AMERICAN JOURNAL OF PHYSIOLOGY
Vol. 226, No. 6, June 1974. *Printed in U.S.A.*

A possible origin of intestinal gradients and their relation to motility

DONALD D. JOB, WILLIAM J. GRIFFING, AND BRUCE E. RODDA
Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, Indiana 46206

JOB, DONALD D., WILLIAM J. GRIFFING, AND BRUCE E. RODDA. *A possible origin of intestinal gradients and their relation to motility.* Am. J. Physiol. 226(6): 1510–1515. 1974.—Sections for electron microscopy were made of longitudinal muscle from the proximal jejunum and distal ileum of cats. Mitochondrial distribution and other morphological features were examined quantitatively to determine whether there were any regional differences. Mitochondria were clustered near the plasma membrane or near the nucleus. Of those near the plasma membrane, the ones in the jejunum were substantially closer on the average than were those in the ileum. This difference alone could account for the slower frequency of electrical slow waves observed in the ileum. Cell diameters were greater in the ileal sections than in the jejunal sections, which could also account for slower slow-wave conduction. The presence of more mitochondria per micrometer of cell perimeter in jejunum than ileum suggests also the basis for a number of metabolic gradients.

intestinal slow waves; metabolic gradients; smooth muscle morphology; slow-wave frequency gradient; smooth muscle electrophysiology

NUMEROUS STUDIES HAVE INDICATED the presence of gradients down the small intestine of mammals. One of the earliest reports on intestinal gradients was on the gradient of mechanical activity by Alvarez (1). Since that time other gradients have been described. Only infrequently, however, has the goal been to explain the basis for the mechanical gradient. Alvarez and Starkweather (2) proposed from limited evidence that the mechanical gradient was due to a metabolic gradient. More recently, the oxygen consumption has been found to decrease aborally in the cat small intestine (12). This gradient, however, was attributed to the mucosal layer rather than to the muscle layer (12).

In addition to gradients in metabolic rates, there have been reports of gradients in substrates or products of metabolism. Hexokinase activity and adenosine triphosphate (ATP) levels have been shown generally to decrease aborally (14, 15). Serotonin also exhibits a diminishing gradient down the small intestine in cats and in other species (13, 28). All these latter gradients and others such as those associated with absorption from the lumen could result from regional differences in metabolism.

The connection between metabolic gradients and mechanical gradients is not obvious. Good evidence is available (3, 4, 5, 8, 10, 22) that slow waves act as pacemakers for the mechanical activity. The other side of the relationship, however, between slow waves and metabolism is not as clear. It is well documented that intestinal slow waves are sensitive to changes in metabolism. Anoxia, for example, is known to inhibit electrical slow waves both in intact animals (7) and in isolated tissue (16). Also, in man, Christensen et al. (6) have shown a direct correlation between thyroid function and slow-wave frequency. The link between metabolism and slow-wave frequency, however, has not been carefully examined until recently. Job (17) has reported that slow waves are sensitive to metabolic inhibitors which interfere with oxidative phosphorylation. Evidence was also presented which led to the suggestion that slow-wave frequency was set by a complex interaction between mitochondria and the plasma membrane.

If slow-wave frequency is determined by interaction between parameters rather than by the parameters themselves, then comparison of different regions of the intestine may give a clue as to which parameters give rise to the different intrinsic frequencies. Three general control mechanisms occur which involve a mitochondria-plasma membrane interaction and which could vary according to region. First, the ionic fluxes or distribution across the membrane could be different. This possibility has been examined in another paper (18). The second area for frequency control would be biochemical in nature. The synthesis rates or amounts of substrate could vary according to the region giving rise to a metabolic gradient. Since in previous studies frequency was relatively stable under varying states of metabolic poisoning, this possibility does not seem likely (17). A third property that could influence frequency would be the spatial arrangements of mitochondria. The distribution of mitochondria could vary in such a way that, by virtue of having fewer mitochondria or mitochondria farther from the membrane, the interaction between energy source and energy sink would be weaker. A decrease in the degree of interaction could cause a decrease in frequency. The exploration of this latter possibility is the principal object of the present study.

MATERIALS AND METHODS

Segments of small intestine, 2–3 cm long, were obtained from cats under α-chloralose anesthesia (65 mg/kg). These segments were either from the proximal portion of the jejunum or the distal portion of the ileum. The mucosal and submucosal layers were removed under Tyrode solution. The remaining cylinder of tissue was slipped over a Plexiglas rod and equilibrated in Tyrode solution at 35–37°C.