Possible Role of Plasma Neurotensin in Regulating the Excitatory Neural Control of the Rectum of the Fowl

Hidenori OHASHI, Seiichi KOMORI, Seong-Chun KWON, and Toshihiro UNNO

Laboratory of Pharmacology, Department of Veterinary Science, Faculty of Agriculture, Gifu University, Gifu 501-11, Japan

(Received 9 June 1988/Accepted 23 August 1988)

ABSTRACT. Effects of neurotensin (NT) applied via the blood vessel on the responses to stimulation of Remak’s nerve (RNS) were investigated in the chicken isolated and perfused rectums. NT (5 ng-2 μg/ml) produced a concentration-dependent inhibition of the constituent contraction but not relaxation of the responses to RNS. In addition, high concentrations of NT (over 80 ng/ml) produced a contraction of the rectal muscle. Propranolol, a beta-adrenoeceptor blocking agent, and guanethidene, an adrenergic neurone blocking agent, were able to reduce the inhibitory effect of NT on the response to RNS while potentiating the contractile effect of NT on the rectal muscle. NT (0.1 and 1 μg/ml), like norepinephrine, decreased the flow rate of perfusate from the isolated rectum which was perfused at a constant pressure. Guanethidene enhanced norepinephrine-induced vasoconstriction, and phentolamine, an alpha-adrenoeceptor blocking agent, plus propranolol was able to abolish it. Either of these prior applications resulted in a small but significant reduction of NT-induced vasoconstriction. These findings suggest that NT in plasma may function as a circulating hormone to exhibit an inhibitory action on the excitatory neural input to the rectum in the chicken, and that catecholamine release from adrenergic nerve terminals by NT may account for some but not all of the activity.—KEY WORDS: chicken, inhibition, neurotensin, rectum, Remak’s nerve.


Remak’s nerve (Nervus intestinalis) is a unique avian autonomic nerve, which may work as efferent pathways for nerve reflexes involved in various functions of the intestine. In the rectal region, the nerve is involved in the regulation of functions to store and expel contents of the rectum. The chicken isolated rectum responds to electrical stimulation of Remak’s nerve with a rapid contraction followed by a long-lasting relaxation. The response appears to be due mainly to stimulation of non-adrenergic, non-cholinergic (NANC) excitatory and inhibitory nerves [1, 2, 12, 15, 16]. Recently, chicken neurotensin (NT), which is identical in biological activities to bovine NT but different in its amino acid composition, has been isolated from the rectum of the chicken [4] and it is considered to be a possible transmitter of NANC excitatory nerves in chicken rectum [6]. Besides, it has been suggested that NT play a role as a circulating hormone in the gastrointestinal tract. This suggestion is based on the findings that the peptide is present in human plasma and its level is elevated following ingestion of meals, especially a high-fat meal [3, 14]. It is possible that changes in plasma level of chicken NT could modulate some processes in the rectum under the control of Remak’s nerve.

In the present study, an attempt has been made to explore the possible function of NT as a circulating hormone by determining how NT applied via the blood vessel alters the responses elicited by stimulation of Remak’s nerve. The present results provide some evidence that NT in plasma can suppress the excitatory neural input to the rectum partially through the release of
endogenous catecholamine from the vascular bed. The physiological meaning of this effect is discussed.

