CHANGES IN RENAL NERVE EFFERENT ACTIVITY IN RESPONSE TO SEROTONIN STIMULATION OF BULBAR NUCLEI

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Data showing the uneven distribution of serotonin in brain-stem nuclei [2, 6-9] indicate the need for a study of the characteristics of its action within single nuclear formations. If injected intravascularly serotonin is known to affect the sympathetic and parasympathetic divisions of the autonomic nervous system [1, 3, 5], whereby it participates in the regulation of activity of, in particular, the cardiovascular system. The effect of serotonin when given by microinjection to the bulbar nuclei on activity of the sympathetic division of the autonomic nervous system has virtually not been studied.

In this investigation changes in efferent sympathetic activity in the renal nerve were studied during microinjections of serotonin into the nucleus of the tractus solitarius and the ventral reticular nucleus — regions of the medulla forming the bulbar level of the cardiovascular center.

EXPERIMENTAL METHOD

Experiments were carried out on 23 cats anesthetized by intraperitoneal injection of a mixture of chloralose (50 mg/kg) and pentobarbital (10 mg/kg). Serotonin creatinine-sulfate (1.5-2 μg in 2-5 μl physiological saline) was injected into the nucleus of the tractus solitarius and into the ventral reticular nucleus [4]. The location of the tip of the microinjector needle was verified in serial brain sections. A pressor carotid sinus reflex was evoked by bilateral compression of the common carotid arteries. The experimental results were subjected to statistical analysis by Student's t-test to assess the significance of differences.

EXPERIMENTAL RESULTS

Under natural conditions the spike flow in the renal nerve has the character of grouped discharges or "volleys," alternating with periods of their absence (intervolley inhibition), typical of postganglionic sympathetic fibers, and synchronized with pulse fluctuations in arterial pressure.

Microinjection of serotonin into the nucleus of the tractus solitarius was accompanied in 24 of 31 experiments by increased activity in the renal nerve, chiefly on account of an increase in frequency of the volley and a decrease in duration of the intervolley interval. The frequency of the volley 1 sec after the beginning of stimulation rose from 24 ± 0.1 to 48 ± 0.7/sec ($P < 0.01$). The most marked quickening of the volleys was observed after 2 sec (on average by 120.8%). A high level of activity was maintained for 20 sec, and complete recovery took place after 60 sec (Fig. 1). The regularity of alternation of volleys and intervolley inhibition was preserved. The amplitude of the spikes did not change. The level of the systemic arterial pressure (SAP) rose as a result of stimulation of the nucleus from 116.7 ± 5.7 to 140.9 ± 8.5 mm Hg ($P < 0.05$) 30 sec after the beginning of stimulation and was completely restored after 3 min. Changes in SAP developed steadily. The SAP level rose by 12, 13.9, 19, and 20.7% after 5, 10, 20, and 30 sec respectively.

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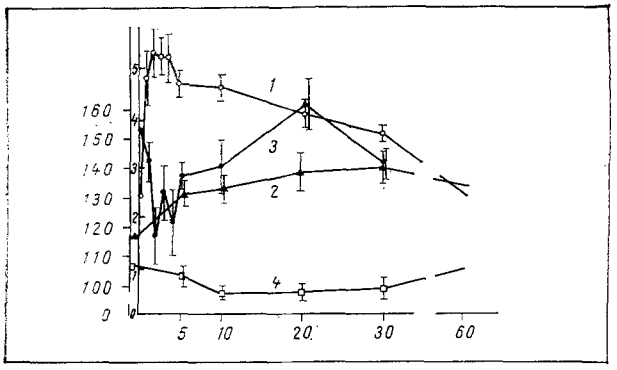

Fig. 1

Fig. 1. Changes in frequency of volleys (1, 3) in renal nerve and in SAP level (2, 4) in response to injection of serotonin into nucleus of tractus solitarius: 1, 2) pressor response, 3, 4) depressor response. Here and in Figs. 2 and 3: abscissa, time (in sec); ordinate, frequency of volleys (number of volleys per second) and SAP level (in mm Hg).

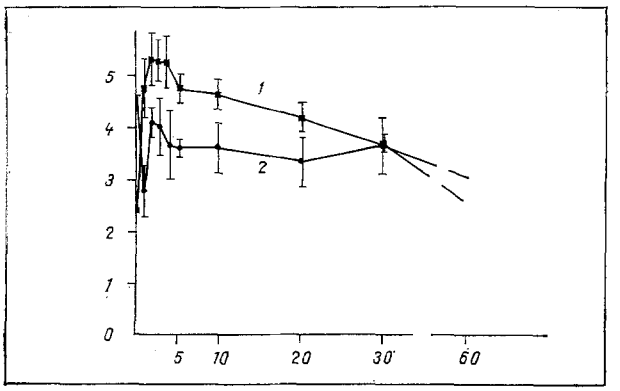

Fig. 2

Fig. 2. Changes in discharge frequency in renal nerve during microinjection of serotonin into the nucleus of tractus solitarius with (1) or without (2) accompanying pressor carotid sinus reflex.

