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Gastric afferents to the paraventricular nucleus in the rat

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Summary. Extracellular recordings were made from vasopressin (AVP) and oxytocin (OXT)-secreting cells in the paraventricular nucleus (PVN) of the hypothalamus in rats anesthetized with urethane–chloralose to determine the effects of electrical stimulation of vagal gastric nerves and gastric distension on their activity. Electrical stimulation of gastric branches of the vagus nerves inhibited 5 and excited 10 of 32 phasically firing neurosecretory cells. Approximately one third of the phasically firing neurosecretory cells (9 out of 29 cells) were transiently inhibited by gastric distension; an effect which was completely abolished by bilateral cervical vagotomy. In contrast, gastric nerve stimulation excited 45 of 72 non-phasically firing paraventricular cells. Thirteen of 77 non-phasically firing cells tested were excited by gastric distension. We conclude that there are some sensory afferent inputs originating from gastric receptors and transmitted by gastric vagal afferents which inhibit the activity of AVP-secreting neurons in the PVN although other inputs excite the cells. Similar inputs also excite some of the putative OXT-secreting neurons in the PVN.

Key words: Paraventricular nucleus – Vagal afferents – Gastric distension – Vasopressin neuron – Oxytocin neuron – Rat

Introduction

The paraventricular nucleus (PVN) and the supraoptic nucleus (SON) of the hypothalamus are well known to be involved in regulating the secretion of the posterior pituitary hormones, vasopressin (AVP) and oxytocin (OXT). The PVN has also been suggested to be involved in the control of the autonomic nervous function (Swanson and Sawchenko 1983).

In the past few years, we have studied the PVN as an integrative site for coordinating neuroendocrine and autonomic functions (Kannan and Yamashita 1983; Yamashita et al. 1983a; Yamashita et al. 1984).

The PVN neurons, including magnocellular neurosecretory cells projecting to the neurohypophysis, have been shown to receive a variety of cardiovascular and visceral afferent inputs (Barker et al. 1971; Koizumi and Yamashita 1978; Calaresu and Ciriello 1980; Yamashita et al. 1989).

Recent studies have demonstrated that plasma AVP and OXT concentrations are differentially influenced by the activation of abdominal vagal afferents. Abdominal vagal afferents activated by gastric distension and the administration of systemic cholecystokinin (CCK) elicit OXT release in the rats (Verbalis et al. 1986; McCann et al. 1989) and AVP release in the monkey (Verbalis et al. 1987). Electrical stimulation of abdominal vagal afferents evokes an increase in plasma AVP concentration, but not OXT concentration in the ferret (Hawthorn et al. 1988). Renaud et al. (1987) reported that the putative OXT-secreting neurons, but not AVP-secreting neurons, in the SON are excited by gastric distension and systemic administration of CCK in the rat, an effect which was probably mediated by the activation of gastric vagal afferents. However the effects of gastric vagal afferents on the magnocellular neurosecretory cells in the PVN have not been examined. Accordingly, we examined the effects of gastric afferent stimulation on the neural activity of the PVN. The present investigation was undertaken to; (1) analyse quantitatively the effects of electrical stimulation of the gastric branches of the vagus nerve on neurosecretory cells in the PVN and to measure the onset latency and threshold of the responses; (2) determine whether the responses were abolished after cervical or abdominal vagotomy; (3) examine the effects of gastric distension in order to elucidate the function of the gastric vagal afferents. A short account of the work has been published elsewhere (Ueta et al. 1986; Ueta et al. 1988).

Methods

Forty three male rats of the Wistar strain, weighing between 350 and 420 g, were anesthetized with α-chloralose (60 mg/kg) and urethane

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(600 mg/kg) given intraperitoneally. A quarter of the initial dose was given as a supplement during the experiment when necessary. The ventral surface of the hypothalamus and the hypophysis was exposed transpharyngeally (Dreifuss et al. 1972). Arterial blood pressure was monitored continuously throughout the experiment with a transducer connected to a cannula in the femoral artery. Body temperature was maintained at 36–38°C by a heating pad. A concentric bipolar electrode (0.6 mm, o.d.) was placed on the junction between the pituitary stalk and the neurohypophysis, through which (negative) monopolar stimulating pulses of 0.5 ms duration and 0.5 mA intensity were applied at 0.83 Hz.

To stimulate the gastric branches of the vagus nerves electrically, the anterior gastric branch was carefully dissected from the surrounding tissue at the junction of the oesophagus and stomach. The nerve was cut peripherally and its central nerve end was placed on a pair of silver electrodes. A mixture of liquid paraffin and vaseline was applied around the nerve so that it was insulated from the surrounding tissues and kept moist. The nerve was stimulated with a train of 3 pulses of 0.5 ms duration at 100–200 Hz and 20–600 μA intensity delivered every 1.2 s. To test the effects of vagal gastric nerve stimulation on the activity of PVN neurons, peristimulus time histograms (PSTHs) were obtained using a signal processor with time bins of 1–2 ms duration. In some experiments, repetitive stimulation with a 60 s train of negative pulses (0.5 ms, 2–50 Hz, 200–600 μA) was used.