MATERIALS AND METHODS

*Animals:* Adult chickens of either sex were obtained from commercial sources. Birds were stunned and bled to death. The whole rectum was excised together with Remak’s nerve, the caudal mesenteric artery and vein. Its lumen was flushed clean with Tyrode solution. The isolated rectum was immersed in a large Petri dish containing Tyrode solution, and the Remak’s nerve trunk was tied off at the anal end with cotton thread, separated by a length of 1 cm of the nerve (as measured from the anal cut end in the oral direction) from the rectal wall and detached carefully from adhering tissues. In some preparations, a few nerve branches originating from Remak ganglia and supplying the organ were cut just after they left Remak’s nerve trunk and were dissected free from the mesentery. The oral cut end of the rectum was ligatured with vessels and Remak’s nerve. An L-shaped glass tube, 7 mm in diameter, was inserted into rectal lumen from the anal cut end up to about 1 cm and then tied together with the rectal wall. The tube served both as a cannula through which mucoid-like liquid was removed from the lumen and as an arm clamping to a rigid upright position. The caudal mesenteric artery and vein were each cannulated with glass tubes with 0.5 and 2.0 mm internal diameters, respectively. All vessels other than those described above were ligatured.

*Perfusion via the blood vessels:* The rectum was mounted horizontally in a 80 ml organ bath filled with Tyrode solution kept at 30±1°C, and perfused with Tyrode solution via the caudal mesenteric artery at a flow rate of 3.0 ml/min by a roller pump (Perista, SJ 1211). The venous effluent was collected in a small chamber via the vein cannula and removed with an aspirator. In experiments where vasoconstrictive effects of drugs were examined, a device for perfusing at a constant pressure was used instead of a roller pump and drops of the venous effluent were recorded. The preparation was initially placed under a resting tension of 5 g and rested for at least 30 min before start of each experiment.

*Nerve stimulation and measurement of mechanical responses:* The anal end of Remak’s nerve trunk was placed in a bipolar suction electrode for electrical stimulation. Special care was taken to avoid dislocation of the stimulating site in an experiment. Trains of square-wave pulses at supramaximal intensity of 0.8 msec duration were applied at various frequencies at an interval of 4 or 6 min from a stimulator (Nihon Kohden, SEN-3013). Changes in tension of the longitudinal direction of the rectum were isometrically measured by a force-displacement transducer (Nihon Kohden, TB 612Z) and recorded on a pen recorder (Hitachi, 056).

*Solutions and drugs:* Tyrode solution was used of the following composition (mM): NaCl 136.9, KCl 2.7, NaH₂PO₄ 0.4, CaCl₂ 1.8, MgCl₂ 2.5, NaHCO₃ 11.9 and glucose 5.6, which was bubbled with air. Drugs used were stropeine sulfate (Tanabe), guanethidine sulfate (Ciba-Geigy), phentolamine mesylate (Ciba-Geigy), propranolol hydrochloride (Sumitomokagaku), adenosine 5'-triphosphate (ATP) (Sigma), alpha, betamethylene ATP (Sigma), human angiotensin II (Peptide Institute Inc., Osaka) and bovine neurotensin (Peptide Institute Inc., Osaka). The stock solutions of all drugs were dissolved in distilled water, made up at 1000 or more times higher concentrations than those used for the experiments, and stored at −20°C. A certain amount of concentrated drug solution was added to Tyrode solution to give the final desired
Role of Plasma Neurotensin in Fowl

Fig. 1. Stimulus frequency-response curve for contractions of the isolated, perfused rectum preparation to Remak's nerve stimulation (square-wave pulses of 0.8 msec duration for 5 sec). Abscissa scale: log stimulus frequency. Ordinate scale: % change in the size of the contractile response (the size of the contractile response at 20 Hz was taken as 100%). Each point represents the mean of 4 measurements; vertical lines indicate S.E.M. A solution containing strophine (250 ng/ml) was perfused at a flow rate of 3 ml/min throughout the experiments.

Concentration, which was used as the perfusing solution for a certain period. The drug was washed away by replacing the drug solution with drug-free solution.

Statistical analysis: Means are expressed with ± means of the standard error. The statistical significance was evaluated by Student's t test for paired samples and P values of 0.05 or less were considered significant.