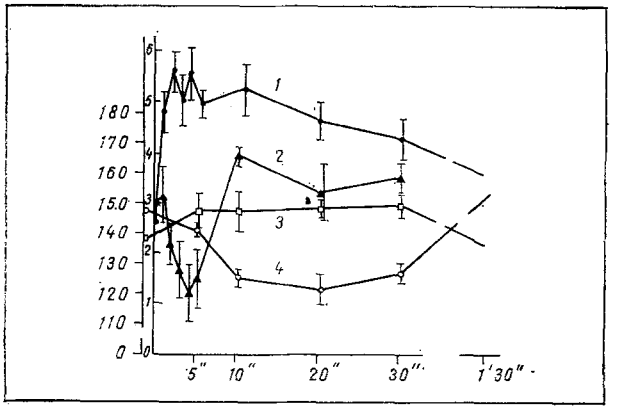

Fig. 3

Fig. 3. Changes in frequency of volleys (1, 2) in renal nerve and in SAP (3, 4) during injection of serotonin into ventral reticular nucleus: 1, 3) pressor, 2, 4) depressor responses.

In seven experiments stimulation of the nucleus of the tractus solitarius was accompanied by a decrease in the discharge frequency in the renal nerve by 57.8% 20 sec after the beginning of stimulation. After 3 sec the frequency of the volleys was reduced by 31.6%, and after 4 sec by 52.6%. During the next 15 sec the frequency of the volleys increased and exceeded the original level by 10.6%. After 30 sec it had fallen again and was 18.4% below the initial level (Fig. 1). Under these circumstances the SAP level fell from 107.8 ± 3.9 to 97.8 ± 3.4 mm Hg ($P < 0.05$) 10 sec after the beginning of stimulation and was restored in the course of 1 min.

Microinjection of serotonin into the nucleus of the tractus solitarius at the height of a pressor carotid sinus reflex was accompanied by a regular decrease in the frequency of volleys in the renal nerve from 4.6 ± 0.5 to 2.8 ± 0.3 volleys/sec ($P < 0.02$) 1 sec after the beginning of injection. During the next 3 sec on average (Fig. 2) the frequency of volleys rose from 2.8 ± 0.3 to 4.1 ± 0.6/sec ($P > 0.5$), i.e., it almost reached its values before stimulation, after which a second phase of a decrease in activity followed, and lasted about 60 sec. After discontinuation of carotid sinus receptor stimulation for 1.5 min the frequency of the volleys (3.25 ± 0.7/sec) was close to its value before development of the pressor carotid sinus reflex (3.1 ± 0.2/sec).

Microinjections of serotonin into the ventral reticular nucleus also was accompanied in most experiments (in 26 of 32) by strengthening of sympathetic activity in the renal nerve. By 1 sec after the beginning of stimulation the increase in discharge frequency amounted to 85%, rising to 119.2% after 2 sec. The increase in the frequency of volleys after 3 sec was 92.3%, after 4 sec 11.3%, after 5 sec 89%, and after 10 sec 100.4%. The frequency of volleys thereupon gradually fell for a period of 1.5 min. After 2 min the frequency of volleys was close to its initial level. The SAP level under these circumstances rose from 138.3 ± 5.8 to 150.2 ± 4.2 mm Hg ($P < 0.05$) 30 sec after the beginning of stimulation of the nucleus.

In six experiments microinjection into the nucleus was accompanied by inhibition of sympathetic activity. Two seconds after the beginning of stimulation the frequency of volleys in the renal nerve decreased by 25%, and after 4 sec the decrease was 58.3% (Fig. 3). A reduction in the frequency of volleys was observed for 10-20 sec. The SAP level fell from 147.0 ± 2.2 to 122.0 ± 5.7 mm Hg ($P < 0.01$). Under these circumstances the increase in SAP was 4.0% 5 sec and 14.3% 10 sec after the beginning of stimulation; after 20 sec it showed its greatest decrease — by 17%, changing to 13.6% after 30 sec. The SAP level 1 min after the beginning of stimulation was 6.1% higher than initially, but after 1.5 min it was close to its initial level (3.4%).

Microinjection of serotonin into the nucleus of the tractus solitarius and into the ventral reticular nucleus was thus accompanied by marked changes in efferent sympathetic activity in the renal nerve and in SAP. These bulbar nuclei have been shown to contain serotonin-receptive neurons, activation of which by serotonin in the doses studied causes predominantly an increase in sympthatic activity in the renal nerve. In some experiments serotonin had an inhibitory effect on efferent activity in the renal nerve. Microinjection of serotonin into the nucleus of the tractus solitarius during bilateral compression of both carotid arteries was accompanied by inhibition of sympathetic activity. The character of the effect of injected serotonin on sympathetic activity was largely determined by the functional state of the structures into which the microinjection was given.

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