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BRIEF COMMUNICATION

Lever-Pressing Behavior Caused by Intraseptal Angiotensin II in Water Satiated Rats[1]

FREDERICO G. GRAEFF, CLEBER G. GENTIL, VERA LÚCIA PERES AND MIGUEL R. COVIAN

School of Medicine and School of Dentistry and Pharmacy, 14.100 Ribeirão Preto, S. P., Brazil

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GRAEFF, F. G., C. G. GENTIL, V. L. PERES AND M. R. COVIAN. *Lever-pressing behavior caused by intraseptal angiotensin II in water satiated rats.* PHARMAC. BIOCHEM. BEHAV. 1(3) 357–359, 1973. –Intracerebral injection of angiotensin II induced drinking behavior in satiated rats. In the present experiments five rats, presenting a positive drinking response to the intraseptal injection of angiotensin II, were trained to press a lever for water in a standard chamber, used for operant behavior studies. The injection of 1 μg of angiotensin II into the septal area of the brain caused the animals, previously satiated in the experimental chamber, to resume lever pressing under a continuous reinforcement schedule of water presentation. The number of responses emitted after angiotensin was considerably higher than after a control injection of saline. This result supports the hypothesis that angiotensin has a dipsogenic action in the CNS that mimicks the effect of water deprivation.

Septal area Angiotensin II Operant behavior

THE intracerebral injection of minute amounts of angiotensin and related peptides has been reported to induce drinking in satiated rats [1, 3, 4]. Most sensitive brain loci include the anterior hypothalamus, preoptic and septal areas, in which consistent dose-response relations between drug and amount of water ingested have been determined [3]. If the action of angiotensin in the CNS is to be interpreted as an increase in thirst, angiotensin effects should mimick other consequences of water deprivation, in addition to increasing the probability of occurrence of the consummatory act. In order to verify if the angiotensin induced drinking can be attributed to motivational change, an experiment was designed to determine if the intracerebral injection of angiotensin would lead rats, that had been previously trained to lever-press for water in a standard operant conditioning situation. to resume responding after being satiated in the experimental chamber.

MATERIAL AND METHOD

Eleven adult male albino rats of the Wistar strain, 200–300 g body weight were kept in individual cages with a food cup filled with a dry mixed diet and a graduated drinking bottle, filled with unfiltered tap water; daily readings were made of the intakes. After a few days, a stainless steel cannula (o.d. 0,71 mm) was stereotaxically implanted in the septal area, according to de Groot's atlas [2], under ether anesthesia. The cannulae were positioned 1,0 mm anterior to the bregma, 0,3 mm lateral to the midline and 6,0 mm below the surface of the skull. Each cannula was provided with a mandrel to prevent its obstruction. One week after recovery from the surgical procedure, injections were made through a dental stainless steel cannula (o.d. 0,31 mm) in unanesthetized and unrestrained rats, in normal water balance. Angiotensin (val-5-angiotensin-II-amide, Hypertensin CIBA) was delivered by a 10 μl microsyringe in a volume of 1 μl of isotonic saline. For this purpose, a polyethylene plastic tube was connected to the inner cannula, which was placed inside the guide cannula and pressed downward to its tip. After the intraseptal injections of angiotensin, the water intake of rats, under usual laboratory conditions of living, was recorded for 1 hr. In this series, five out of the eleven animals ingested more than 10 ml of water during the 60 min period after the injection of 1 μg of angiotensin and were selected for use in the following experiment.

The five animals were trained to press a lever (15 g minimum pressure) placed 9 cm above the grid floor of a standard E3125D chamber (Grason-Stadler), currently used for operant behavior studies and obtained at least 200

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reinforcements, under a continuous reinforcement schedule (CRF) of water presentation, before being submitted to the test situation. Each reinforcement consisted in the presentation to the animal of 0,03 ml of water, for 3 sec. Standard electromechanical equipment (Grason-Stadler) was employed for automatic programming and recording. Lever-pressing responses were recorded in a digital counter and in a Gerbrands cumulative recorder.

Rats were deprived of water for 24 hr before the experimental session. Each animal was placed inside the experimental chamber and allowed to respond, under a CRF schedule of water presentation until the following satiation criterion was met. If the animal did not emit a sequence of at least two reponses in succession, during 5 min, he was considered as satiated. After satiation, the animal was removed from the experimental chamber and intracerebrally injected with 1 μg of angiotensin.

