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28 November 1955

"Whirling Behavior" in Dogs as Related to Early Experience

In the course of 3 years of experimentation on the relationship of early experience in dogs (Scottish terriers) to their later behavior, there has appeared an interesting phenomenon that is worth reporting separately (*1*). This is the occurrence of "whirling fits" in a number of dogs that were restricted during early life.

Restriction is imposed by rearing the experimental animals from 1 to 8 or 10 months of age in isolation cages (one dog per cage) that are so constructed that the dog inside each can never see any more than the floor of the cage above or the ceiling of the room. By means of a small side compartment adjoining the living space and separated from it by a sliding panel, feeding and cleaning can be accomplished without exposing the restricted animal to the outside environment. After the period of restriction is over, the experimental "Scotties" are compared by means of psychological tests with their littermates which have been reared normally as pets in homes.

Many striking differences have appeared between the normal and the restricted dogs in all phases of behavior, including intelligence, activity, emotionality, and social behavior. These are reported in full elsewhere (*2*). More bizarre than any of these effects of early restriction are the afore-mentioned whirling fits. These have appeared in eight out of eleven severely restricted animals. The three exceptions, while highly active and excitable, have not, to our knowledge, shown the extreme behavior discussed here.

Whirling can be described as follows: very rapid, jerky running in a tight circle; shrill, agonized yelping; barking and snarling; and tail snapping and tail biting. The syndrome may last from 1 to 10 minutes. It is usually heralded by certain characteristic signs. The dog suddenly becomes motionless, cocking its head up and back, as if looking at its own tail. It begins to growl viciously, and its eyes take on a glazed expression. These signs may continue for a minute or two, increasing in intensity until the full-blown fit occurs. To all appearances, whirling does not seem to be under voluntary control but to be "driven." The dog does not seem to be able to control its behavior and cannot usually be distracted even by fairly intense stimuli.

Whatever its nature and causes, whirling is a peculiar and striking form of behavior that is worth further investigation. Several points concerning it should be noted. In the first place, it seems to vary in degree, with respect to both intensity and duration.

Second, although many of the fits appear to occur spontaneously (in that the immediate causes are not known), they usually seem to be set off by some change in the stimulus-environment. This change may be anything from the mere introduction of a food dish into the cage to electric shock or restraint in a harness for a period of time.

Third, all the dogs showing whirling fits shared, to some degree, a common ancestry. All were descendants of three Scotties purchased from Hamilton Station, Bar Harbor, Maine, and bred, within themselves and to outside dogs, for several generations. However, the three animals not showing this behavior were also related to this strain. Consequently, it is difficult to make any obvious inferences concerning the possible genetic origin of the trait.

Fourth, all dogs showing whirling have had a background of severe restriction in early life. None of their normal littermates have shown such behavior. At the same time, since the three exceptions have also undergone restriction, this kind of early experience is not a sufficient condition for the appearance of the symptoms, although it may be a necessary one.

In view of the foregoing points, it is difficult to know what ultimate factors predisposed some animals to whirling fits. Diet is a possible explanation, although it could not be the only cause, since all the animals in the laboratory were fed the same amount and type of ration made up according to the specifications of several experts in dog care. All dogs received, during a typical week, meat (liver, Pard, hamburger), dog biscuits, Purina Dog Chow, vegetables, cod-liver oil, and milk while they were puppies. The restricted animals showed appetites as good or better than normals. At the same time, we cannot rule out the possibility that this diet might have been inadequate for dogs raised in severe restriction, even though it appeared to be adequate for dogs living in normal environments.

The possibility that whirling was caused by a specific irritation in the tail —thus causing the circling and tail snapping—is unlikely. It does not seem reasonable to suppose that such extreme behavior could be set off so easily and set off only under special conditions involving a change in the sensory environment. When tail injuries did occur, they appeared definitely to be the result rather than the cause of whirling. Consequently, we are inclined to feel that the behavior is central and not peripheral in origin.

Finally, it must be mentioned that the dogs were constantly checked for signs of worms and distemper by examination of their feces and by noting any decline in appetite. There was no evidence of ill health among any of the experimental dogs during their period of restriction. After removal from restriction, they were examined more carefully by a veterinarian, with negative results.

