

Intestinal Motility as Influenced Through Extrinsic Nerves as a Result of Central Stimulation by Bulbocapnine.

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Bulbocapnine has been shown to stimulate both sympathetic and parasympathetic centers¹ and to change the level of blood sugar of rats by way of the vago-insulin and sympathetic-adrenal systems. The present study was undertaken to observe the effect of this drug on intestinal motility and rate in dogs. This rate has been shown to be very constant for any given level of intestine.²⁻⁷

Methods. Trained dogs with exteriorized loops of small intestine in continuity, with blood supply intact, enclosed in bipediced tubes of skin⁸ were used. Records were made from the loops by a 2 tambour air-displacement system. Group 1 had intact nerve supply, Group 2 bilateral vagotomies, Group 3 bilateral splanchnicotomies. The dogs were fasted 18 hr. Control readings for character and rate of intestinal contractions were obtained at the start of each experiment. Intestinal contractions were recorded continuously. Blood sugar levels (Folin-Wu) were determined as controls and after bulbocapnine at 15, 45, and 90 min, and later as indicated.

Each group of animals contained some whose loops were located just below the

duodenum and others with loops placed just above the ileo-colic sphincter. These levels may behave differently.⁹ Bulbocapnine phosphate was administered subcutaneously, usually in doses of 25-30 mg/kg.

Results. Group 1. Normal dogs. Six animals were used. In 5 of these there was a complete inhibition of intestinal activity. The remaining dog showed increased amplitude of contractions. There was no correlation between increased amplitude of contractions and fall in blood sugar, or vice versa. For instance, of the dogs showing the 2 highest elevations of blood sugar levels after bulbocapnine, the intestine of one was inhibited and the amplitude of intestinal contractions of the other was augmented. Intestinal effects usually preceded the changes in blood sugar levels. The established rate of contraction was not changed in any instance.

Group 2. Splanchnicotomized dogs. Seven animals made up this series. After bulbocapnine all showed an increase in amplitude of intestinal contractions. Blood sugar levels were unchanged in 6 of 7 cases. In the seventh animal there was an elevation of 26 mg %. Rates of intestinal contraction were uninfluenced.

Group 3. Vagotomized dogs. Five dogs comprised this group. Amplitude of contraction of loops of intestine at low levels was inhibited after bulbocapnine, those located high in the jejunum presented increased amplitude of contractions. Blood sugar was elevated in 4 cases, unchanged in a fifth. There was no change in the rate of contraction.

Two dogs with normally innervated Thiry-Vella fistulae of the jejunum (recorded by a

¹ Feldman, J., Cortell, R., and Gellhorn, E., *Proc. Soc. Exp. Biol. and Med.*, 1941, **46**, 157.

² Oppenheimer, M. J., and Mann, F. C., *Am. J. Digest. Dis.*, 1941, **8**, 86.

³ Oppenheimer, M. J., and Mann, F. C., *Am. J. Digest. Dis.*, 1941, **8**, 90.

⁴ Douglass, D. M., and Mann, F. C., *Am. J. Digest. Dis.*, 1939, **6**, 318.

⁵ Douglass, D. M., and Mann, F. C., *Am. J. Digest. Dis.*, 1939, **6**, 434.

⁶ Douglass, D. M., and Mann, F. C., *Am. J. Digest. Dis.*, 1940, **7**, 53.

⁷ Castleton, K. B., *Am. J. Physiol.*, 1934, **107**, 641.

⁸ Biebl, M., *Klin. Wchsch.*, 1930, **9**, 1674.

⁹ Oppenheimer, M. J., and Glyer, N. M., *Am. J. Digest. Dis.*, 1941, **8**, 471.

distending balloon) were tested for comparison. Although blood sugar was elevated in both, in neither case was the character or rate of contraction of the intestine changed. A dog with a completely denervated exteriorized loop⁸ showed no changes in blood sugar levels nor in intestinal activity after bulbocapnine.

There was a definite threshold for dosage with bulbocapnine. Twenty mg per kg which produce catalepsy, are ineffective for blood sugar and intestinal motility. Twenty-five to 30 mg per kg always produced a change in amplitude of intestinal activity, usually after a short period of hyperkinesia.

Hippus of the pupil and alternating tachycardia-bradycardia were added evidence of mixed sympathetic and parasympathetic activity.

Discussion. In normal rats the blood sugar is uniformly elevated after bulbocapnine.¹ In dogs this level may either rise or fall. Evidently in the latter test animal sympathetic predominance is by no means uniform. The intestine is, in contrast, regularly inhibited. When vagus influences act alone the blood sugar level is usually unchanged while the amplitude of intestinal activity was uniformly augmented. This finding may be compared with that in rats where the blood sugar level is depressed 15 mg % in adrenalectomized cases.¹ Lastly, when the splanchnics act unopposed blood sugar is elevated in most cases. However, intestinal segments highly placed showed augmented amplitude while those situated lower down were inhibited. In rats after bulbocapnine there was a large elevation of blood sugar if the vagi were cut.¹ Hence, as far as the intestine is concerned the splanchnic mechanism gives variable results depending on the level of intestine studied.

Thus it may be pointed out that as a result of central stimulation by bulbocapnine the intestinal responses and blood sugar fluctuations may behave differently, even though both are activated by the same dual (Group 1) or single (Group 2 and 3) efferent mechanism. The vagus effect on motility may be similar to the high intravesical pres-

ures found in the urinary bladder.¹⁰ One can better understand the increased activity of highly placed intestinal loops as a result of sympathetic stimulation when it is pointed out that bulbocapnine causes a peripheral vasodilatation¹¹ which may reverse the usual action of the extrinsic nerves.¹²

Thiry-Vella fistulæ show no effect after bulbocapnine possibly because distension markedly influences reflex responses.¹³ The Biebl loop,⁸ as used in this study is recorded without distension.

Threshold observations confirm the work of Spiegel.¹⁴ Bulbocapnine, like several other agents,^{2-7, 9} did not change the rate of intestinal contraction.

Conclusions. 1. Although bulbocapnine acts centrally and stimulates both sympathetic and parasympathetic mechanisms, in dogs it showed qualitative and quantitative differences between its effects upon the level of blood sugar and upon intestinal activity. 2. In normal dogs under bulbocapnine either mechanism may predominate in respect to blood sugar levels. Sympathetic effects were most important for intestinal motility. Amplitude of contraction was diminished. 3. In vagotomized dogs loops of intestine placed just below the duodenum showed augmented amplitude of contraction after bulbocapnine, those placed just above the ileo-cecal valve were inhibited. Blood sugar was elevated in most cases. 4. In splanchnicotomized dogs the vagus mechanism is activated by bulbocapnine in respect to amplitude of intestinal contractions but not for blood sugar levels. 5. Bulbocapnine does not change the rate of intestinal contractions.

¹⁰ Kolb, L. C., and Langworthy, O. R., *J. Pharm. Exp. Therap.*, 1938, **63**, 108.

¹¹ Molitor, H., *J. Pharm. Exp. Therap.*, 1938, **62**, 16.

¹² Wiggers, C. J., *Physiology in Health and Disease*, Lea & Febiger, Philadelphia, 1939.

¹³ Youmans, W. B., Meek, W. J., and Herrin, R. C., *Am. J. Physiol.*, 1937, **120**, 750; 1938, **124**, 470.

¹⁴ Spiegel, E. A., *Dtsch. Z. f. Nervenheilk.*, 1932, **124**, 104.