After the injection animals were immediately replaced inside the experimental chamber, under the same CRF schedule conditions. Animals were allowed to level-press for water, until the above satiation criterion was met.

In a control session, undertaken 7 days after, the same sequence of events followed, except that each animal was injected with 1 μl of saline instead of angiotensin and remained in the experimental chamber, after the intracerebral injection, exactly the same time that particular animal had spent after agiotensin, in the test session.

RESULTS

The cumulative records in Fig. 1 and Table 1 clearly show that every one of the five animals used responded considerably more after angiotensin than in the control session. Gross-behavioral changes were absent after the injection of angiotensin. Lever-pressing behavior and water licking showed the same topographical characteristics, as in the preceding satiation period.

TABLE 1

NUMBER OF LEVER-PRESSES EMITTED BY WATER SATIATED RATS AFTER THE INTRASEPTAL INJECTION OF ANGIOTENSIN II

Animals	Treatment	
	Angiotensin* (1 μg)	Control
R 3	75	28
R 4	106	45
R 14	113	0
R 15	71	0
R 18	207	36
Mean ± S.E.M.	114.4 ± 24.6	21.8 ± 9.3

*Rats were injected with 1 μg of angiotensin, dissolved in NaCl 0.9% solution, immediately before the experimental session. In control experiments, animals were injected with 1 μl of NaCl 0.9% solution, only.

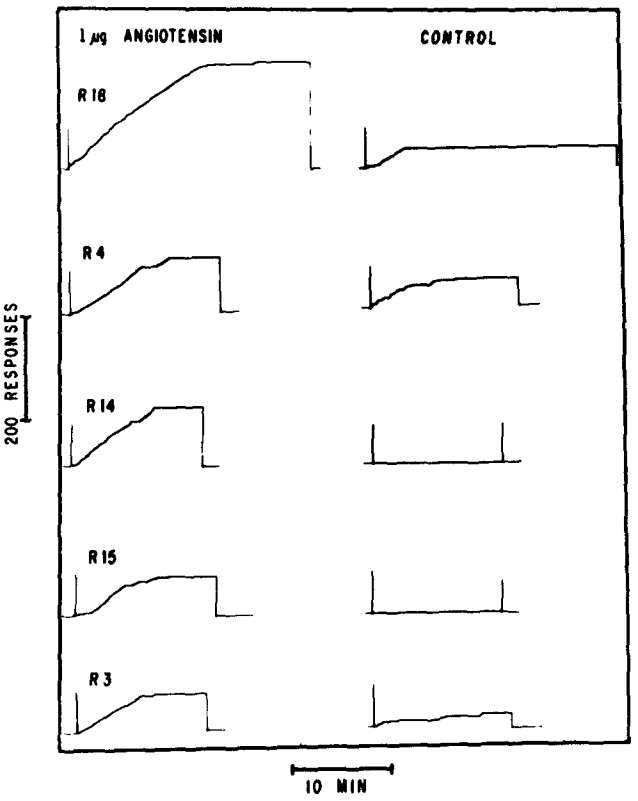

FIG. 1. Cumulative records of performance of five rats, previously satiated in the experimental chamber, after the intraseptal injection of angiotensin or saline (control). Every lever-pressing response was followed by water presentation (CRF) and caused the recording pen to move upward by 0.25 mm.

DISCUSSION

These results demonstrate, that the intracerebral injection of angiotensin mimicks the effect of water deprivation, in the sense that it increases the probability of occurrence of a learned response, previously associated with water presentation. The preceding evidence supports the hypothesis that angiotensin has a dipsogenic action on the central nervous system. In addition, present results suggest that the use of operant behavior techniques may provide a better method to assess the motivational effect of angiotensin, than the currently used, amount of water consumed method. With the latter technique ingested liquid probably triggers homeostatic responses that tend to inhibit drinking behavior, thus counteracting the drug effect. In contrast, with operant procedures, the amount of water ingested after angiotensin can be reduced to a minimum, by the use of intermittent schedules of reinforcement, in which only a fraction of the total number of responses are followed by water presentation.

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