To distend the stomach, a thin latex balloon connected to a polyethylene catheter with 0.8 mm diameter was inserted into the stomach. After laparotomy, a small cut was made near the pylorus of the stomach. Before inserting the balloon, the stomach contents were removed by repeated flushing with warm saline. After the balloon was inserted, it was secured in place with a purse string suture. In some experiments, another similar balloon was placed in the peritoneal cavity between the stomach and the diaphragm on the left side. After these procedures, the abdominal wall was closed with sutures. The polyethylene catheter connected to the balloon was connected to a three-way tap with one arm connected to a syringe and the other arm to a low-pressure transducer to measure the pressure within the balloon. The stomach was distended by injecting 1–12 ml air within 2–3 s and distension was maintained for 30–100 s. To study the effects of vagotomy, the bilateral cervical vagus nerves were dissected from the surrounding tissue in the neck and loops of thread were tied loosely around them so that the nerves could be readily exteriorised and severed.

For recording the neural activity of PVN neurons, a glass microelectrode (tip diameter less than 1 μm; DC resistance of 15–30 MΩ) filled with 2% Pontamine Sky Blue in 0.5 M sodium acetate was introduced into the PVN region. Action potentials were displayed on a storage oscilloscope and photographed when required. PVN neurosecretory neurons were identified by antidromic activation following stimulation of the pituitary stalk using the criteria of constant latency at threshold, frequency following at 100 Hz and collision with spontaneous spikes.

Criteria for responses, excitation or inhibition following gastric stimuli are as follows. (1) Responses to electrical stimulation of gastric branches of the vagus nerves with a single shock on neurosecretory cells were accessed on the basis of PSTHs. (2) Responses to repetitive electrical stimulation of the gastric branches of the vagus nerves and to gastric distension on non-phasically firing neurosecretory cells were judged to have responded as excitation or inhibition when its firing rate changed by more than 20% comparing the mean firing rate for a period of 1 min before, with that for 30 sec after stimulation or distension. (3) The criteria used for classifying phasically firing neurosecretory cells are described in detail in the Results.

After each experiment, the last recording site was marked by iontophoretically deposited dye (with 5 μA, for 5 min). The brain was removed. Frozen sections cut at 40 μm were mounted and stained with neutral red. The positions of the recording sites were reconstructed from frontal sections using the atlas of König and Klippel (1963).

Results

A total of 210 spontaneously firing neurons were identified as magnocellular neurosecretory cells in the PVN by antidromic stimulation of the pituitary stalk. Magnocellular neurosecretory cells were divided into two groups on the basis of their firing patterns; 61 were classified as "phasically firing cells" which showed alternating periods of activity and silence, and 149 cells as "non-phasically firing cells".

Electrical stimulation of gastric branches of the vagus nerves with a single shock

Phasically firing neurosecretory cells. The responses of 32 phasically firing neurosecretory cells to electrical stimulation of gastric branches of the vagus nerves with a single shock were examined using peristimulus time histograms (PSTHs). Ten neurons (31%) were excited (Fig. 1A) and five neurons (16%) were inhibited (Fig. 1B). The remaining neurons showed no response. The excitatory and inhibitory responses were more pronounced when the stimulating current was increased and in 2 cases a simple excitatory response changed to excitation followed by inhibition. We found no cells in which an excitatory or inhibitory response was reversed by increasing or decreasing the strength of the stimulus pulses. The threshold

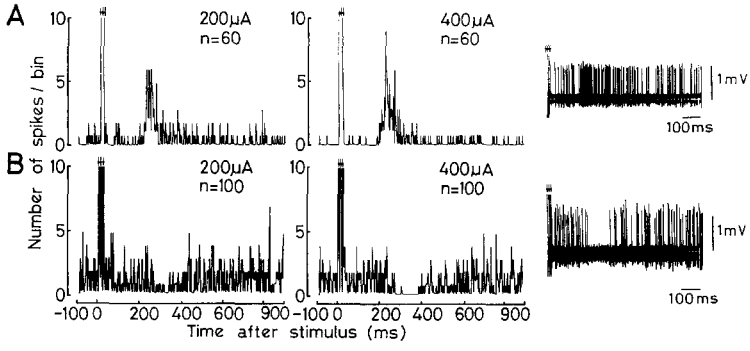

Fig. 1A, B. The effects of electrical stimulation of the gastric branches of the vagus nerves with a single shock on the activity of phasically firing neurons in the PVN. **A** An example of a neuron which was excited. **B** An example of a neuron which was inhibited. Left and middle panels show a peristimulus time histogram. Intensity of the electrical stimulation is indicated by numbers (μA) in each case. *n*: numbers of sweep. Three arrows indicate the time of stimulation. The right panels are oscilloscope traces of action potentials taken simultaneously at the time of left (**A**) and middle (**B**) panel (20 sweeps superimposed)