Results

Responses to stimulation of Remak's nerve: Electrical stimulation of Remak's nerve (RNS) elicited a biphasic response in the rectum, consisting of an initial rapid contraction and a subsequent long-lasting relaxation. Main constituents of the response were preserved in the presence of atropine (500 ng/ml) and guanethidine (1 µg/ml). The pharmacological properties indicate its non-adrenergic, non-cholinergic nature, as previously reported by Takewaki et al. [16]. Figure 1 shows the stimulus frequency-contractile response relationship. Trains for 5 sec of stimulus pulses were applied at various frequencies at a 4 or 6 min interval. The magnitude of the contractile response varied in a frequency-dependent manner, and the maximal response was obtained at 20 Hz. The response magnitude was rather reduced when stimulus frequency was increased to 30 Hz or 40 Hz.

Effect of NT on the contractile responses: As contractile responses to RNS at 10 Hz were recorded every 4 min, NT was applied to the rectum for 90 sec at five different concentrations (5 ng/ml-2 µg/ml) in random order by perfusing Tyrode solution containing this peptide via the caudal mesenteric artery. In the present experiments, bovine NT was used because synthetic chicken NT is not available yet. NT invariably reduced the contractile responses to RNS. The effect of NT, 500 ng/ml, is shown in Fig. 2: The maximal reduction of more than 75% was observed in the first response from the NT application. The inhibitory effect faded gradually with time after termination of the NT application and was completely reversed within 30 min. When the concentration was higher than 80 ng/ml, NT produced a small and transient contraction of the rectum preceding the inhibition of the responses to RNS. Figure 3A shows plots of the maximal reduction of the contractile responses to RNS and the time required for recovery from the inhibitory effect against NT concentration. With concentrations of 5, 20, 80, 500 and 2000 ng/ml, NT reduced the contractile responses by 28±6, 51±1, 67±5, 75±7 and 86±4% (n=5 to 7), respectively. The IC50 value for the maximal reduction of the contractile response to RNS was 19±3 ng/ml (n=3). The time required for recov-
Fig. 2. The effect of neurotensin, 500 ng/ml, (NT, □) on the contractile responses in the isolated, perfused rectum preparation to stimulation of Remak's nerve (square-wave pulses of 0.8 msec duration at 10 Hz for 5 sec). A solution containing atropine (250 ng/ml) was perfused at a flow rate of 3 ml/min throughout the experiment. Neurotensin was applied by perfusing its solution for 90 sec via the arterial cannula.

Fig. 3. Concentration-response curves for the inhibitory effect of neurotensin on the contractile responses to stimulation of the trunk (A) and branches (B) of Remak's nerve (●, square-wave pulses of 0.8 msec duration at 10 Hz for 5 sec) and for the time required for recovery from the inhibitory effect (○), in the isolated, perfused rectum preparation. In A and B, abscissa scale: -log concentration of neurotensin (NT); left ordinate scale: % change in the size of the maximally-reduced contractile responses (the size of the contractile response for the immediately preceding period in normal solution was taken 100%); right ordinate scale: the time required for complete recovery. Each point represents the mean of 5 to 7 measurements in A and of 5 to 11 measurements in B; vertical lines indicate S.E.M. A solution containing atropine (250 ng/ml) was perfused at a flow rate of 3 ml/min throughout the experiments. Neurotensin was applied by perfusing its solution for 90 sec via the arterial cannula.
Fig. 4. The effect of neurotensin, 500 ng/ml, (NT, •) on the contractile responses of the isolated, perfused rectum preparation to stimulation of the trunk (●) and branches (○) of Remak's nerve (square-wave pulses of 0.8 msec duration at 10 Hz for 7 sec). A solution containing atropine (300 ng/ml) was perfused at a flow rate of 3 ml/min throughout the experiment. Neurotensin was applied by perfusing its solution for 90 sec via the arterial cannula.

er from the inhibitory effect was also concentration-dependent (see Fig. 3A). When perfused in concentrations higher than 500 ng/ml, NT produced a strong contraction of the circular muscle of the rectum by which tension development in the longitudinal direction was appreciably prevented. This led to an exaggerated result of the inhibitory effect of NT. In all experiments, the constituent relaxation of the nerve-mediated responses remained almost unchanged after the perfusion of NT.

