AUTONOMIC RESPONSES DURING CONTRACTION OF SKELETAL MUSCLES IN FREELY BEHAVING CATS

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Contraction of the gastrocnemius muscle was induced in intact cats by stimulating the nerve to that muscle through an implanted electrode at strengths expressed in multiples of the threshold level for motor response. Reflex changes in blood pressure and heart rate developed during contraction of the gastrocnemius muscle if unaccompanied by reflex pain. In the curarized animal painless and threshold painful activation of the nerve caused no autonomic changes. The autonomic reflexes observed during contraction of muscles in intact animals can serve as a model of changes in the hemodynamics and respiration in man during physical work.

KEY WORDS: *blood pressure; stimulation of nerve; contraction of muscle.*

A reflex rise of blood pressure (BP) during contraction of skeletal muscles in anesthetized or decerebrate animals is associated with activation of muscular afferents of groups III and IV [9, 18]. It is known, however, that group III-IV afferents convey impulses from muscle pain receptors [13, 14]. Under acute experimental conditions it is impossible to distinguish the nociceptive afferent flow along group III-IV fibers from the non-nociceptive flow associated with physiological contraction of skeletal muscles. The investigation described below was accordingly carried out to study reflex autonomic responses evoked by contraction of a skeletal muscle in intact cats under conditions of free behavior, so that nociceptive and non-nociceptive experimental effects could be differentiated.

EXPERIMENTAL METHOD

Altogether 27 experiments were carried out on 15 cats. Under pentobarbital anesthesia (40 mg/kg, intraperitoneally), 5-6 days before the experiments under sterile conditions a stimulating electrode was implanted on the nerve to the gastrocnemius muscle, a bipolar myographic electrode introduced into the gastrocnemius muscle and, in some experiments, a silicone-treated tube was inserted into the trachea. To inject the substances and record BP, venous and aortic catheters were introduced [3] and filled with a 6% solution of gelatin with heparin (2000 units/ml).

The stimulating electrode was made from silver wire 0.1 mm in diameter and a length (10 mm) of silicone rubber tube. The electrodes were fixed and insulated in the rubber tube by means of KLT-30 silicone sealing compound. Branches of the nerves to the gastrocnemius muscle supplying the lateral and medial heads were separated from the tibial nerve at a distance of 20-25 mm from the muscle and placed inside the electrode. The myographic electrodes were made from flexible multistrand stainless steel wire with vinyl insulation (AS-632 wire, Cooner Sales, USA). The stages in the making of the stimulating electrode and a scheme showing insertion of the stimulating and myographic electrodes are given in Fig. 1.

The threshold (T) of activation of the nerve to the gastrocnemius muscle, the average value of which was 0.172 V, was determined from the appearance of the M-response on the electromyogram (EMG). Tetanic contractions of the muscle were induced by electrical stimulation of the nerve (voltage from 1 to 10 T, frequency 50 Hz, pulse duration 0.1 msec).

BP was recorded by the EMP-34 electromanometer. The heart rate (HR) was determined continuously by an analog time interval meter [4], triggered by the BP pulse wave.

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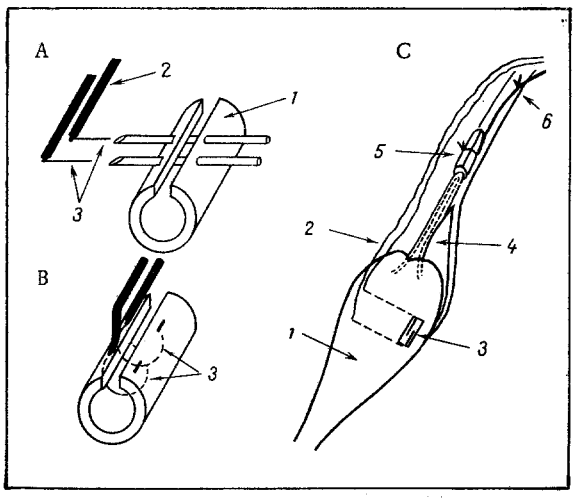

Fig. 1. Construction of stimulating electrode and scheme showing layout of electrodes. A, B) Stages in making stimulating electrode: 1) silicone rubber tube; 2) wire leads; 3) silver wire electrodes; C) scheme showing arrangement of implanted electrodes: 1) gastrocnemius muscle; 2) AS-632 wire, bared part of which acts as EMG electrode; 3) silicone rubber fixing plate; 5) stimulating electrode; 6) level of fixation of leads to membrane of sciatic nerve.