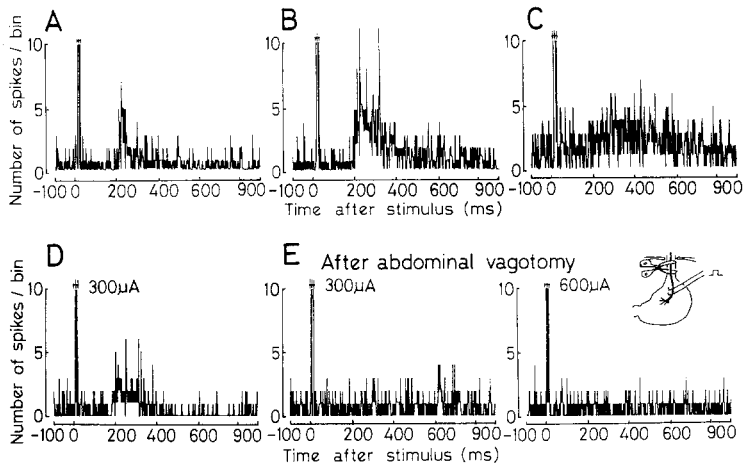

Fig. 2A–E. The excitatory effects of single shock electrical stimulation of the gastric branches of the vagus nerves on the activity of non-phasically firing neurons in the PVN. **A** A non-phasically firing neuron which showed short duration excitation. **B** and **C** Example of neurons which showed larger responses. Similar responses were also observed on phasically firing neurons. **D** and **E** Were obtained from the same neuron. The excitatory response was completely abolished after abdominal vagotomy. Each panel shows a peristimulus time histogram. Intensity of the electrical stimulation is **A**: 400 μA, **B**: 600 μA and **C**: 600 μA. Numbers of sweeps are 60 (**A**), 100 (**B**), 100 (**C**) and 30 (**D** and **E**). Three *arrows* indicate time of stimulation

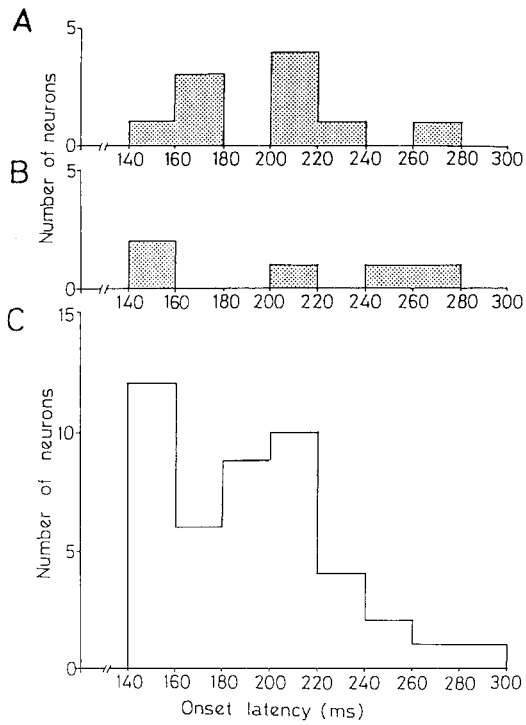

Fig. 3A–C. Frequency distribution of the onset latency of excitatory and inhibitory responses to electrical stimulation of the gastric branches of the vagus nerves on the neural activity of the neurosecretory cells in the PVN. **A** Frequency distribution of the onset latency of excitatory responses of phasically firing neurons ($n=10$). **B** Frequency distribution of the onset latency of inhibitory responses of phasically firing neurons ($n=5$). **C** Frequency distribution of the onset latency of excitatory responses of non-phasically firing neurons ($n=45$)

current was approximately 50–100 μA. The onset latency of the excitatory responses was between 140 and 280 ms (mean ± S.D., 194 ± 12, $n=10$) (Fig. 3A) and that of the inhibitory response was between 140 and 280 ms (Fig. 3B).

Non-phasically firing neurosecretory cells. The responses of 72 non-phasically firing neurons to single shock electrical stimulation of the gastric nerves were also examined. Forty-five (63%) neurons were excited, and the remaining 27 neurons showed no change in firing rate. The pattern of the responses varied from neuron to neuron (Fig. 2A–C), but increasing the strength of stimulation never changed the pattern of the responses of any of the cells we recorded. The variation of the excitatory responses was similar to that seen in phasically firing neurons. Inhibitory responses were never observed. The threshold for excitatory responses of non-phasically firing neurons was similar to that of the phasically firing neurons and the onset latency varied between 156 and 300 ms (mean ± S.D., 194 ± 6) (Fig. 3C). There was no significant difference in the onset latency of the excitatory responses between phasically and non-phasically firing neurons. The responses of 2 neurons excited by stimulation of vagal gastric nerves were re-examined after section of the abdominal vagus nerves. In each case the excitatory response was completely abolished after the abdominal vagotomy (Fig. 2D, E).