Effect of neurotensin on the contractile responses to stimulation of branches of Remak's nerve: When the trunk of Remak's nerve is stimulated to elicit rectal responses, ganglionic transmission occurs in the nerve pathways [5]. In an attempt to see whether NT acts at the ganglion to inhibit the contractile responses, effect of NT on contractile responses to stimulation of branches of Remak's nerve, which originate from cells in the ganglia of Remak's nerve trunk and run to the rectum, was investigated. In comparison with that elicited by RNS, the response to stimulation of the branches (postganglionic nerve stimulation) was small in magnitude, but had a similar pattern, consisting of an initial, brief contraction followed by a prolonged relaxation (Fig. 4). In every experiment, the contractile responses were inhibited by NT. The results are summarized in Fig. 3B. Following perfusion for 90s in five different concentrations of 5, 20, 80, 500 and 2000 ng/ml, the responses were reduced by 24±8, 45±6, 62±8, 86±3 and 75±12% (n=5 to 11), respectively. The value for each NT concentration was not significantly different from that in the case of RNS. This suggests that NT may exhibit its action at the neuromuscular junction or the smooth muscle cells.

Repetition of neurotensin application: As shown in Fig. 5, when NT (100 ng/ml) was perfused over a period of 15 min, the inhibitory effect on the contractile response to RNS gradually faded even during the perfusing period. Such a long exposure to NT rendered the preparation less sensitive to subsequently-applied NT. This inhibitory
response to NT exhibited desensitization and the desensitization subsided slowly with time (see also Fig. 5).

Effects of ATP and alpha, beta-methylene ATP on the contractile responses: RNS elicits excitatory junction potentials (EJP)s which result from increased membrane permeability to ions, and the EJPs are thought to be the initial membrane responses leading to the contractile responses [8, 12, 15]. NT produced an increase in membrane permeability to ions resulting in membrane depolarization in smooth muscle cells of chicken rectum (unpublished data). Thus, NT must be capable of decreasing the EJP amplitude and this inhibitory effect on the neuromuscular transmission could be responsible for the inhibition of the contractile responses. To elucidate this aspect, adenosine 5'-triphosphate (ATP) and its stable analogue, alpha, beta-methylene ATP, which have been reported to exert a strong depolarizing effect on the smooth muscle membrane resulted from an increase in membrane conductance [7], were applied in the same way as NT and their effects on the contractile response to RNS were investigated.

Perfusion of ATP (lower than 40 µg/ml) had little or no effect on the contractile responses. With ATP in a concentration of 40 µg/ml, a reduction in the magnitude was observed only in the first contractile response from the end of the ATP application, as shown in Fig. 6. When perfused in a concentration of 1 µg/ml, alpha, beta-
methylene ATP itself induced a contraction whose magnitude was about 40% of the contractile response to RNS with having almost no effect on the contractile response to RNS (see also Fig. 6). Thus, it seems unlikely that the inhibitory effect of NT on the contractile responses is attributable totally to its direct action on the effector cells to increase membrane conductance.

**Effects of angiotensin II and norepinephrine:** NT has been reported to produce vasoconstriction in the rat coronary vessel [13] and in the present experiments, perfusion of NT was frequently followed by a decrease in diameter of the visible arteries of the preparation. To investigate whether the activity of NT as a vasoconstrictor can account for the inhibitory effect, human angiotensin II and norepinephrine, which are known as powerful vasoconstrictors, were perfused and their effects on the contractile responses to nerve stimulation were examined.

