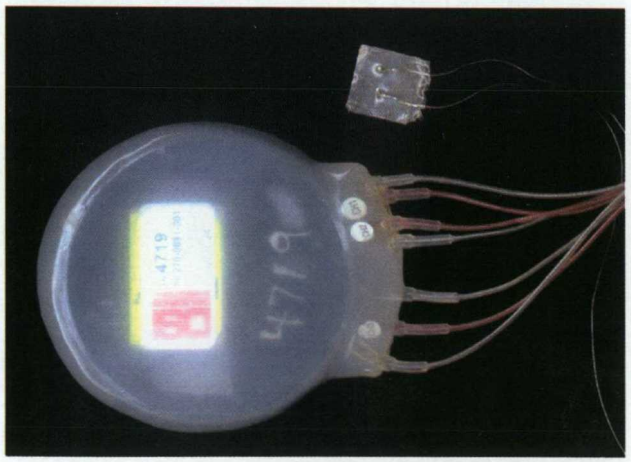
Newborn piglets offer an excellent model for studying the human digestive system, enabling us to learn much about our own physiology and to develop treatment methods for many illnesses

Mammals depend completely upon their mothers at birth, even though all the organs necessary for independent survival do develop in the fetal stage. One such organ is the alimentary canal, which primarily functions though contractile action. Gut mobility plays a key role in the processes of digestion, i.e. grinding up, mixing, and transporting food materials through successive digestive tract sections, enabling nutritive substances to be absorbed. The development of contractile action begins at an early fetal stage in mammals (around the 12th week of pregnancy in humans) but continues long after birth.

Birth and the first several days of life are a critical time for newborns, requiring very rapid adaptation to life outside the uterus. This pertains in particular to the alimentary canal, which suddenly becomes responsible for gathering and absorbing the nutrients necessary to facilitate the growth and development of the entire organism. The first observations and studies of contractile activity date back to the early 19th century. Contractions in rabbit stomach and intestine muscles were registered in 1869. A few years later, in 1893, Santiago Ramón y Cajal discovered the alimentary canal cells responsible for generating and maintaining the basic electric rhythm of the organ's smooth muscles - called interstitial Cajal cells.



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This telemetric implant with biopolar electrodes of our own design, implanted in piglets, collects data about intestinal contractile activity

Keeping time "in three"

Small intestine motor activity in both humans and animals shows characteristic models of muscle action. The interdigestive electromyographic (EMG) activity of the digestive tract, repeating in a 1-2 hour cycle, is described as a migrating myoelectric complex (MMC) which consists of 3 phases. Phase 1 is characterized by a lack of action potentials, phase 2 by the presence of regularly appearing action potentials accompanied by peristaltic movements (mixing food material), while phase 3, involving the presence of regular muscle electrical activity, is responsible for propelling food along the intestine. In weaned piglets, the ingestion of solid food disrupts the established digestive tract activity and initiates the appearance, for 1-2 hours, of a digestive rhythm similar to phase 2 of the MMC, i.e. increased peristaltic intestine activity.

Digestive tract motor activity begins to develop during the prenatal period, depending on the specific species of mammal. Pioneering research on small intestine activity was carried out on dog and sheep fetuses. Electrodes implanted on the serous membrane of the small intestine and connected to an electromyograph were used to register the activity of intestinal muscles. Initially such activity was disorganized, yet as the fetus developed it became more regular and proceeded along increasing lengths of the intestine. Several days prior to birth and on the day of birth, sheep fetuses already showed regular digestive tract activity. Puppies, however, were seen to still have "fetal" activity even after birth, with models characteristic of the normal digestive system only appearing on the 16th day of life.

The first recording of small intestine motor activity in humans was carried out in premature babies

Scott Bauer/USDA

The processes of digestion and alimentary tract development proceed very similarly in human babies and piglets

born between the 28th and 32nd week of pregnancy. Individual action potentials were then noted, with 1–2-minute action complexes appearing increasingly more frequently, similar to the "fetal" complex in sheep and goats. Between the 34th and 36th week of pregnancy, human fetuses show an increased duration and number of action potentials, and between the 37th and 46th week, the three-phase MMC is recorded. Also significant is the fact that fetuses develop a sucking and swallowing reflex as early as around the 16th week of pregnancy, enabling them to take in from 4 to 450 ml of amniotic fluid per day. The hormones and growth factors such fluid contains boost the development of the alimentary canal and give the child a "head start" after birth. Small intestine activity is chiefly regulated by the enteric nervous system (ENS), which begins to develop in humans around the 9th week of pregnancy. This is also stimulated by many gastrointestinal hormones, such as: motilin, cholecystokinin, gastrin, glucagon, vasoactive intestinal peptide, and gastric inhibitory peptide.

The mystery of digestion

Premature babies do not have a fully developed nervous system, and so such children may experience trouble with proper intestinal activity, or even a complete absence of it. Related problems include food tolerance complications, intestinal stasis, and also overgrowth of bacterial flora. Because many studies are not carried out on children themselves, researchers look to animal models. Newborn piglets have proven to offer an ideal model for studying the development of the human digestive system. Piglets' digestive tract goes through the same developmental stages and functional changes as seen in human babies, such as the change in stomach pH and the secretion of various digestive enzymes when shifting from milk to solid food.

Nevertheless, small intestine motor activity in newborn piglets remains in large part a mystery, chiefly due to methodological difficulties. Up until now, the earliest that digestive motor activity was registered was in 12-day animals. A new "telemetric" method, which takes measurements using small electrodes placed in the intestines, ensures that the animals can move about freely and remain in contact with one another, thus minimizing stress.