Repetitive electrical stimulation of the gastric branches of the vagus nerves

Phasically firing neurosecretory cells. The responses of 10 phasically firing neurosecretory cells to repetitive electrical stimulation of the gastric branches of the vagus nerves were examined.

Two of three neurons which were inhibited by electrical stimulation with a single shock were also inhibited during repetitive stimulation at 400 μA and 50 Hz (Fig. 4A). When the intensity of the electrical stimulation was increased to 600 μA, the spontaneous firing was more clearly inhibited. The effects of changing the frequency of stimulation between 20 and 50 Hz were also examined. As stimulus frequency increased, the spontaneous firing was progressively inhibited (Fig. 4A). Though the neuron presented in Fig. 4A did not show a typical phasically firing pattern, it was inhibited by peripheral baroreceptor activation induced by i.v. administration of phenylephrine (4–8 μg), which is typical of AVP-secreting cells (Harris 1979).

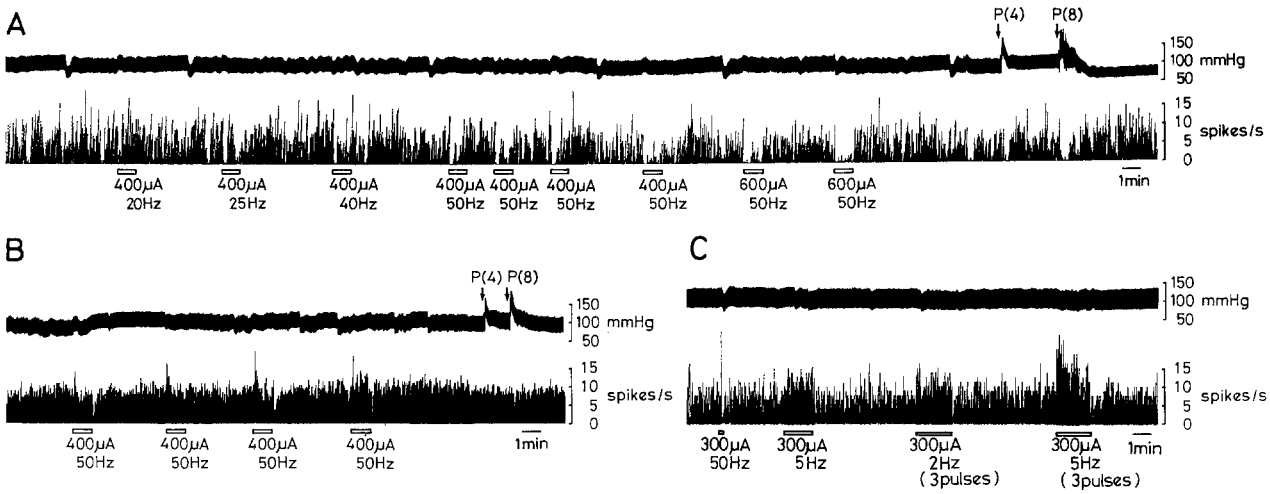

Fig. 4A–C. The effects of repetitive stimulation of the gastric branches of the vagus nerves on the activity of neurosecretory cells in the PVN. **A** The inhibitory effect of repetitive stimulation of the gastric nerves on neural activity. This neuron was also inhibited by i.v. injection of 4 or 8 μg phenylephrine (P). **B** The transient excitatory effect of trains of stimuli (400 μA, 50 Hz) applied to the gastric nerves on the activity of a non-phasically firing neuron. The trains induced a transient excitation followed by inhibition but was unaffected by phenylephrine injection (P; 4 or 8 μg per animal i.v.). **C** The tonic excitatory effect of trains of stimuli (single pulses at 50 Hz or 5 Hz: group of 3 pulses at 100 Hz repeated at 2 Hz or 5 Hz) on non-phasically firing neuron. In each panel the *upper trace* shows arterial blood pressure and the *lower trace*, a rate meter record (spikes/s). The numbers under the bars indicate stimulation parameters

5 neurons excited by electrical stimulation with a single shock had no response during repetitive electrical stimulation. The remaining 2 cells had no response to either electrical stimulation with a single shock or repetitive electrical stimulation.

Non-phasically firing neurosecretory cells. Seven neurons which were excited by single shock electrical stimulation were tested with repetitive stimuli at 300–400 μA and 2–50 Hz. Five of 7 neurons were excited by repetitive stimulation. Both transient excitation (Fig. 4B) in 2 neurons and tonic excitation in 3 neurons (Fig. 4C) were seen. The neuron in Fig. 4B showed transient excitation followed by quiescence when the stimulation stopped. In this case, there were changes in blood pressure but the changes were variable. There appeared to be no correlation between the changes in firing rate and changes in blood pressure and the neuron was not inhibited by phenylephrine-induced baroreceptor activation. The sustained responses are also shown in Fig. 4C.

