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**Change in Blood Glucose Level in Rats
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16. Abstract

Experiments were carried out on male white rats divided into 4 groups. In group 1 the blood glucose level was determined immediately after immobilization and in the other 3 groups 2 hours following immobilization the blood glucose level was determined every 20 minutes for 3 hours 40 minutes by the glucose oxidase method. Preliminary immobilization for 2 hours removed the increase in the blood glucose caused by the stress reaction. By the 2nd hour of immobilization in the presence of continuing stress, the blood glucose level stabilized and varied within 4.2 ± 5.5 and 4.7 ± 8.1 mg %. Within 2 hours after the immobilization, the differences in the blood glucose level of the rats from the control groups were statistically insignificant.

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CHANGE IN BLOOD GLUCOSE LEVEL IN RATS AFTER IMMOBILIZATION

R. D. Platonov G. M. Baskakova, S. A. Chepurinov

In experiments on intact rats, changes in blood glucose level were studied through time (after each 20 minute period in the course of 3 hours 40 minutes) using the glucose oxidation method. It was shown that the preliminary immobilization in the course of 2 hours removes the increase in blood glucose level, which provokes a stress reaction. Blood glucose level in the stabilization period changes from 42 ± 5.5 to 47 ± 8.1 mg %. After 2 hours following immobilization, the difference in blood glucose level of the rats from the experimental and the 3 control groups was not statistically authentic. /37

The non-pharmacological immobility is the bondage of animals to the experimental table provoking a strong reaction, being built up from the psychoemotional state and muscular tension along with periods of freedom of movement¹⁴. For the rat being tied in a position at the spine is an especially strong stressor influence, in so far as the vestibular reflections act upon the endurance mechanisms of the vegetative regulation⁹. The investigations carried out in the last few years⁴ show that along with this, a remarkable change in the vascular system has been observed, which guarantees hemostasis. One of the most important sensory demonstrations of an increase in stress in the response to immobilization is the carbohydrate metabolism. Even in 1878 it had been discovered (see 5), that the procedure of tying a cat to a bench, and likewise, painful irritation provoked hyperglycemia in these animals. With the development of the presentation concerning the role of the limbic structures in neuroendocrinal regulation² it was established that the change in carbohydrate metabolism in the presence of stressor influences might occur through a change in the activity of these structures". The results of electrophysiological experiments and experiments with the destruction of the limbic structures testify to this.^{8, 12} In neuroendocrinal investigations on small animals with simultaneous registration of electroencephalograms, during decapitation are excluded, the puncture of veins along with several bonds is more convenient than habituation of channels.

In the present work, the results of the study of the change in blood glucose level in rats after immobilization are presented.

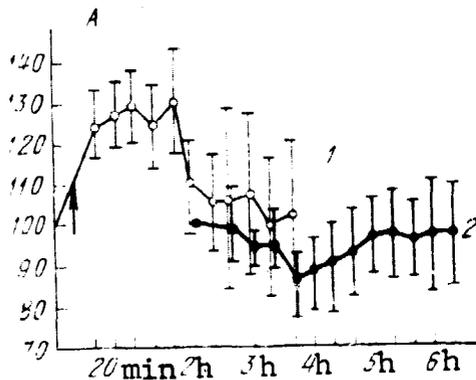
The experiments were carried out on 25 male white rats weighing 175-200 grams divided into 4 groups. In one group, the determination of

blood glucose level was begun immediately after tying them to the table; in the other three it was begun after the preliminary 2 hour immobilization (done by tying the animals to the table). Blood from the veins was taken according to the method worked out in the laboratory by B. A. Kudryashov, after each 20 minute interval in the course of 3 hours 40 minutes. Blood glucose levels were determined using V. K. Gorogetskiy's glucose oxidation method. Glucose levels after 20 minutes up to the introduction of a physiological solution in the lengthy counts were taken from 100% of the animals and the concentration of glucose at each point of the curve were obtained with them. In the animals of one group the blood glucose level was determined on the basis of a preliminary 4 day introduction of desoxycorticosterone (intraperitoneally from the count 5.7 mg /kg , daily according to 138 0.25 part of this dosage) the experiment began after the introduction of all obstructive doses after 3 hours following the last introduction of the hormone. For statistical calculations, of the results, the criteria of the authenticity of differences according to St'yudent was used.

