TRANSFER OF CONDITIONED HYPOGLYCEMIA IN DOGS

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It has been shown experimentally [1, 2, 7, 8] that the blood sugar level of animals and man can be controlled by a conditoned reflex. In particular, conditoned hypoglycemia can be produced in dogs if in a series of experiments instad of glucose, an equal volume of physiological saline is injected [8]. Meanwhile, studies of transfer of acquired skills with the aid of brain extract or cerebrospinal fluid (CSF) from trained animals (donors) to untrained animals (recipients) have shown that neurohumoral transfer of behavioral skills is possible [3-5].

The aim of the present investigation was to produce conditoned hypoglycemia in donor dogs and to transfer this reflex neurohumorally to recipient dogs. To assess the degree of transfer a chemical method of analysis was chosen, because it enables the degree of transfer of the state from the donor to the recipient animal to be detrmined more precisely than by a biological method.

EXPERIMENTAL METHODS

Experiments were carried out on adult mongrel dogs into whose jugular vein a long-term standard catheter 1 mm in diameter was inserted. The background blood sugar level (BSL) was determined in all the dogs 3 days after the operation and the orienting reaction to the experimental situation was extinguished. To do this, in three or four experiments an acoustic stimulus was presented to the dogs for 20 sec: white noise with an intensity of 60 dB. At the 19th second after the beginning of the experiment 60 ml of physiological saline was injected through the catheter. After determination of BSL in the donor dogs, the conditoned reflex was formed. The conditoned stimulus was the same white noise, which was applied at the 15th minute after the beginning of the experiment, and the unconditioned stimulus consisted of injection of 20% glucose solution (0.8 g/kg of the dry substance). The degree of consolidation of the reflex was judged from the results of control experiments, in which instead of glucose, the donors were given an injection of an equal volume of physiological saline. Blood was taken from the cathether every 10 min from the beginning of the experiment. Blood sugar curves were plotted from the data of the control experiment (Fig. 1). A donor was considered to be ready if conditioned-reflex changes in BSL took place. After the background experiments 1 ml of CSF was taken from the recipient dogs and used for testing compatibility between donor and recipient. They were then given an injection of CSF from the prepared donors. The operation of CSF exchange was carried out under thalamonal (fentanyl) anesthesia, for which purpose CSF taken by cisternal puncture from the donor in a volume of 0.5 ml was injected into a recipient. Experiments with the recipients began 24 h after this procedure, when the conditoned stimulus was applied and physiological saline injected. BSL was determined with the "glucose enzyme" kit (Lachema, Czechoslovakia). The optical density of the samples was determined on an SF-16 spectrophotometer. To analyze relative changes in BSL the coefficient of change of BSL (CCBSL) was calculated by the equation:

$$CCBSL_{exp} = \frac{C_{exp}}{C_{av}} \text{ (in conv. units)}; \; C_{av} = \frac{C_1 + C_2}{2},$$

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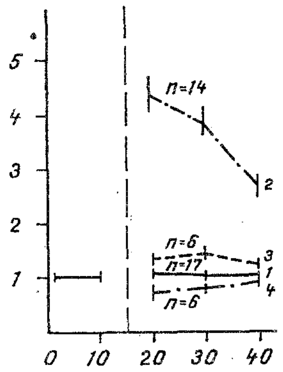

