CHANGES IN EXCITABILITY OF THE VAGUS NERVE FOLLOWING PROTEIN SENSITIZATION VIA THE TONSIL

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In acute experiments on 33 rabbits an increase in excitability of the vagus nerve was found after general sensitization of the animal. In rabbits sensitized via the tonsil this increase was more marked than in rabbits sensitized transperitoneally. Excitability of the central segment of the divided vagus nerve was increased more then that of the peripheral segment by both methods of sensitization.

Both theoretically and practically the study of the mechanism of the heart lesions associated with diseases of the tonsils is a complex problem. Among the various factors linking the tonsil with the heart, great importance is attached to disturbances of vagus nerve excitability [6, 8, 10, 14, 18-20].

Previous investigations [11] showed that in experimental inflammation of the tonsils marked disturbances of excitability arise in the vagus nerve center and, to a much lesser degree, in the cholinergic structures of the heart.

Since sensitization of the body from a focus in the tonsils is considered to play an important role in the pathogenesis of tonsillogenic cardiopathies it is important to study changes in the excitability of the vagus nerve during sensitization produced by injection of the sensitizing agent into the tonsil compared with that observed after sensitization by other routes. In general sensitization has a well-marked effect, although differing according to results obtained by different investigators, on excitability of the vagus nerve [1-5, 7, 15-17].

The object of the investigation described below was to compare the excitability of the vagus nerve in animals after sensitization with horse serum by transtonsillar and transperitoneal routes.

EXPERIMENTAL METHOD

Thirty-three rabbits weighing 2-2.5 kg were divided into 3 groups with 11 animals in each group. In group 1 the excitability of the vagus nerves was studied after intraperitoneal sensitization. For this purpose, fresh horse serum in a dose of 1 ml/kg body weight was injected 4 times intraperitoneally at intervals of 2-3 days. The rabbits of group 2 were sensitized with the same dose of serum by injection into the tonsil. Using a fine needle with guard fitted to a syringe the serum was injected deep into the fauces between the pillars to a depth of 3 mm. The pharynx was illuminated by a mirror while the injection was given. The reference points were the masses of proliferation of lymphoid tissue which in rabbits are the analogs of the palatal tonsils. The injections were repeated 4 times at intervals of 2-3 days. Group 3 (the control) consisted of 11 unsensitized rabbits.

Excitibality of the vagus nerve was determined under acute experimental conditions in relation to square pulses applied at 50/sec. Platinum electrodes were placed on the exposed cervical trunk of the vagus nerve. To prevent the nerve from drying, it and the electrodes were covered with cotton wool soaked in warm physiological saline. As a rule, when the stimulation was repeated the polarity of the current was changed. After excitability of the intact nerve trunk had been studied the nerve was divided,

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both ends were taken up on ligatures, and the excitability of the central and peripheral ends of the divided nerve was measured in succession. Investigations were carried out both on the left and on the right nerve trunks. The duration of stimulation did not exceed 1 sec. The stimulation was repeated at intervals of 5-20 sec. Pulses were generated by a "Neurovar" (Alvar) stimulator. The intensity of stimulation was determined from the voltage of the current at the output of the generator. In all experiments stimulation began at subthreshold intensity and was gradually strengthened until the threshold effect appeared. This was detected by the response in the electrocardiogram, the pneumogram, and the tachogram, which were recorded simultaneously in different channels of a polyphysiograph (Galileo) with appropriate attachments.

The excitability of the nerve was studied in all sensitized rabbits 3 weeks after the last injection of horse serum. The rabbits were then given the reacting dose of serum intravenously, and the degree of sensitization was assessed from the severity of the manifestations of anaphylactic shock.

EXPERIMENTAL RESULTS

The investigation showed that sensitization of the animals, both intraperitoneally and by injection into the tonsil, increased the excitability of the vagus nerve as shown by a regular lowering of the thresholds of stimulation in the sensitized animals compared with the intact.

Equally regularly a difference was found in the degree of increase of excitability of the vagus nerve in the rabbits sensitized with horse serum intraperitoneally and in the rabbits receiving the same dose of serum by injection into the tonsil. In particular, the mean threshold of excitation of the vagus nerve trunk in intact (unsensitized) rabbits was 0.61 ± 0.07 V, while in rabbits sensitized by intraperitoneal injection of the serum it was 0.33 ± 0.08 V ($P < 0.02$). In rabbits sensitized by the transtonsillar route, the thresholds of stimulation were lower still, namely 0.21 ± 0.07 V.

Lowering of the threshold of stimulation as a result of sensitization was also observed when the excitability of the divided ends of the vagus nerve was investigated. However, the decrease in threshold of stimulation of the peripheral end of the divided vagus nerve after sensitization was less marked than the decrease in thresholds of stimulation of the central end.

A highly significant fact was that sensitization by intraperitoneal injection of horse serum and by injection into the peritonsillar region gave rise to different increases in the excitability of both peripheral and central ends of the divided vagus nerve: in both cases sensitization by the intraperitoneal route gave a smaller increase in excitability than sensitization by injection into the tonsil. In particular, whereas in intact animals the mean threshold of stimulation of the peripheral end of the vagus nerve was 1.07 ± 0.1 V, in animals sensitized intraperitoneally the threshold was reduced to 0.85 ± 0.08 V, and in animals sensitized by injection into the tonsil it was lower still, namely 0.7 ± 0.05 V (in both cases $P < 0.05$).

The thresholds of stimulation of the central end of the nerves in the sensitized animals were lowered by a much greater degree: their mean values were 0.29 ± 0.1 V in the animals sensitized intraperitoneally and 0.17 ± 0.05 V in animals sensitized by the transtonsillar route. In unsensitized animals the threshold was 0.49 ± 0.1 V.

The general patterns described above were found equally when excitability of the vagus nerve was determined on the opposite side.

The results given above thus indicate that the immunological response of the animal, in the form of protein sensitization, is accompanied by increased excitability of the vagus nerve, which is bound to affect the functional state of the heart. Meanwhile, sensitization arising from the region of the tonsil has a particularly marked effect on excitability of the vagus nerve, and this must be taken into account as a significant factor in the pathogenesis of tonsillogenic cardiopathies. In view of the results of the writers' previous investigations [11, 12], showing the high resorptive activity of the tissues of the tonsils and peritonsillar region in relation to labeled proteins, it can be assumed that the high activity of sensitization through these tissues, as reflected by changes in the excitability of the vagus nerve, is connected with the rapid and complete absorption of the sensitizing agent. At the same time, however, the possibility of reflex effects from the powerful reflexogenic zone of the tonsil and its surrounding tissues as an explanation of this fact cannot be ruled out.

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