It is recognized ¹³ that the maximum loss of the adrenocorticotrophic hormone (ACTH) and the glucocorticoids occurs in the first minute following stressor influence, and after 2-2.5 hours the blood catecholamine content drops. In order to clarify how these hormonal changes affect the summary index of the carbohydrate metabolism as well as the blood glucose level, a comparison was made between changes in the quantity of blood glucose in the rats from 20 minutes following bondage to 2 hours 20 minutes, following bondage. An intravenous injection of a physiological solution was a supplementary stressor influence. Then after each 20 minute interval blood was taken from the veins, therefore a painful stress in both groups was identical. However, it is on the basis of this, that the difference in blood glucose levels was observed in comparison with the preliminary immobilization of the rats and animals from which blood was taken immediately following bondage. In figure A (curve 1) it is shown that, in the first 2 hours the glucose level increased to 132% according to the relationship with the norm. After this, the concentration of blood glucose decreases, and, gradually, almost returns to normal, without taking into account the fact that painful stressor irritation is repeated. In the following 2 hours, the character of the change in blood glucose levels in the animals of this group was the same as following a preliminary 2 hour immobilization

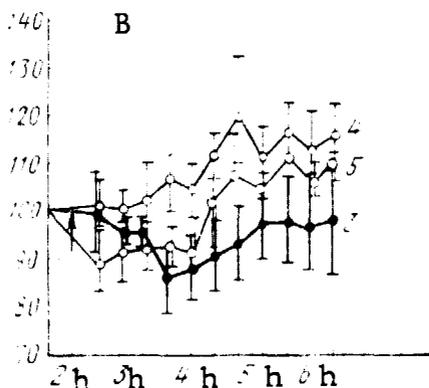
(fig. A, interval 2-3 hours 40 minutes).

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Change in blood glucose levels.
A--without preliminary immobilization;
B--with preliminary immobilization.

1--immediately following bondage (n=5), 2--after 2 hours following bondage (n=10), 3--control with the injection of physiological solution (n=5), 4--control without injection of physiological solution (n=5), 5--control with the injection of physiological solution after a 4 day injections of desoxycorticosterone (n=10). Arrows point out the moment of the introduction of physiological solutions.



Comparing curves 1 and 2 according to Styudenta's criteria of difference we discovered the authenticity of the difference that testifies to the non-homologous selection physiologically this may be interpreted as the influence of stress from immobilization in the first group.

The results obtained permit us to consider that towards the second hour of immobilization in the presence of continued stress or influence, blood glucose levels are stabilized and vary from 42 ± 5.5 to 47 ± 8.1 mg.%.

Because we did not determine the hormonal levels in the blood, a series of experiments were done with the notable exception of waste of glucocorticoids, raising the blood sugar levels in the 39 presence of stress.³ It is agreed in the literary data^{10,15} that hydrocortisone and dexamethasone impede the adrenocorticotropine function of the hypophysis and lower the ACTH content in the blood^{10,15}. The effect of stressor irritation under these conditions does not provoke an increase in the secretion of ACTH, and

consequently, also glucocorticoids.⁶ We used desoxycorticosterone - a hormone, according to its proximity to the aforementioned effect.

In fig. B (curve 5), the graph presents the change in blood glucose level during the previous injection of desoxycorticosterone. It is logical to note some decrease (about 11%) in the blood glucose level in the first 20 minutes of the experiment. Meanwhile, on curve 3 (immobilization + the injection of a physiological solution) an insignificant decrease blood glucose level is noted only after an hour following the beginning of the experiment. Obviously, in the animals of the 4th group the secretion of ACTH is suppressed and therefore the rise in the glucose level provoked by the effect of the glucocorticoids, does not occur. Towards the 4th or 5th hour of immobilization the blood glucose level is normalized, then a slight increase is observed. Having examined curve 3, it is logical to note that the blood glucose level changes very little in the course of the entire experiment. The slight hypoglycemia arising after 3 hours 20 minutes, is statistically not reliable. The animals did not experience any sort of influence, except the puncture of the veins and immobilization, there was no statistically accurate difference in the blood glucose level depending on the time of immobilization. The fact that all of curve 4 is located higher than curves 3 and 5, may be explained by the fact that the initial glucose level at the norm in these animals is higher (112 ± 6.5 mg.%) than in the animals of the second group (103 ± 3.3 mg.%) and the 4th group (56 ± 9.4 mg.%).