Fig. 1

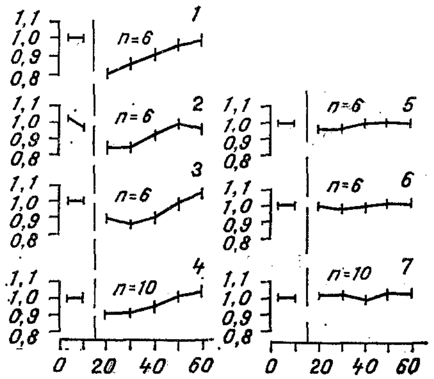

Fig. 2

Fig. 1. Changes in BSL in donor dogs during conditioning. Abscissa, time of bginning of experiment (in min); ordinate, BSL (in conv. units). 1) Background sugar curve (acoustic stimulation was followed by injection of physiological saline); 2) sugar curve in experiment with unconditioned stimulus (conditioned stimulus was followed by intravenous injection of glucose solution); 3) hyperglycemic sugar curve in first and second control experiments; 4) isoglycemic sugar curve in third and fourth control experiments. Vertical broken line indicates time of presentation of conditioned stimulus. Portion of curve corresponding to 1-10 min after begining of experiment common to all curves. n) Number of animals.

Fig. 2. Changes in BSL in recipient dogs after injection of CSF from donor dogs. 1-6) 1, 2, 3, 5-7, 14, and 17 days respectively after transfer; 7) control recipients. Remainder of legend as to Fig. 1.

where C_1 is the absolute BSL in the first blood sample taken, C_2 the absolute BSL in the second blood sample, C_{exp} the absolute BSL in any experimental sample, and C_{av} the average BSL. To estimate changes in BSL, the data were subjected to statistical analysis [6].

EXPERIMENTAL RESULTS

In the course of the experiments the dogs jumped peacefully on to a table in the experimental room and stayed there without fixation for 80-90 min. In the background experiments fluctuations of BSL in the dogs relative to the initial value amounted to 0.04 ± 0.02 conv. unit; the random character of fluctuations of the background blood sugar curves was confirmed, moreover, by plotting an averaged curve based on the results of 17 background investigations (Fig. 1, I). It can be concluded from the data obtained in the background experiments that two or three exposures to white noise and injection of physiologgical saline had no significant effect on BSL in the dogs.

In the control experiments the three donor dogs received, instead of the unconditioned stimulus (glucose), an injection of the equivalent volume of physiological saline. In this way it was possible to judge the process of formation of hypoglycemic response. These experiments were carried out during conditoning after 5, 10, 15, and 20 experiments with injection of glucose.

The results obtained during conditoning of the donor dogs showed that the formation of this process takes place in two stages: I) elevation of BSL compared with the initial level in control experiments (hyperglycemic). II) Depression of BSL compared with the initial value in control experiments (hypoglycemic). The averaged data, which reflect the hyper- and hypoglycemic character of the change in BSL during conditioning, are given in Fig. 1. The mean increase compared with the initial level was 0.18 conv. units (Fig. 1, 3), the mean decrease 0.25 conv. unit (Fig. 1, 4). The original level was restored after 40 min.

Having obtained experimental conditoned reflex hypoglycemia an attempt was made to model this state in the recipient dogs. BSL of all recipients was observed to be lower than initially 5-15 min after presentation of the conditioned stimulus, and this was followed by a return to the background value. Averaged graphs for different times after transfer of the conditioned reflex are given in Fig. 2. The lowering of BSL by 0.2 conv. units below the initial level on the first day after transfer was maximal, for on the second day the decrease was 0.15 conv. unit and on the third day it was 0.09 conv. unit, and showed no definite time course: on the 5th-7th day it was 0.11 conv. unit lower than on the third day, on the 14th day the decrase was not significant (0.05 conv. unit), and on the 17th day there was no decrease (Fig. 2).

Thus after injection of CSF from animals with an established conditioned reflex into recipients, after presentation of the conditioned stimulus to the latter a distinct hypoglycemic response was observed and was maintained for 5-7 days after injection of the donors' CSF. Under these circumstances the changes in BSL developed in a similar way to those in the donors. Evidently CSF of the donor animals contained specific chemical factors which, when injected into intact animals, induced corresponding intracentral readjustment, analogous to those in the donor animals. In turn, as a result of these readjustments, the recipients acquire the characteristic conditioned reflex of the donors. Incidentally, by contrast with previous investigations [3-5], the present one is an example of transfer of an autonomic (in fact, corticovisceral) reflex.

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