The effect of bradykinin on the electrical activity of rat jejunum

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Summary. Bradykinin increased the potential difference across both the jejunum and colon of the rat. This effect was significantly reduced by indomethacin, suggesting that it was mediated by prostaglandins. The possibility that bradykinin may contribute to the diarrhoea of the carcinoid syndrome by inducing a net secretory state in the intestine is discussed.

Certain pathological conditions, such as the carcinoid syndrome, are associated with an elevation of blood kinin levels[1]. One of the symptoms of such conditions is diarrhoea and the possibility that the kinins may contribute to this state by inducing net secretion in the intestine has been investigated.

The intestinal tract is normally polarised, the plasma being electropositive with respect to the lumen. This transmural potential difference results from the active transport of ions by the intestine[2-4] and can therefore be used as an index of net ion movement provided that any resistance changes are taken into account. The potential difference was measured across segments of rat jejunum and proximal colon using the in vivo preparation described by Hardcastle and Eggenton[5]. The kinin used in this study was bradykinin and it was administered i.v. in doses ranging from 0.01 µg to 6 µg, each dose being washed in with 0.2 ml isotonic saline.

Bradykinin caused a rapid and transient increase in the potential difference across both the jejunum and the colon. Typical responses are shown in figure 1. The transient nature of the response is likely to be due to the rapid destruction of bradykinin within the body[6]. The increased potential difference induced by bradykinin could be due to increased cation absorption, enhanced anion secretion or a combination of both. The fact that an inhibition of fluid absorption by everted sacs of rat small intestine has been observed in response to this kinin[7], suggests that it induces a net secretory state.

The effect of bradykinin depended on the dose administered and a sigmoid relationship between the dose and the response was obtained both in the jejunum and the colon (figure 2). The kinins are potent vasodilators and have been shown to influence blood flow in the intestine[8]. However, other vasodilators, e.g. the ganglion-blocking agent pentolinium, do not affect the transintestinal potential difference[9] and it seems unlikely, therefore, that the effects of bradykinin reported here can be attributed to an effect on the circulation.

Bradykinin has been shown to exert its effects in several tissues by increasing their production of endogenous prostaglandins[10]. I.v. administered prostaglandins (PGE_1 and PGE_2) also increase the jejunal and colonic potential differences in the rat[11], producing responses which have very similar characteristics to those caused by bradykinin. This suggests that prostaglandins could be involved in the actions of bradykinin on the intestine. Indomethacin, a potent inhibitor of prostaglandin synthesis[12], was therefore administered s.c. at a dose of 16 mg/kg and its influence on the response to bradykinin determined. Although indomethacin caused no change in the endogenous potential differences, it can be seen clearly that it reduced the effects of bradykinin both on the jejunum and the colon (figure 2). The maximum jejunal response was reduced significantly ($0.01 > p > 0.001$) from 4.1±0.6 mV (6) to 2.9±0.6 mV (4)

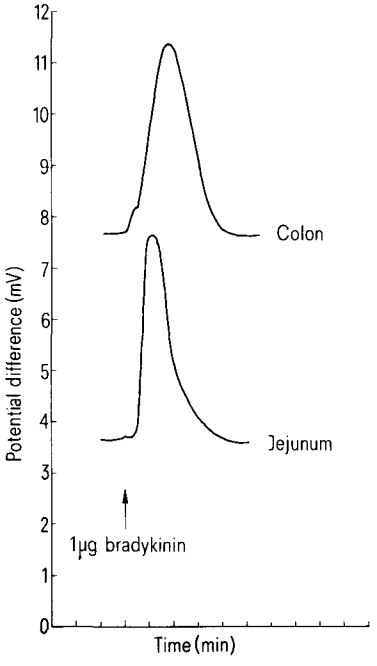

Fig. 1. Typical responses of rat jejunum and colon in vivo to bradykinin. Bradykinin was administered i.v. at a dose of 1 µg and the potential differences across jejunum and colon recorded simultaneously.

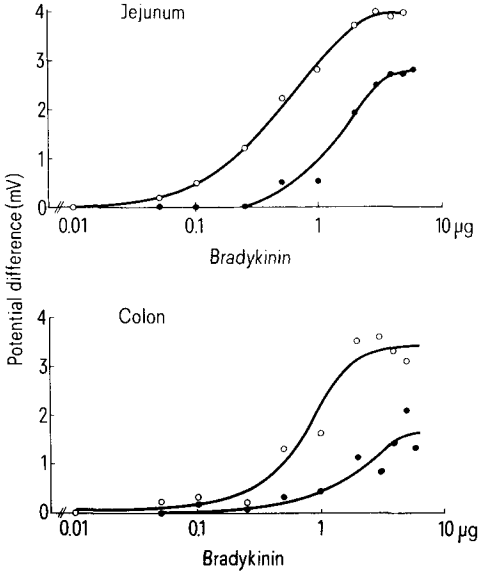

Fig. 2. Relationship between the dose of bradykinin administered and the increased potential difference across rat jejunum and colon in vivo. ○ Control (each point represents the mean of observations from 6 animals), ● responses after 16 mg/kg indomethacin s.c. (each point represents the mean of observations from 4 animals).

