

# CHANGES IN THE SENSITIVITY OF THE CAROTID SINUS RECEPTORS DURING AGING

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Translated from *Byulleten' Éksperimental'noi Biologii i Meditsiny*,

Vol. 54, No. 8, pp. 37-40, August, 1962

Original article submitted June 23, 1961

Reflexes from the carotid sinus receptors play an important role in the regulation of various vital functions. The pattern of formation of reflexes from the carotid sinus region in early ontogenesis has been studied in detail [3, 4,9], yet, so far as we know, no experimental investigation of these reflexes during aging has been undertaken. We can cite only clinical observations concerning the changes in Czermak's sinus reflex in elderly and old people [10,11].

It was considered important to study the changes in the reflexes from the pressure and chemical receptors of the carotid sinus region at this age period in response to the action of mechanical and chemical stimuli.

## EXPERIMENTAL METHOD

Investigations were conducted on 80 rabbits and 25 cats in acute and chronic experiments under chloral hydrate or urethane anesthesia. Fifty of the animals were young (1-1½ years) and 55 were old (rabbits aged 3½-4 years, cats aged 8-10 years). The blood pressure in the carotid artery (by means of a mercury manometer) and the respiration (by means of a tracheal cannula or a cannula connected to the nasal cavity) were recorded in these animals. The mechanoreceptors of the carotid sinus were stimulated by compressing the common carotid artery and by orthostatic tests, and the chemoreceptors were stimulated by injecting chemical stimuli into the isolated carotid sinus and by means of the technique used in S. V. Anichkov's laboratory. This method consists of the intravenous injection of substances which act reflexly on the respiration and circulation, by stimulating the chemoreceptors of the carotid region [1,2,6,7]. As chemical stimuli we used nicotine and cytisine (cholinomimetic substances) and sodium sulfide (an anoxic agent).

## EXPERIMENTAL RESULTS

The experiments showed that the sensitivity of the mechano- and chemoreceptors of the carotid sinus undergoes various changes during aging.

The pressor reflexes caused by compression of the common carotid arteries were smaller in magnitude in the old animals than in the young. In the young rabbits, for instance, the elevation of the arterial pressure after compression of the carotid arteries was 30-60 mm Hg (20 experiments), and in the old rabbits 15-35 mm Hg (25 experiments). Similar results were described by V. V. Frol'kis [8].

An indirect idea of the change in sensitivity of the mechanoreceptors of the carotid sinus was given by experiments involving orthostatic tests, in which the animals were transferred into a vertical position – with the head downward or upward. When the head was turned downward the pressure measured in the carotid artery rose, and when the head was turned upward, the pressure fell. Reflexes from the mechanoreceptors of the carotid sinus are known to play an important part in the restoration of the initial level of the blood pressure during orthostatic tests. The experiments showed that the rise and fall of the general arterial pressure in the old animals during the orthostatic tests were more marked than in the young, which indicates that the reflexes from the mechanoreceptors of the carotid region become weaker during aging. This was confirmed by experiments in which the orthostatic tests were studied before and after denervation of the carotid sinuses. These showed that after denervation more marked changes in the blood pressure were observed in the young animals than in the old.

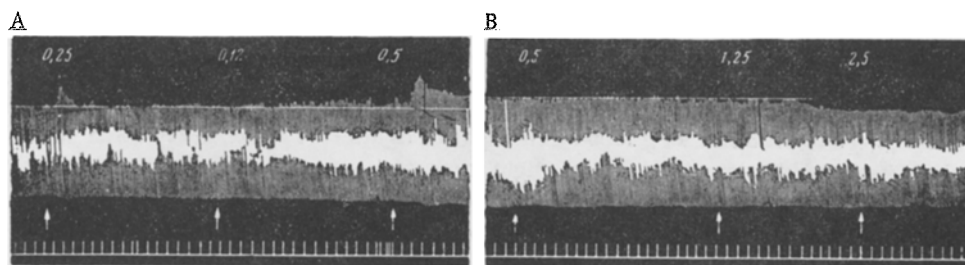


Fig. 1. Changes in respiration in an old rabbit after intravenous injection of sodium sulfide before (on the left) and after (on the right) denervation of the carotid sinuses. Significance of the curves (from above down): pneumogram; time marker (5 sec). The arrow points to the time of injection of the sodium sulfide.

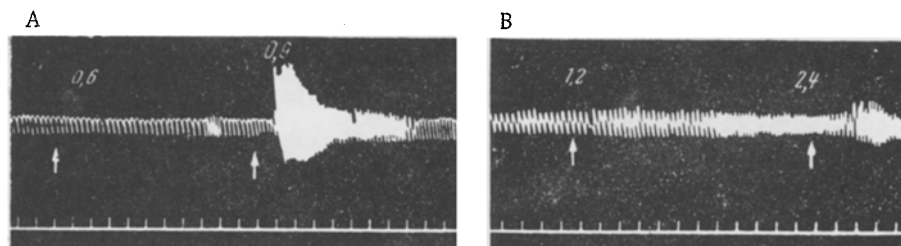


Fig. 2. Change in the respiration of a young rabbit after intravenous injection of sodium sulfide before (on the left) and after (on the right) denervation of the carotid sinuses. Legend as in Fig. 1.