To assess the effect of activation of the afferent fibers under the stimulating electrode changes in autonomic functions in response to stimulation of varied intensity were investigated in each animal before and during the action of a muscle relaxant. A solution of listhenon was injected intravenously. After respiration stopped the animal was intubated and artificially ventilated. The endotracheal tube was smeared with amethocaine ointment.

During the experiment the animal was kept in a chamber measuring 500 × 500 × 600 mm. The indices studied were recorded on the Mingograph-34 instrument.

EXPERIMENTAL RESULTS

Stimulation of the nerve with a strength of 1 T caused no change in the indices recorded. During stimulation of the nerve with a strength of 2 T or more the limb was fully extended at the ankle and slightly flexed at the knee and hip, i.e., the thigh was drawn up toward the abdomen. The animals responded quietly to this contraction. BP, HR, and the respiration rate all rose (Fig. 2). Changes in the mean values of BP and HR were statistically significant during stimulation with a strength of 2 T. The mean BP in this case increased from 88 ± 3.4 to 102 ± 4.0 mm Hg ($P < 0.01$) and HR from 164 ± 7.3 to 183 ± 6.4 beats/min ($P < 0.05$). With an increase in the strength of stimulation the autonomic changes were greater. A sharp change in the autonomic response was observed when the painful level was reached, as shown by the animal's giving a single vocal response. A nociceptive response was observed in most animals to activation of the nerve with a strength of 6-8 T or more (Fig. 3).

To obtain data for the mean value of the maximal autonomic changes observed during painless stimulation, the results of individual experiments were aggregated depending on the time of appearance of a nociceptive response. During painless stimulation the mean increase in BP was from 90 ± 4.0 to 112 ± 3.5 mm Hg ($P < 0.001$), whereas during threshold painful stimulation of the nerve it rose from 89 ± 3.6 to 124 ± 3.6 mm Hg ($P < 0.001$). HR rose correspondingly from 169 ± 7.0 to 211 ± 6.3 beats/min ($P < 0.001$) and from 170 ± 6.4 to 221 ± 6.7 beats/min ($P < 0.001$).

A nociceptive response to stimulation of the motor nerve could be due either to activation of pain receptors within the muscle or to direct stimulation of afferent pain fibers. To facilitate the subsequent analysis, the nerve was stimulated for a short time (under 5 sec) by pulses with parameters sufficient to cause excitation of group III-IV afferents: 10 V, 2 msec. In response to this stimulation the animals developed a generalized pain response:

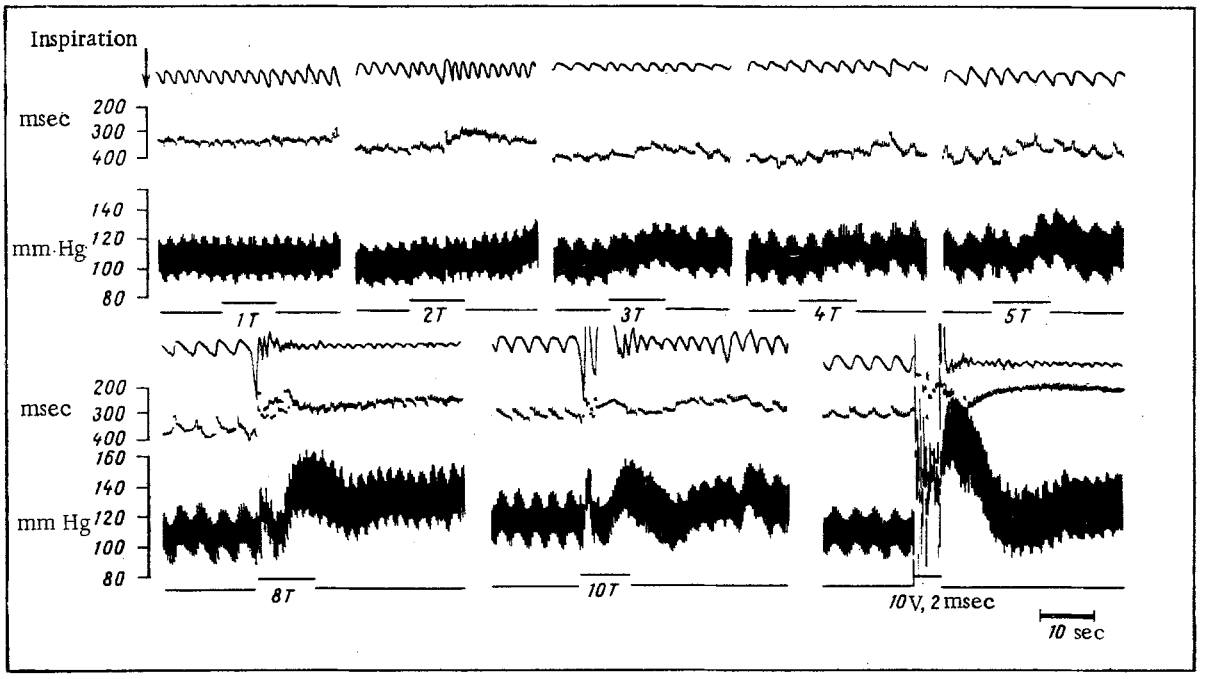

Fig. 2. Autonomic responses in intact cat during contraction of gastrocnemius muscle evoked by stimulation of nerve to that muscle. From top to bottom: respiration, interval between successive cardiac contractions, blood pressure, marker of stimulation. 1 T, 2 T, etc.: strength of stimulation of nerve in motor thresholds. Vocal response recorded on respiration curve during stimulation of nerve with strengths of 10 T and 10 V.

a loud cry and violent motor excitation. BP rose sharply and HR increased (Fig. 2).

The role of the contracting muscle in the genesis of painful and painless autonomic responses was determined in experiments in which a muscle relaxant was given. During stimulation of the nerve with a strength of between 1 and 8-10 T no changes in BP or HR occurred in the curarized animals. Painful stimulation of the nerve (10 V, 2 msec, 50 Hz) was accompanied by a marked increased in BP in the curarized animals. The magnitude of the pressor response was equal to or even greater than that of the response in the intact animals, and the increase in BP in the curarized animals lasted 3 to 4 times longer.

The results of the experiments on intact unanesthetized animals showed that reflex changes in BP, HR, and the respiration rate can arise in the absence of any signs of a pain response. It can tentatively be suggested that the autonomic changes observed were due to contraction of the triceps surae muscle and not to direct activation of afferent nerve fibers beneath the electrode. Such a conclusion is based on the following argument. The strength of stimulation of the motor nerve not evoking a pain response was 3-4 T or, sometimes, 6-8 T, as determined electromyographically from the appearance of the M response. The thickest and most easily excitable afferents of muscular nerves in cats are known to be activated at 1.4-1.8 T [12, 16]. Increasing the strength of stimulation to 4-5 T led to activation of all the group I fibers and some of the group II fibers [2, 20], but this was not accompanied by the appearance of somato-sympathetic reflexes [10, 15, 20]. On the other hand, stimulation of a motor nerve with a strength of 3-4 T is sufficient to cause excitation of most motor axons. In the present experiments this was confirmed by the fact that the magnitude of the M response during stimulation of this strength was maximal, and a further increase in the strength of stimulation caused no increase in the M-response.