Angiotensin II (0.1–2 μg/ml) inhibited the contractile responses. The inhibitory effect of angiotensin II (2 μg/ml) was very similar in the magnitude to that of NT, 100 ng/ml, but slightly shorter in the duration, as shown in Fig. 7. Even in preparations which were in the state of desensitization to NT, the inhibitory response to angiotensin II (100 ng/ml) was observed. It was also found that
Fig. 7. Comparison between the inhibitory effects of neurotensin, 100 ng/ml, (NT, □) and angiotensin II, 2 μg/ml, (Ang, □) on the contractile responses of the isolated, perfused rectum preparation to Remak's nerve stimulation (square-wave pulses of 0.8 msec duration at 10 Hz for 5 sec). A perfusing solution contained 500 ng/ml atropine was perfused at a flow rate of 3ml/min throughout the experiment. Neurotensin and angiotensin II were applied by perfusing their solutions for 90 sec via the arterial cannula.

Table 1. The effects of propranolol plus phenolamine and guanethidine on the neurotensin-induced contraction and neurotensin-induced reduction of the contractile response to Remak's nerve stimulation in the isolated, perfused rectum of the chicken

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Propranolol (500 ng/ml) plus phenolamine (1 μg/ml)</th>
<th>Guanethidine (1 μg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Contraction</td>
<td>100%</td>
<td>150–370% (n=4)</td>
<td>170–300% (n=4)</td>
</tr>
<tr>
<td>Reduction</td>
<td>68.6±3.2% (n=7)</td>
<td>*13.8±5.3% (n=4)</td>
<td>*39.8±6.8% (n=4)</td>
</tr>
</tbody>
</table>

Mean±S.E. mean is shown. Control: effects of neurotensin (100 ng/ml) before treatment with drug. Statistical significance is shown as *p<0.01 compared with the control.

an antagonist against angiotensin II, [Sar¹, Ala⁸]-angiotensin II, reduced the inhibitory effect of angiotensin II, but did not affect the inhibitory effect of NT. Thus, the inhibition produced by angiotensin II is mediated through activation of its receptors. Norepinephrine (up to 85 ng/ml) had little effect on the contractile response to RNS, and at higher concentrations, it was effective in reducing the nerve-mediated contraction. After treatment of the preparation with propranolol (500 ng/ml) plus phenolamine (1 μg/ml) which was able to decrease markedly this inhibitory effect of norepinephrine, the contractile responses to RNS were slightly reduced in magnitude, and NT (100 ng/ml) was found to exert a stronger contractile effect on the preparation with reducing its inhibitory effect on the nerve-mediated response. Qualitatively similar
Fig. 8. The effects of norepinephrine and neurotensin on the flow rate of perfusate in the isolated, perfused rectum preparation. Upper panel: the effects of norepinephrine, 85 ng/ml (A and B) and neurotensin, 100 ng/ml (C and D); A and C, 30 min after treatment with phentolamine (1 µg/ml) plus propranolol (500 ng/ml) (open columns); B and D, 20 min after treatment with guanethidine (1 µg/ml) (open columns). In A–D, hatched columns indicate the control effects before either of these pre-treatments, and the half open and half hatched region expresses overlap. The results were obtained in one preparation. Right panel, the effects of norepinephrine, 170 ng/ml (A and B) and neurotensin, 1 µg/ml (C and D); A and C, 30 min after treatment with phentolamine (1 µg/ml) plus propranolol (500 ng/ml) (open columns); B and D, 20 min after treatment with guanethidine (1 µg/ml) (open columns). In A–D, hatched columns indicate the control effects before either of these pre-treatments, and the half open and half hatched region expresses overlap. The results were obtained in another preparation. Perfusion of a solution at a constant pressure (100 cm H₂O) was used throughout the experiments. The number of drops of the venous effluent of every 30 sec was counted, and the results are expressed as a percentage of the control value for a period of 30 sec immediately before application of these drugs (the first column in every case).
effects were obtained with guanethidine (1 μg/ml). The obtained results are summarized in Table 1. The reduction of the inhibitory effect of NT on the nerve-mediated contraction was maximal in the first application of NT from the start of treatment with guanethidine and became smaller as NT application was repeated. These findings suggest NT may release catecholamine from adrenergic nerve terminals as its indirect action. 