Responses to gastric distension

Phasically firing neurosecretory cells. The responses of 29 phasically firing neurosecretory cells to intragastric distension were examined. To test the effects of gastric mechanoreceptor activation, the intragastric balloon was inflated during a spontaneously occurring burst of spikes. When evaluating an inhibitory response in a phasically firing neuron, it was critically important to decide whether a silent period which occurred after gastric distension was a direct consequence of the stimulus rather than a spontaneously occurring silent period. In the present study neurons were regarded as having responded if the following two criteria were satisfied. First, the neuron was completely inhibited immediately after injection of 4–8 ml of air. Second, the inhibitory response could be repeated at least 5 times. Nine (31%) of 29 neurons tested were inhibited by distension of the intragastric balloon and the remaining 20 (69%) were not affected. No neurons were excited by gastric distension. Figure 5 shows a representative example of inhibited cell. Gastric distension with 4 ml of air completely inhibited the activity of the neuron and when a smaller volume of air (1, 2 or 3 ml) was used, the magnitude of the inhibitory effect was directly related to the volume injected. The amount of air required to produce an inhibitory response varied from neuron to neuron but in most cases, 4 ml was sufficient to inhibit spontaneous activity completely. The pattern and duration of the inhibitory period following gastric distension also varied considerably between neurons, ranging from a very transient inhibition to complete inhibition throughout the period of gastric distension. For example, the neurons illustrated in Fig. 5A and 6A were inhibited by injection of 4 ml but not by 2 or 3 ml of air injection. However in every test, inhibition occurred immediately after the onset of inflation of the balloon. To control for nonspecific effects of distension of the abdominal wall or of intraperitoneal pressure, another similar balloon was placed between the stomach and the abdominal wall. None of the neurons tested ($n=5$) showed any apparent change in spike frequency when the balloon placed in the peritoneal cavity was inflated with the same volume of air that was effective when injected into the intragastric balloon (Fig. 6A).

Three neurons inhibited by gastric distension were tested again after the left and right cervical vagus nerves had been severed. The inhibitory effect of gastric distension was completely abolished after bilateral vagotomy, as shown in Fig. 6B.