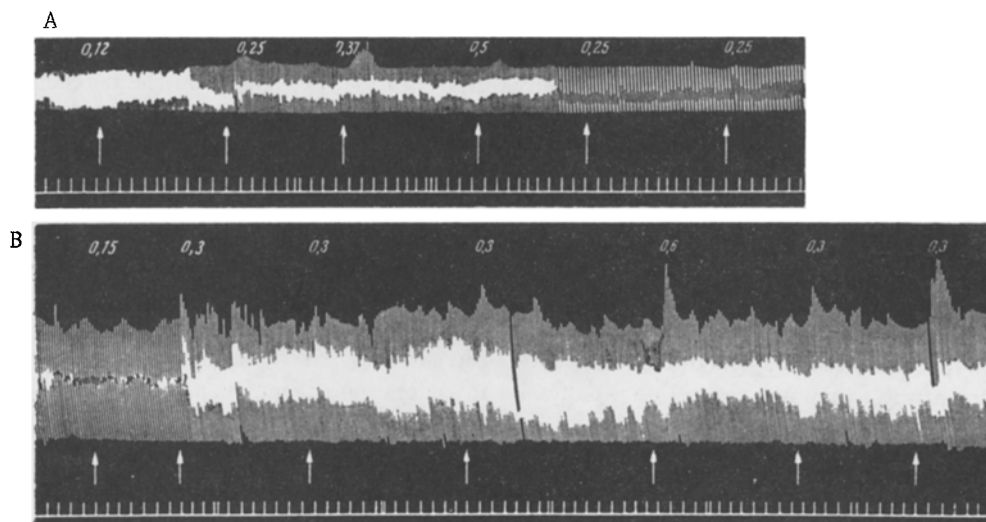


Fig. 3. Change in respiration of an old (upper pneumogram) and a young (lower pneumogram) rabbit during the repeated (interval 5-10 min) intravenous injection of sodium sulfide. Legend as in Fig. 1.

In the next series of experiments we studied the sensitivity of the glomus to the action of various chemical stimuli – sodium sulfide, cytosine, and nicotine.

These experiments showed that the old animals were more sensitive to the action of chemical stimuli than the young. For instance, after the intravenous injection of sodium sulfide into the old rabbits, marked dyspnea developed in response to a dose of  $0.25 \pm 0.015$  mg/kg (27 experiments), and in young rabbits in a dose of  $0.47 \pm 0.031$  mg/kg (30 experiments). The threshold doses of cytosine for the young cats (9 experiments) varied from 1.4 to 5  $\mu$ g/kg, with an average value of  $3.15 \pm 0.47$   $\mu$ g/kg, and for the old cats (12 experiments) it varied from 0.4 to 1.8  $\mu$ g/kg, with an average value of  $0.81 \pm 0.13$   $\mu$ g/kg.

During the intravenous injection of nicotine (9 experiments on cats and rabbits), the average threshold dose for the old animals was  $3.2 \pm 0.72 \mu\text{g/kg}$ , and for the young animals  $6.5 \pm 1.3 \mu\text{g/kg}$ . The difference between the mean values in all the experimental series was significant.

After denervation of the carotid sinuses, injection of the chemical agents in the same doses did not cause the development of dyspnea. An interesting fact was brought to light here: After denervation of the carotid sinuses in young animals it was possible to produce a very slight increase in respiration by means of a 4- to 5-fold increase in the threshold dose of sodium sulfide, while in old animals even a tenfold increase in the dose was quite ineffective in most of the experiments (Figs. 1 and 2). The same results were observed with cytosine: After denervation of the carotid sinuses the threshold dose of cytosine for the young cats had to be increased two- or fourfold, and for the old cats eight- to tenfold.

These results show that the difference which emerged in the sensitivity of old and young cats to the action of chemical stimuli was associated with an increase in the sensitivity of the carotid sinus receptors themselves, and not of the nerve centers. This conclusion was confirmed by experiments in which chemical stimuli, usually nicotine, were injected into the isolated carotid sinus. When nicotine was introduced directly into the sinus, we found that the reactions of the blood pressure and respiration developed at the same time. If threshold doses were used, only the blood pressure was changed, but as the dose was increased, respiration also was affected. The reactions of the blood pressure were variable: smaller doses gave rise to pressor reactions, larger doses to depressor, in agreement with the findings of Teng Si-hsien [5].

In the old rabbits (5 experiments) the injection of 0.2 ml of 0.001% nicotine solution into the perfused carotid sinus caused a pressor, or sometimes a depressor reflex action on the blood pressure. In the young animals (5 experiments), in order to obtain the same effect, the dose of nicotine had to be increased to 0.5 ml of a 0.001% solution, or even 0.2 ml of a 0.01% solution.

The young and old animals reacted differently to the repeated action of small doses of chemical stimuli, whether injected intravenously or into the perfused, isolated sinus. In old animals, after 5 or 6 injections at intervals of 5-10 min of threshold and superthreshold doses of sodium sulfide or cytosine, the effect began to diminish, and at the end of the experiment the threshold dose was quite ineffective. In young animals we did not observe such a rapid decrease in the sensitivity of the carotid sinus receptors to the action of chemical stimuli (Fig. 3).

Hence, in old animals, variable changes in the sensitivity of the mechano- and chemoreceptors of the carotid sinus develop. The reflexes from the mechanoreceptors of the carotid sinus are weakened and the sensitivity of the chemoreceptors in the same area is increased. However, the reflexes from the chemoreceptors are unstable in old animals, and they rapidly diminish when the action of the stimulus is repeated.

#### SUMMARY

In experiments on animals (rabbits and cats) of various age groups, a study was made of the reflexes from the mechano- and chemoreceptors of the carotid sinus. In old animals the changes occurring in the sensitivity of mechano- and chemoreceptors are not uniform. The pressor and depressor reflexes from the mechanoreceptors are weakened, and the sensitivity of chemoreceptors of the carotid area increases. The reflexes in old animals are not stable: with repeated action of the stimulus they decline rapidly and an adaptation phenomenon occurs.

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