The data we obtained concerning the blood glucose level in rats (34 ± 5.6 mg.%), and concerning the increase of it in the first period of stress - the acute phase, as well as the size of the maximum hyperglycemic loss in the response to immobilization (60 ± 2.4 mg. %) is in agreement with the results of other authors.^{1,3} As can be seen, after 2.5 hours the stressor hormonal responses are stabilized. Obviously, because of this, the term 2.5 hours after immobilization is used along with the investigation of multiple-stressor influence and the processes of adaption to it.^{12,14}

With the end of our acute phase of stress, a slight, slow increase in the blood glucose level in all control groups in that number and on the basis of the blocked secretion of ACTH. It may be suggested that in this case the change in stipulated influence on the carbohydrate metabolism of adrenaline and those viscera-visceral reflexes, is transferred along the sympathetic paths, arising in the presence of pain and loss of blood. An insignificant hypoglycemia of short duration

along with the injection of physiological solution requires a complete explanation. In any case this may not be explained by the inclusion of the somatotropic hormone with its insulin-like effect in the stressor reaction, as far as, according to V. P. Fedotov and Ya. A. Sokolov⁷, that of the rats is distinguished from that of the primates the even stronger stress after laparotomy, does not provoke a rapid separation of somatotropic hormone in the vascular system. Undoubtedly, prolonged immobilization and increased blood loss leads to a more significant change in the blood glucose level.

REFERENCES

1. Bondarenko, M. F., "The activity of lipoprotein lipase of the stomach muscles in the presence of experimental diabetes in connection with stress," Probl. endokrinologii, 16, 2, (1970).
2. Vein, A. M., Solov'eva, A. D. "The limbico-reticular complex and the vegetative regime," Nauka., Moscow., (1973).
3. Ivanova, I. I., Lapshina, V. F., "Stress in the presence of alloxanic diabetes in rats," Bull. eksperim. biologii i meditsiny., 10, (1972).
4. Kudryashov, B. A., Lomovskaya, E. G., Shapiro, F. B., Lyapina, L. Ya., "The influence of adrenalectomy and the injection of corticosterone on fibrolytic activity of a complex combination of heparin in the blood after immobilization," Fiziol. zhurn., 59, 7., USSR., (1973).
5. Mintyushov, M. I., "The function of the great hemisphere of the brain and the blood sugar level," Nauka, Moscow-Leningrad., (1964).
6. Timofeeva, N. O., "Electrophysiological analysis of the participation of the limbic structures of the brain in the organization of behavior," Avtoref. kandid. diss., Moscow (1972).
7. Fedotov, V. P., Sokolov, Ya. A., "The Basic principles, some results, and perspectives of application of a radioimmunological method of the separation of albuminous hormones," in Sovremennye voprosy endokrinologii, "Meditsina," Moscow (1972).
8. Chepurnova, N. E., Chepurnov, Ya. A., Tong Fyuk Khao., "The participation of the amigdala in the reactions of the limbic system on the somatotrophic hormone of hypophis." Vest. Moskovsk. un-ta, ser. biologii i pochvovedeniya, 2, (1974).
9. Akkert, K., Gernandt, B. E., "Neurophysiological study of vestibular and limbic influences upon vagal outflow." EEG Clin. Neurophysiol., 14, 904-914, (1962).
10. Ashfold, A., Jones, J. I. M., "The assay of corticotropin in hypophysectomized and in cortisone-treated rats." Brit. Journ. Pharmacol. and Chemother., 20, 95-98, (1963).

11. Klemm, W. R , "Correlation of hippocamel theta rhythm, muscle activity and brain stem reticular formation activity. Commun. Behav. Biol., pars A5., 147-151, (1970).
12. Kvetnansky, R., "Transsynaptic and humoral regulation of adrenal catecholamine synthesis in stress," in: Frontiers in Catecholamine Research, B, London, (1973).
13. Kvetnansky, R., Weise, V. K., Gewirtz, G. P., Kopin, I. J., "Synthesis of catecholamines in rats during and after immobilization stress," Endocrinol., 89, 46-50, (1971).
14. Kvetnansky, R., Weise, V. K., Kopin, I. J., "Elevation of adrenal tyrosine hydroxylase and phenyletanolamino-N-metyl transgerase by repeated immobilization of rats," Endocrinol., 87, 744-749, (1970).
15. Sirett, N. E., Gibbs, F. B., "Dexamethasone suppression of ACTH release: effects of the interval between steroid administration and the application of stimuli known to release ACTH," Endocrinol., 85, 355-359, (1969).

Recommended by the chairman of the dept. of human and animal physiology of the Moscow State University imeni M. V. Lomonosov.