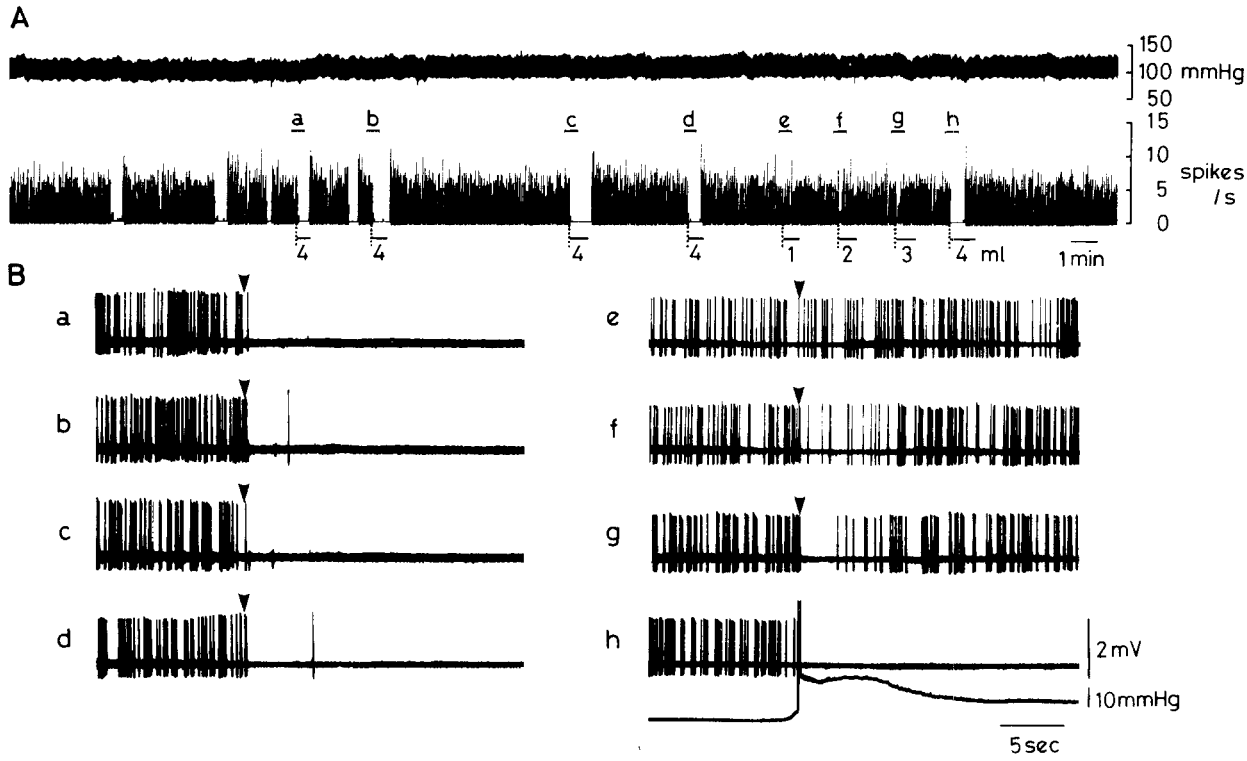

Fig. 5A, B The inhibitory effect of gastric distension on the activity of a phasically firing neuron in the PVN. **A** A polygraph record. *Upper trace*, arterial blood pressure. *Lower trace*, a rate meter record (spikes/s): numbers under bars indicate the volume of air (ml) injected to the intragastric balloon. Note that the inhibitory responses to gastric distension are reproducible. **B** Oscilloscope records taken simultaneously at the time of the marks (⊓) indicated by a–h in **A**. *Dotted lines* (**A**) and *arrowheads* (**B**) indicate onset of gastric distension respectively. The record in Bh shows action potentials of the phasically firing neuron (*upper trace*) and the intragastric pressure record (*lower trace*). Note that the early transient peak in the pressure record trace represents a recording artifact

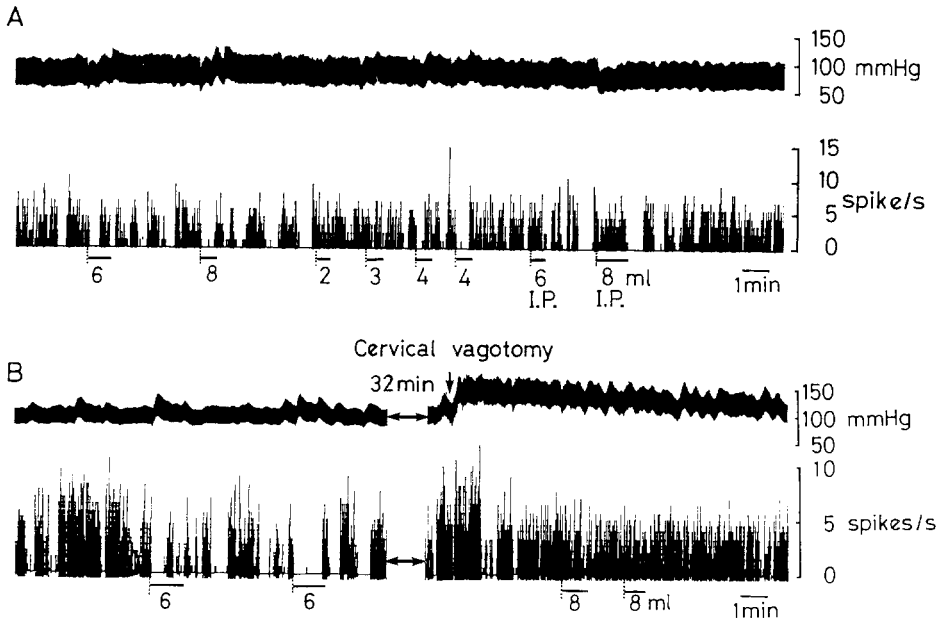

Fig. 6. A The effects of inflation of an intraperitoneally (I.P.) placed balloon on a phasically firing neuron which was inhibited by gastric distension. The numbers under the bars indicate the volume of air (ml) injected into the gastric or intraperitoneal balloon. Note that inflation of the intraperitoneal balloon had no effect on the neural activity. **B** The effects of severing both cervical vagus nerves on the activity of a phasically firing neuron which was inhibited by gastric distension. In each panel the *upper trace* shows arterial blood pressure and *lower trace* a rate meter record (spikes/s). Severing both the left and the right vagus nerve (Cervical vagotomy) completely abolished the inhibitory response induced by gastric distension. *Dotted lines* indicate the onset of gastric distension

Non-phasically firing neurosecretory cells. To compare the responsiveness of the two groups of neurosecretory neurons, we also tested the responses of 77 non-phasically firing neurons to gastric distension with a volume of air (4–12 ml) which had been shown sufficient to inhibit a substantial number of phasically firing neurons. The majority of non-phasically firing neurons (60 cells, 78%) showed no significant change of firing rate after gastric distension. Among 17 responsive neurons, 13 (17%) were excited (Fig. 7A, B) and 4 (5%) inhibited. Two types of