and that in the colon was decreased significantly ($0.05 > p > 0.01$) from 3.9 ± 0.8 (6) to 1.7 ± 0.7 mV (4). The inhibitory effect of indomethacin cannot be attributed to a nonspecific action since it did not significantly affect ($p > 0.05$) the maximum increase in potential difference induced by acetylcholine (3.5 ± 0.3 mV (6) in the jejunum and 6.3 ± 1.0 mV (6) in the colon). These observations support the hypothesis that the increased transintestinal potential difference induced by bradykinin is mediated by an increased production of endogenous prostaglandins.

Cyclic AMP is thought to be involved in the secretory states induced by both prostaglandins[13] and bradykinin[7], and this lends further support to the suggestion of a link between bradykinin and prostaglandins. Bradykinin not only increases the transintestinal potential difference in vivo but is also effective in an in vitro preparation, indicating a direct action on the tissue. Sheets of rat jejunum and colon respond to the addition of 50 µg bradykinin to the serosal fluid with transient rises in the potential differences of 1.3 ± 0.2 mV (6) and 3.2 ± 0.8 mV (7), respectively. From simultaneous resistance measurements the change in the current generated by the tissues can be calculated using Ohm's law. In the jejunum bradykinin increased the current by 17.4 ± 3.1 µA/cm^2 (6) and in the colon by 31.7 ± 6.6 µA/cm^2 (7). Thus the rise in potential difference results from an alteration in net ion transport and does not simply reflect a change in tissue resistance. The carcinoid tumour secretes many biologically active substances and 5-hydroxytryptamine has already been implicated as the cause of the diarrhoea associated with this syndrome[14]. In view of the action of bradykinin demonstrated in this study it would appear that the kinins may also play a contributory role.

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The transcendental meditation technique, adrenocortical activity, and implications for stress

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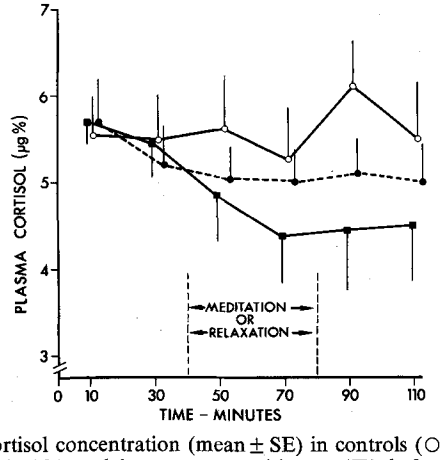
Summary. The practice of the transcendental meditation technique in subjects eliciting this state regularly for 3–5 years is correlated with acute decline of adrenocortical activity not associated with sleep during the practice.

Increased adrenocortical hormone levels in the circulation are well established correlates of both acute and chronic stress[1]. However, natural states characterized by acutely decreased adrenocortical activity have not been identified. The technique of transcendental meditation (TM) is a widely practiced, reportedly relaxing[2] mental practice which requires no special circumstances except ordinary considerations of comfort[2]. This practice has been reported to induce, within 30 min, a physiologic state characterized by decreased oxygen consumption, carbon dioxide elimination, and arterial lactate; major redistribution of blood flow[4]; and EEG changes[3]. To see whether these apparent relaxing effects are reflected in endocrine changes, change of plasma concentration of cortisol was measured. Also, since the beneficial effects purportedly associated with meditation may be simply due to sleep or drowsiness accompanying relaxation, the endocrine changes were correlated with occurrence of sleep. We report here a marked decline of plasma cortisol consistent with complete inhibition of adrenocortical activity in long-term practitioners during meditation. This decline was not found to be related to sleep during meditation. The conclusions of this study are at variance with those of Michaels[5].

Materials and methods. Plasma cortisol values were measured in 30 normal day-active young adult volunteers (University students). 15 long-term regular practitioners (8 men and 7 women, ages 22–29) and 15 controls (7 men and 8 women, ages 20–27), were studied; the controls were restudied after 3–4 months of regular TM practice. The long-term practitioners had been practicing the technique from 3 to 5 years. Transcendental meditation is practiced twice daily for 20–40 min by the regular practitioner. All observations were made between 12.00 and 16.00 h, a period of relative stability of mean plasma cortisol concentration[6].



Plasma cortisol concentration (mean ± SE) in controls (○) restudied controls (●) and long-term practitioners (■) before, during and after meditation or rest.