In three control experiments on anesthetized animals stimulation of the nerves to the gastrocnemius muscle through the implanted electrode, with a strength of 3 T, was shown to cause maximal contraction of the triceps surae muscle. Curarization of the animal also demonstrated that, in the absence of muscular contraction in the unanesthetized cats, no autonomic responses arose to stimulation of the nerve with strengths of 2-4 T or more.

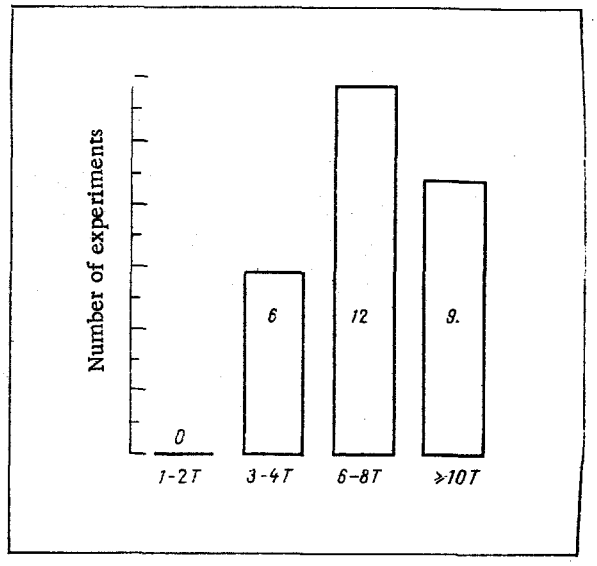

Fig. 3. Frequency of appearance of threshold nociceptive response (ordinate) depending on intensity of stimulation (abscissa).

Under chronic experimental conditions it is impossible to rule out activation of joint receptors, which could also lead to a reflex increase in BP, HR, and the respiration rate [7]. However, the influence of the joint receptors was evidently small in the present experiments, for movement of the limb at the joints was of short duration and occurred only once (at the beginning of stimulation), whereas in the experiments of Barron and Coote [7], movement in the joint occurred twice per second for 3 min.

The pain threshold, determined from the vocal response, was most frequently 6-8 T. The response was observed only at the beginning of stimulation and there was no after effect. Integration of this vocal response takes place at the bulbar level [11]. It is impossible to explain these results, on the basis of existing neurophysiological data on the thresholds of activation of different groups of muscle afferents [2, 12], by excitation of afferent pain fibers, for stimulation at 6-8 T does not affect group III, or still less, group IV fibers [20], which carry impulses from pain receptors [8, 13, 14]. Curarization, which itself does not affect action of the the afferents beneath the electrode, abolished the autonomic responses to threshold nociceptive stimulation. On the other hand, deliberate excitation of group III-IV fibers of the nerves to the gastrocnemius muscle gave identical autonomic responses in the intact and curarized cats. This suggests that in response to threshold nociceptive stimulation summation of the afferent flow from the contracted muscle with the additional flow of impulses takes place in the fibers with the lowest pain thresholds, and the combined afferent flow reaches the level of the pain threshold [1, 5]. This would explain the absence of autonomic changes in the curarized animals.

The investigation showed that reflex changes in BP, HR, and the respiration rate can be obtained in intact animals by indirect electrical stimulation of a skeletal muscle. Reflex autonomic responses observed in such animals can be used as a model for hemodynamic changes appearing in man during the performance of physical work [6, 17, 19].

LITERATURE CITED

1. A. V. Val'dman, The Neuropharmacology of Narcotic Analgesics [in Russian], Moscow (1972).
2. P. G. Kostyuk and N. N. Preobrazhenskii, Mechanisms of Integration of Visceral and Somatic Afferent Signals [in Russian], Leningrad (1975).
3. O. S. Medvedev, Fiziol. Zh. SSSR, No. 9, 1473 (1974).
4. O. S. Medvedev and A. A. Gorynya, Fiziol. Zh. SSSR, No. 9, 1440 (1975).
5. V. M. Khayutin, L. A. Baraz, E. V. Lukoshkova, et al., in: Neutral Mechanisms of Pain (Proceedings of an All-Union Symposium) [in Russian], Leningrad (1973), pp. 26-29.