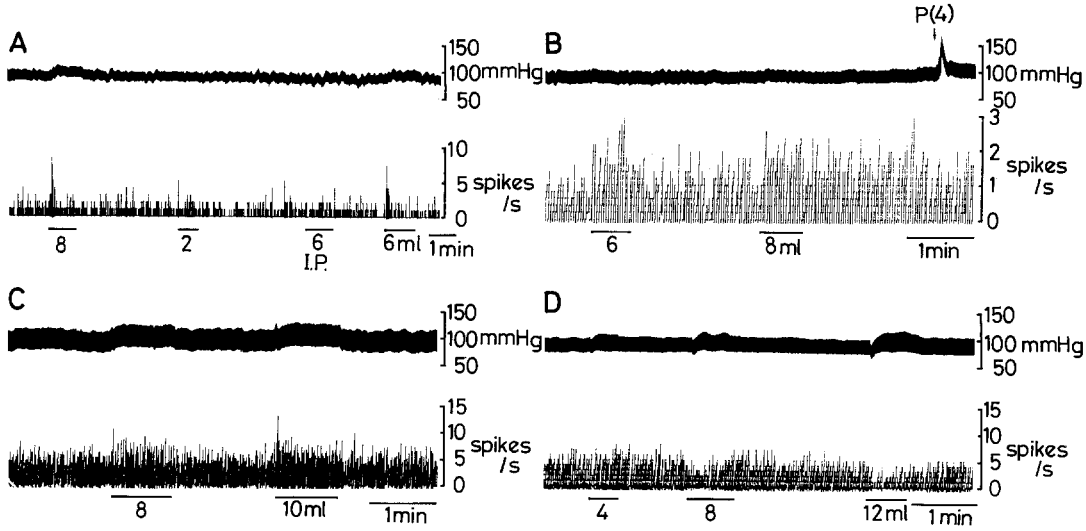

Fig. 7A–D. The effects of gastric distension on non-phasically firing neurons (**A, B**) and putative parvocellular neurons (**C, D**) in the PVN. **A** A transient excitatory response. Inflation of intraperitoneal balloon (I.P.) had no effect on the neural activity. **B** A tonic excitatory response. The neuron was unaffected by i.v. injection of 4 μg phenylephrine (P). **C, D** An excitatory response and an inhibitory response of putative parvocellular neurons, respectively

excitatory responses were observed: 9 cells responded with a transient increase in firing rate which occurred only when the pressure was increasing (Fig. 7A), while the other 4 neurons showed an increase in firing rate which continued throughout the period of gastric distension (Fig. 7B). There was no correlation between the basal firing rate and the pattern of the response.

In the present study, arterial blood pressure and heart rate either did not change or slightly decreased during gastric distension with 2–4 ml of air (Fig. 5, 6, 7). However, a bigger volume of air (6–12 ml) produced a slight pressor response in some experiments (Fig. 6, 7). The increase in blood pressure induced by gastric distension was not always accompanied by a decrease in the firing rate of the tested neurons so the decrease in firing rate was probably not the result of inhibition by the baroreceptor reflex.

Unidentified neurons within the PVN. To compare the responsiveness between neurosecretory neurons and parvocellular neurons, we also tested the responses of 31 PVN neurons, which did not respond to antidromic stimulation of the pituitary stalk, to gastric distension. Gastric distension excited 5 and inhibited 5 of 31 neurons tested (Fig. 7C, D).

Discussion

The present data provide direct evidence that the vagal afferents from the stomach influence some magnocellular neurosecretory cells of the PVN in the rat. Our experiments using electrical stimulation of gastric branches of the vagus nerves showed that phasically firing neurons in the PVN received both excitatory and inhibitory inputs from the stomach, while the non-phasically firing neurons received only excitatory inputs. We also showed that gastric distension inhibited the activity of phasically firing neurons in the PVN. There is good evidence that cells which fire phasically are AVP secreting neurons, while non-phasically firing cells constitute a mixed population containing a majority of OXT cells and a minority of AVP secreting neurons (Harris 1979; Poulain et al. 1977; Yamashita et al. 1983b).

Our results are thus consistent with the possibility that activation of gastric mechanoreceptors may be one of the physiological factors which are involved in suppresion of plasma AVP concentration. A rapid fall in plasma AVP concentration after drinking has been reported in many species (Arnauld and du Pont 1982; Geelen et al. 1984; Thrasher et al. 1981, 1987; Blair–West et al. 1985, 1987). It has been postulated that this may be the result of inhibition of AVP release which may be mediated by neural inputs to the hypothalamus following activation of receptors in the oropharynx and stomach during drinking. Earlier studies indicate that stimulation of oropharyngeal receptors modulates the activity of SON and PVN cells (Nicolaïdis 1969; Sakaguchi et al. 1989). Our results showed the putative AVP-secreting neurons in the PVN were also inhibited by the activation of gastric mechanoreceptors. Although many reports suggest that gastric distension is less important in inhibiting AVP secretion than oropharyngeal stimulation (Blair–West et al. 1985; Thrasher et al. 1987; Thompson et al. 1987; Salata et al. 1987), it is also possible that gastric mechanoreceptors are to some extent responsible for the rapid fall of plasma AVP concentration which occurs during drinking.