Accordingly, there are considerable grounds for supposing that whirling is dependent, at least partly, on the conditions of restriction imposed during early life. Whether or not it can properly be described as epileptiform is a moot point. None of the parasympathetic components of true seizures were ever observed in the dogs. On the other hand, the gross features of its expression would suggest that it is essentially a related phenomenon.

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References and Notes

1. The observations reported here are part of a project of the McGill Psychological Laboratory supported by a grant-in-aid from the Rockefeller Foundation. The behavior described in the article has been filmed, and the film will soon be available.
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1 November 1955

Action of Some Centrally Acting Drugs on Ion Transport in Red Cells

Stimulation of excitable tissue is known to be followed by a decrease in membrane potential, which is accompanied by an increased permeability of the tissue to sodium and potassium (*1*). Thus, the cell, on stimulation, loses potassium and gains sodium. During recovery, sodium is removed from the cell and potassium is replaced. The recovery process depends on the active transport of one or both cations, since the movement is against the concentration gradient.

When human blood is refrigerated, the

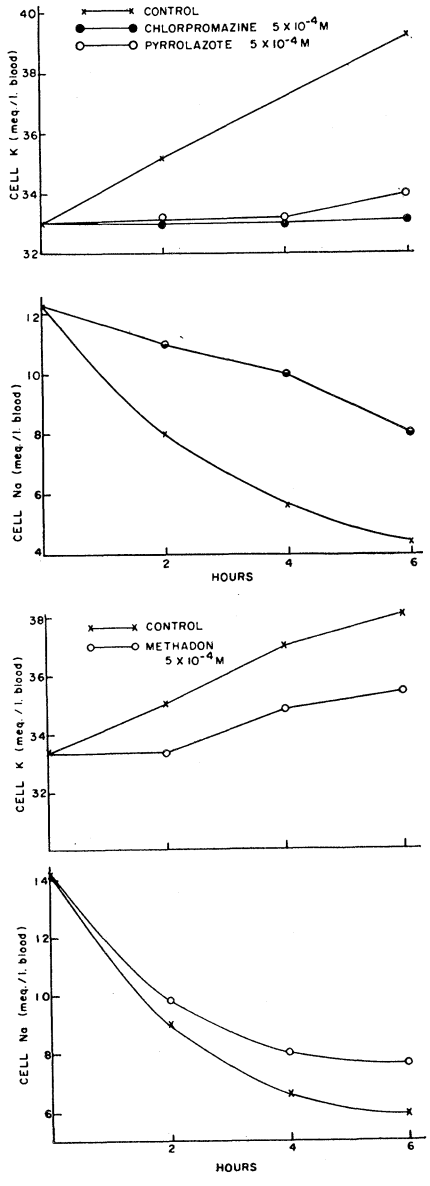

Fig. 1. Erythrocyte sodium and potassium plotted against time.

erythrocytes lose potassium and gain sodium. On warming to 37°C in the presence of the appropriate substrate, potassium is replaced in, and sodium removed from, the cell (*2*). There is no proof at present that the mechanism for active transport of cations is the same in all tissues, but it is likely that the fundamental process is, at least, similar.

The action of certain drugs that affect the central nervous system has been tested on the transport of sodium from, and potassium into, erythrocytes of blood that had been refrigerated for several days and then incubated at 37°C.

Freshly drawn human blood was defibrinated by shaking it with glass beads under sterile conditions and was stored in the refrigerator at about 5°C for 3 to 5 days. During this time, the erythrocytes lost potassium and gained sodium. On removal of the blood from the refrigerator, glucose (1 mg/ml blood) was added to it; sodium chloride solution (0.9 percent) was added to the control suspension (0.1 ml/ml blood); and the drug, which was dissolved in sodium chloride solution (0.9 percent), was added to the experimental suspensions. The blood was incubated at 37°C, and, at intervals of about 2 hours, 1-ml samples were removed and centrifuged. The plasma was removed from each sample, and the cells were washed with sucrose solution (9.8 percent) and hemolyzed by the addition of distilled water. The protein was precipitated by adding trichloroacetic acid to the hemolyzate to give a final concentration of 5 percent. The filtrate was used for the determination of sodium and potassium, using the Beckman DU spectrophotometer with flame attachment.