6. M. Alam and F. H. Smirk, J. Physiol. (London), 89, 372 (1937).
7. W. Barron and J. H. Coote, J. Physiol. (London), 235, 423 (1973).
8. P. Bessou and Y. Laporte, C. R. Soc. Biol. (Paris), 152, 1587 (1958).
9. J. H. Coote, S. M. Milton, and J. F. Perez-Gonzalez, J. Physiol. (London), 215, 789 (1971).
10. J. H. Coote and J. F. Perez-Gonzalez, J. Physiol. (London), 208, 261 (1970).
11. B. Dahlstrom, G. Paalzow, and L. Paalzow, Life Sci., 17, 11 (1975).
12. R. M. Eccles and A. Lundberg, Arch. Ital. Biol., 97, 199 (1959).
13. M. Franz and S. Mense, Brain Res., 92, 369 (1975).
14. A. Iggo, J. Physiol. (London), 155, 52P (1961).
15. K. Koizumi and C. M. Brooks, Ergebn. Physiol., 67, 1 (1972).
16. K. Kubota, Y. Iwamura, and Y. Niimi, J. Neurophysiol., 28, 125 (1965).
17. A. R. Lind, S. H. Taylor, P. W. Humphreys, et al., Clin. Sci., 27, 229 (1964).
18. D. I. McCloskey and J. H. Mitchell, J. Physiol. (London), 224, 173 (1972).
19. J. H. Mitchell and K. Wildenthal, Annu. Rev. Med., 25, 369 (1974).
20. A. Sato and R. F. Schmidt, Physiol. Rev., 53, 916 (1973).

BLOOD PRESSURE REFLEXES TO STIMULATION OF TIBIAL NERVE A FIBERS IN MESENCEPHALIC AND BULBAR CATS

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The role of the various subgroups of A fibers of the tibial nerve (pulse frequency of electrical stimulation 10/sec) in the formation of reflex changes in blood pressure (BP) was investigated in unanesthetized cats with total transection of the brain stem at the level of the pontomedullary junction (bulbar animals) or at the rostral border of the mesencephalon (mesencaphalic animals), and also in anesthetized cats with an intact brain. The lowest thresholds for the reflexes were found in anesthetized animals with an intact brain, the highest in bulbar cats. Excitation of A fibers in anesthetized cats with an intact brain evoked only depressor reflexes. In some bulbar and mesencephalic animals only pressor reflexes appeared. In the experiments of this group excitation of fibers with a conduction velocity of over 15 m/sec in mesencephalic cats evoked reflexes of near maximal strengths, whereas in bulbar cats excitation of thinner A fibers also was necessary. In unanesthetized animals disconnection of the suprabulbar structures thus lowers the sensitivity of the central mechanisms of vasomotor regulation to impulses in low-threshold A fibers. No such effect was found in another group of experiments in which depressor reflexes appeared in response to stimulation of fast-conducting A fibers only. In these experiments, if slower A fibers also were stimulated, the reflexes became pressor but the difference between their magnitude in the bulbar and mesencephalic cats was not significant.

KEY WORDS: *decerebration; somatic afferents; blood pressure reflexes; general anesthesia.*

In the classical view reflex responses of the blood pressure (BP) to somatic nerve stimulation remain normal (i.e., the same as in animals with an intact brain) provided that connections are preserved at least with the pontobulbar region of the brain [4, 11]. This view is supported by the absence of changes in these reflexes after decerebration not only in acute [9, 10] but also in chronic experiments [13]. In these cases reflexes in anesthetized animals with an intact brain were regarded as "normal." However, other workers [1, 2, 5-8]

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