Our results can help us learn what stimulates and what inhibits digestive tract activity not only in piglets, but also in humans

Our research has also employed an artificial sow system, which enables newborn piglets to be raised under laboratory conditions. The system simulates the piglet's biological feeding cycle, providing milk substitute in the right quantities (34 ml per feeding) and frequency (every 75 minutes, 20 times a day). In their fifth day of life, the piglets had bipolar electrodes implanted on the serous membrane of the duodenum (E1 and E2) and small intestine (E3), linked to a three-channel telemetric implant subsequently placed between the oblique stomach muscles. Signals began to be recorded immediately after the surgery, using data archiving equipment.

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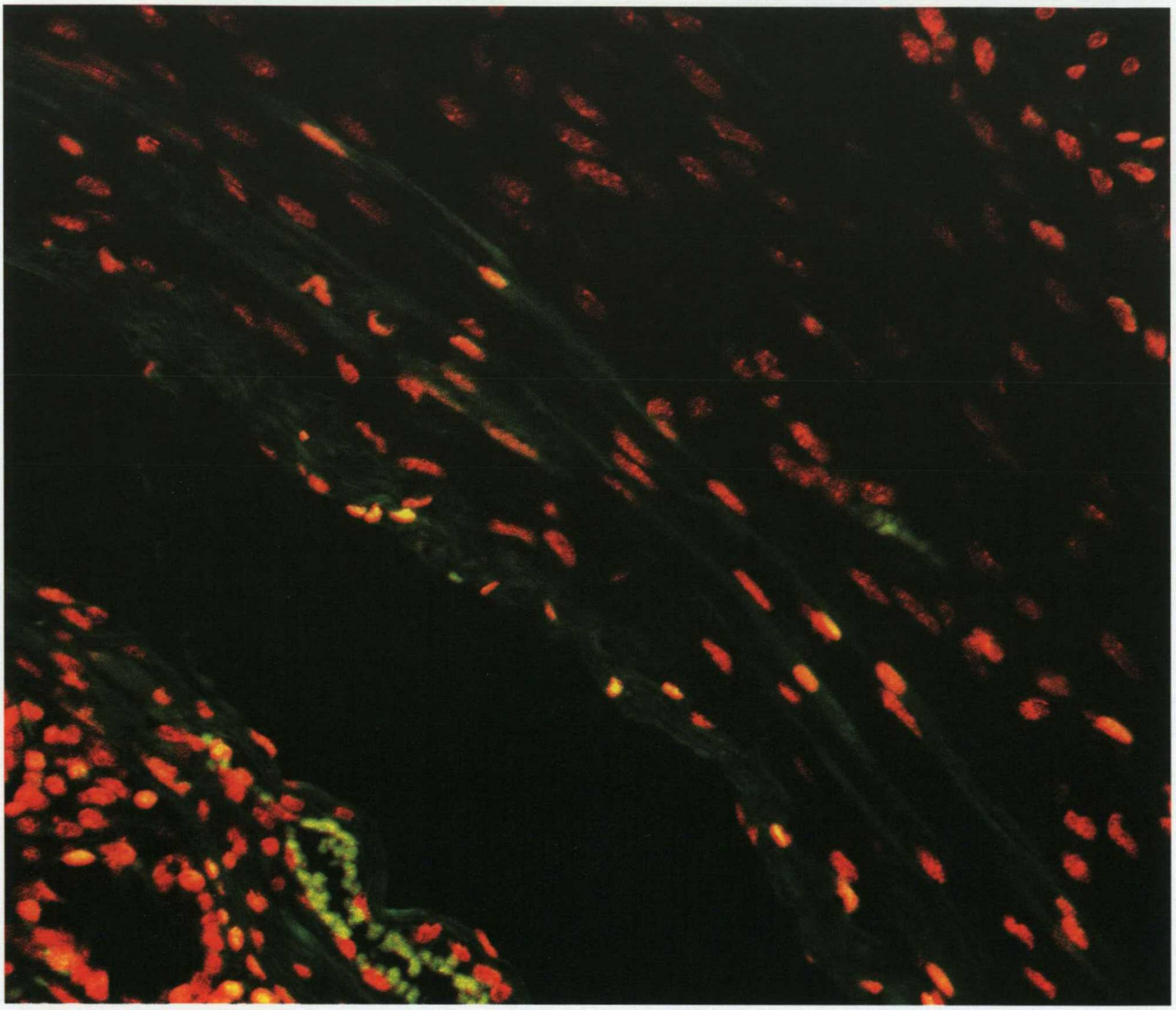

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Central small intestine muscular tissue in a 7-day-old piglet, with spindle-shaped interstitial Cajal cells visible in green

Pioneering research

We are the first research team in the world to produce evidence of regular contractile activity in piglet small intestines on their 6th day of life. Unfortunately, our results do not allow us to assert whether such activity also occurs during fetal life in piglets (or in humans or sheep), or whether it appears immediately after birth, as in the case of puppies. Moreover, we are the first team in the world to telemetrically register the contractile activity of small intestine smooth muscles in piglets during their shift from milk feeding to solid food. Despite the fact that we are at the beginning of our research, we can already say significantly more about digestive system activity in the first, critical days of life in newborn piglets. Our results can also help us learn how intestinal activity is affected by the bioactive factors contained in milk - i.e. what stimulates and what inhibits digestive tract activity. Not only in piglets - our results can be quite easily extrapolated to human babies. ■

Further reading:

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