The drugs that were tested on the extrusion of sodium from, and uptake of potassium by, red cells were morphine sulfate ($10^{-3}M$), pentobarbital sodium ($2 \times 10^{-3}M$), methadone (*3*) (2.5 and $5 \times 10^{-4}M$), cocaine ($3 \times 10^{-4}M$), Pyribenzamine (*4*) ($3 \times 10^{-4}M$), chlorpromazine (*5*) (2.5 and $5 \times 10^{-4}M$), and Pyrrolazote (*6*) ($5 \times 10^{-4}M$). Three of these drugs—namely, methadone, chlorpromazine, and Pyrrolazote—inhibited both sodium and potassium transport. The results of a typical experiment are shown graphically in Fig. 1. This effect is similar to that described by Schatzmann (*7*) and by Glynn (*8*) for certain cardiac glycosides. The other drugs had no effect under our experimental conditions.

The concentrations of methadone that were used are sufficient to inhibit glycolysis and carbohydrate oxidation by brain tissue (*9*). However, the concentrations of the phenothiazine drugs that were used in these experiments had no effect on either glycolysis or oxidation of glucose by brain tissue. Thus, inhibition of transport cannot be correlated with inhibition of glycolysis in the case of the phenothiazine drugs.

The concentrations of phenothiazine drugs that were used in these experiments to inhibit ion transport are several times greater than those required to inhibit hemolysis by lysolecithin (*10*).

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25 November 1955

Enzymatic Detoxification Mechanism for Viadril

The structural similarity of the steroid anesthetic, Viadril (*1*) (pregnan-21-ol-3,-20-dione 21-hemisuccinate) (*2*), to substrates of several enzymes currently under investigation (*3–5*) has suggested that related reactions may be involved in its detoxification. Thus, Viadral might be reduced at the 3-position (reaction 1), and then be conjugated as the glucuronide (*6*). Alternatively, the following sequence of reactions may occur: esterase action on Viadril to produce succinate and pregnan-21-ol-3,20-dione (reaction 2), reduction of the steroid moiety catalyzed by 3α-hydroxysteroid dehydrogenase (reaction 3), and conjugation. These possibilities have been investigated, utilizing enzyme systems (*7*) partially purified from rat liver. The reactions examined were

$$\text{Viadril} + \text{DPNH} + \text{H}^+ \rightleftharpoons \text{pregnane-3}\alpha,\text{21-diol-20-one 21-hemisuccinate} + \text{DPN}^+ \quad (1)$$

$$\text{Viadril} + \text{H}_2\text{O} \rightarrow \text{Pregnan-21-ol-3,20-dione} + \text{succinate} \quad (2)$$

$$\text{Pregnan-21-ol-3,20-dione} + \text{DPNH(TPNH)} + \text{H}^+ \rightarrow \text{pregnane-3}\alpha,\text{21-diol-20-one} + \text{DPN}^+\text{(TPN}^+\text{)} \quad (3)$$

Reaction 1 was reversibly catalyzed by an ammonium sulfate fraction of rat liver that, when it was added to Viadral and DPNH, caused a rapid oxidation of the reduced pyridine nucleotide as measured in the spectrophotometer at 340 mμ. TPNH did not function in this reaction. When 3α-reduced Viadril (pregnane-3α, 21-diol-20-one 21-hemisuccinate) was incubated with the enzyme preparation and DPN^+, a prompt reduction of the pyridine nucleotide was observed. With 3β-reduced Viadril as substrate, DPN^+ was not reduced. It is of interest to note that reaction 1 was also catalyzed by αBAD (*3*) that was obtained from an organism isolated by enrichment culture. In the presence of DPNH, this enzyme reversibly reduces 3-ketosteroids with a terminal carboxyl group. Viadril was reduced to 3α-reduced Viadril by the enzyme at 40 percent of the rate of the reduction of ketocholanic acid.