Furthermore, it is possible to explain why gastric distension only inhibited one third and excited none of the phasically firing cells tested, despite the observation that electrical stimulation of the vagus nerves inhibited some and excited other phasically firing cells, if the electrically-induced excitation of phasically firing cells was due to

stimulation of chemo and/or nociceptive afferents rather than mechanoreceptor afferents (Leek 1977). The question might be resolved by studying the effects of stimulation of other gastric receptors on the neurosecretory cells, especially chemoreceptors which are sensitive to water and changes of temperature, pH and osmolality in the stomach rather than mechanoreceptor influences.

Electrical stimulation of vagal afferents excited two thirds of the non-phasically firing neurosecretory cells tested. The results suggest that putative OXT cells receive excitatory inputs from gastric receptors. This finding is in agreement with the observation that activation of gastric vagal afferents stimulate OXT release in rats (Verbalis et al. 1987). A possible explanation for the small number of neurons excited by gastric distension may be that the degree of distension used in this study was comparatively small. We found that approximately 4 ml of air used for gastric distension was the threshold to induce changes in the firing rate of neurosecretory cells (Fig. 5). Larger amounts of injected air might have activated higher threshold mechanoreceptors or nociceptive receptors. Our findings are entirely consistent with a recent study performed in the SON reporting that gastric distension by a comparatively large amount of air excited putative OXT cells (Renaud et al. 1987). We observed both transient and tonic excitatory responses of non-phasically firing cells following gastric distension. As there are high- and the low-threshold gastric mechanoreceptors, we postulate that the high-threshold mechanoreceptors are activated transiently by the dynamic phase of gastric distension and low-threshold mechanoreceptors are sensitive to steady distension (Davison and Clarke 1988). In our study, the stomach was distended rapidly. The high-threshold gastric mechanoreceptors may thus have been activated only transiently.

The functional significance of plasma increased OXT level during activation of gastric afferents is unknown. It has been suggested that activation of gastric afferents excites parvocellular oxytocinergic pathways from the PVN as well as the magnocellular OXT-secreting system from the neurohypophysis (McCann et al. 1989). Actually, we observed excitatory or inhibitory effects of gastric distension on the putative parvocellular neurons in the PVN. Furthermore, it has been suggested that central projections from the PVN might integrate neuroendocrine, autonomic and behavioral responses such as control of gastric acid secretion, inhibition of gastric emptying and feeding (Rogers et al. 1986; Banks and Harris 1987; McCann et al. 1989).

Previous work has shown that gastric distension may either increase or decrease the discharge of spontaneously active hypothalamic neurons (Anand and Pillai 1967). However, the afferent pathways mediating the response have not been established. We found that transection of the abdominal vagus nerves abolished the responses of neurosecretory cells to electrical stimulation of the gastric branches of the vagus nerves. As it is difficult to investigate the effects of abdominal vagotomy on the responses of neurosecretory cells to gastric distension without losing the neuron recorded, we carried out the experiment by bilateral cervical vagotomy. We found that bilateral cervical vagotomy abolished the responses to gastric distension. Our findings that bilateral section of the cervical vagus nerves and abdominal vagotomy completely abolished the responses of PVN neurosecretory cells to gastric distension and electrical stimulation, respectively, are compatible with earlier anatomical and electrophysiological studies (Harding and Leek 1973; Barber and Burks 1983; Nosaka 1984; Gonzalez et al. 1986). They suggest that the primary sensory afferent fibers from gastric mechanoreceptors travel in the vagi and project to the nucleus of the tractus solitarius (NTS) in the dorsomedial medulla (Harding and Leek 1973; Barber and Burks 1983; Gonzalez et al. 1986). A direct-pathway from the NTS to the PVN carrying afferent impulses from visceral receptors has already been demonstrated (Nosaka 1984). Another recent study has revealed that presumed A1 catecholaminergic cells in the caudal ventrolateral medulla which project directly to the PVN receive synaptic inputs from the cervical vagus nerve (Kannan et al. 1986). Thus the neurosecretory neurons in the PVN probably receive information from the stomach via a direct projection from the NTS and/or a polysynaptic route involving the A1 catecholaminergic neurons in the ventrolateral medulla, although the possible existence of other afferent pathways cannot be excluded at present.

Our results are thus consistent with the existence of sensory afferent inputs originating from gastric receptors and transmitted by gastric vagal afferents which inhibit the activity of AVP-secreting neurons in the PVN and that these inputs also excite some of the putative OXT-secreting neurons in the PVN. Further study will be necessary to clarify the central afferent pathway from the NTS to the neurosecretory cells in the PVN.

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