Effects of angiotensin II, norepinephrine and neurotensin on the flow rate of the perfusate: In order to confirm vasoconstrictive effects of angiotensin II, norepinephrine and NT, identical experiments were performed with perfusion at a constant pressure instead of perfusion at a constant flow. Changes in the flow rate were measured by recording drops of the venous effluent. At a perfusion pressure of 100 cm H₂O or so, the flow rate was found to reach a level as fast as in the perfusion at a constant flow (3 ml/min). When norepinephrine or NT was perfused in concentrations high enough to produce the inhibitory effect on the nerve-mediated contraction, the flow rate was significantly reduced. The reduction of the flow rate was elicited even when the concentration of norepinephrine was decreased to 85 ng/ml which was ineffective in inhibiting the nerve-mediated contraction. However, angiotensin II (up to 10 μg/ml) had no effect on the flow rate. As shown in Fig. 8, the effect of noradrenaline (85 ng/ml or 170 ng/ml) was enhanced by guanethidine (1 μg/ml), but markedly reduced by phentolamine (1 μg/ml) plus propranolol (500 ng/ml). On the other hand, the effect of NT (100 ng/ml or 1 μg/ml) was reduced after prior application of guanethidine or phentolamine plus propranolol, and the reduction was greater in the effect elicited by the higher concentration of NT (170 ng/ml) (see also Fig. 8). This finding indicates involvement of endogenous catecholamines in the vasoconstrictive effect of NT.

DISCUSSION

The present results showed that NT applied via the blood vessel exerts an inhibitory effect on the mechanical responses to excitation of non-adrenergic, non-cholinergic (NANC) nerves by Remak's nerve stimulation in the chicken isolated, perfused rectum. The inhibition is unlikely to be due to prevention of impulse initiation or impulse conduction in the nerve fibers, since it was graded and concentration-dependent over a wide range of concentrations. The nerve fibers responsible for the response have been shown to consist of C fibers [11], and if NT, like TTX, prevents initiation or conduction of nerve impulses, the inhibitory effect should be substantially in an all or nothing fashion. This view is consistent with the fact that NT had no effect on the constituent relaxation of the responses to RNS. The effectiveness of NT in suppressing the contractile responses to stimulation of the nerves at their postganglionic site [5] can be interpreted as an indication that its site of action is more peripheral than the ganglionic transmission. It is possible that NT reduced either the amount of neurotransmitter release responsible for the contractile response or the sensitivity of the smooth muscle to the transmitter. As mentioned above, NT had no effect on the constituent relaxation of the response to RNS. Because of the similar mechanisms underlying nerve impulse-evoked release of neurotransmitters, it seems unlikely that NT reduced the amount of transmitter release from the excitatory nerves driven by stimulation of Remak's nerve.

NT is not to act simply as an antagonist against the transmitter substance, since it has contractile effect on the smooth muscle
of chicken rectum. Furthermore, NT, like the excitatory transmitter, produced an increase in membrane conductance resulting in membrane depolarization of the rectal muscle (unpublished observations). The fact that alpha, beta-methylene ATP which increases profoundly the membrane conductance of the rectal muscle [7] had virtually no effect on the neurally-induced contraction suggests that the effect on the membrane conductance may not account for the inhibition of the contractile response to RNS produced by NT.

Angiotensin II had the inhibitory effect on the contractile response to RNS as did NT, and the effects of angiotensin II and NT appeared to be exerted through activation of the respective receptors. It is clear that these peptides did not act by the same mechanism, a marked vasoconstriction, since angiotensin II did not act as a vasoconstrictor in the chicken rectum. In similar experiments where perfusion via the blood vessel of the isolated rectum was achieved at a constant pressure, norepinephrine (85 ng/ml) was not less potent than neurotensin (100 ng/ml) in reducing the flow rate of the perfusate while having little effect on the contractile response to RNS. This serves to rule out the possibility that the vasoconstriction accounts for the inhibition of the contractile response to RNS elicited by NT. In most preparations pre-treated with propranolol plus phentolamine or guanethidine, NT produced a greater contraction of the rectum and was less effective in inhibiting the contractile response to RNS, suggesting that NT releases norepinephrine from adrenergic nerve terminals: In normal preparations, the smaller activity of NT to contract the rectal muscle can be explained as a consequence of counteraction of its direct action by the released norepinephrine, and the greater activity to inhibit the contractile response to RNS can be explained as a consequence of summation of the effects of NT and the released norepinephrine. The distribution of adrenergic nerve fibers in chicken rectum and the adrenergic inhibition of its mechanical activity mediated by beta-receptor have been reported [9, 10]. The indirect action of NT is also suggested by the observations on the flow rate that the vasoconstrictor effect was reduced after treatment with guanethidine or phentolamine plus propranolol. Adrenergic nerve terminals present in the blood vessels seems to serve as the source of this catecholamine, because when added to the bathing solution, NT could not exert its catecholamine-releasing action in the same preparation. The activity of NT to inhibit the nerve-mediated contraction can be explained only partially by its catecholamine-releasing action, since neither guanethidine nor blockers of alpha- and beta-adrenoceptors were able to reverse completely the inhibitory effect of NT. Underlying mechanisms of the main effect of NT remain to be determined.

In conclusion, the data presented in this paper show that when perfused via the caudal mesenteric artery, NT can reduce the excitatory input to the rectum from Remak's nerve in the chicken, and that this effect on the neuromuscular transmission can be explained partially by its catecholamine-releasing action. The present data also suggest a possible physiological role of NT in plasma as a circulating hormone: If the plasma level of NT is elevated as a consequence of the release following various stimulations such as ingestion of a meal, the peptide could reduce the sensitivity of the rectum for excitatory signals via Remak's nerve.

ACKNOWLEDGEMENTS. We wish to thank the Fugaku Trust for Medical Research for supporting part of this work.
要約

鳥類結直腸の神経による興奮性支配の血中ニューロテンシンによる調節の可能性：大橋秀法・小森成一・橋成春・海野年弘（岐阜大学農学部野戦医学学科家畜薬理学講座）——ニワトリから摘出した結直腸を血管から人工栄養液で灌流しながら、レマック神絵刺激（RNS）により発生する結直腸収縮反応に対する血管から適用した場合のニューロテンシン（NT）の作用を検討した。NT（5 ng-2 μg/mL）は、RNSで発生する反応の中で、収縮要素を用量依存的に抑制したが、弛緩要素には影響を及ぼさなかった。高濃度のNT（80 ng/mL以上）では、結直腸収縮も発現した。アドレナリン作動性β2受容体遮断薬のプロプラノロールとアドレナリン作動性ニューロテンシン遮断薬のアガネチシンは、NTのRNSによる収縮反応抑制効果を弱める一方で、NTの結直腸収縮効果を増大した。NT（0.1 μg/mL・1 μg/mL）は、ネコエピネフリンと同様に、定圧灌流下の結直腸標本からの灌流液の流出速度を低下した。アガネチシンはノルエピネフリンのこの血管収縮効果を増大し、アドレナリン作動性α受容体遮断薬のフェントラミンとプロプラノロールとの併用はこの効果を発現しなかっただけである。これらどちらの前処置によっても、NTの血管収縮効果は抑制された。これらの成績は、血中NTがホルモン様に作用してニワトリの結直腸に対する興奮性神経支配を抑制する可能性とこの効果の発現にはNTによりアドレナリン作動性神経から遊離されるカテコールアミンが一部関与することを示唆している。