Time Course of Radiation-induced Taste Aversion Conditioning

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CARROLL, M. E. AND J. C. SMITH. Time course of radiation-induced taste aversion conditioning. PHYSIOL. BEHAV. 13(6) 809–812, 1974. — Taste aversion conditioning was used to define the onset and duration of the period after exposure to 100 R gamma radiation which was most aversive to the animal. Rats were irradiated and then allowed to drink a saccharin solution. A significant decrement appeared in their cumulative intake, compared to sham animals at 90 min postexposure. When time delays between 0–90 min were imposed between offset of the radiation beam (US) and onset of saccharin exposure (CS), the time at which a significant decrement in saccharin drinking occurred remained constant at 90 min. With US–CS delays of 2, 4, and 6 hr a weaker aversion was found in terms of the time span before a significant decrement in the irradiated groups’ saccharin drinking rate appeared. Groups which were irradiated then allowed access to tap water for 24 hr, either immediately or 1.5 hr after radiation offset, showed no decrement in their water drinking rate with respect to a sham control. The procedures used in this experiment provide a method for measuring the latency of onset of subtle physiological effects.

Taste aversion X-irradiation Saccharin Backward conditioning

IT is well known that it is possible to condition a taste aversion in rats using ionizing radiation as the unconditioned stimulus (US) [3,9]. No unconditioned response (UR) to the radiation exposure has been observed [4]. There are no observable signs of immediate sickness following the irradiation as there are with certain drugs such as lithium chloride and apomorphine hydrochloride which have successfully been used in taste aversion conditioning [4,8]. Attempts have been made to determine the physiological basis of the aversive characteristic of the irradiation by testing the effects on taste aversion conditioning of partial body exposures [2] of blocking drugs [10] and by removal of the stomach [5]. Hunt et al. [6] irradiated one partner of a parabiont pair of rats and found that if the non-X-ray exposed member of the pair tasted saccharin (CS), he subsequently avoided the sweet taste, giving evidence that indicates a humorally mediated physiological response.

There is considerable evidence that there is a rather long latency between the radiation exposure and this strong aversive characteristic which, when paired with the novel taste solution, results in a subsequent taste aversion [1, 7, 12]. Evidence from the taste aversion literature indicates that the aversive characteristic of the irradiation which results in the subsequent conditioned taste aversion does not occur during the exposure period. Rather, one can infer from the data that this noxious experience becomes most intense 30–90 min after the exposure. In studies using the classical conditioning paradigm typically the CS would precede the US, i.e., the irradiation would follow the saccharin drinking period. It has been shown, however, that strong taste aversions can be produced if the rat does not have access to the saccharin solution until after the radiation exposure. Morris and Smith [7] presented rats with a saccharin CS 0.5, 1.0 and 6.0 hours after a 100 R X-ray exposure. They reported a subsequent aversion in the 0.5 and 1.0 hr delay groups but not in the 6.0 hr group. We subsequently reanalyzed their data and found that the 1.0 hr delay group showed significantly greater saccharin aversion than the 0.5 hr group. Barker and Smith [1] have recently tested several delay intervals between US and CS and demonstrated the most profound aversion when the CS was presented after a 30 min delay. These studies were conducted by pairing the irradiation and the saccharin drinking on one day and testing for aversion the following day.

We wanted a more direct measure in order to observe immediate signs of the onset of this aversive characteristic following radiation exposure. Garcia et al. [4] exposed rats to 200 R (in 3 min) and recorded licking to a saccharin solution during the exposure and for the subsequent 17 min. They found no decrement in drinking by comparing these rats to sham-irradiated controls. The earlier data of Morris and Smith [7] and Barker and Smith [1] indicate

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that the aversive period is most noxious at 30–60 min post-exposure. It was probable that Garcia et al. [4] saw no
direct decrement in saccharin drinking since they only
measured for 20 min from the onset of exposure.

In an earlier study Smith and Schaeffer [12] irradiated
rats with 100 R over 75 min and then subsequently re-
corded cumulative licks from a pair of bottles for 15 hr,
one containing saccharin and one containing water. Their
data revealed that drinking on the saccharin bottle ceased
after 20 min (95 min after onset of the gamma rays) where-
as sham-irradiated rats continued to drink. The results of
this study indicate that a decrement in drinking saccharin
can be seen if the test is long enough. However, two other
major factors could account for the difference between
these data and those of Garcia et al. [4]. (1) The radiation
exposure dose was 200 R in 3 min (66.67 R/min) in the
Garcia study, and in the Smith and Schaeffer study it was
100 R in 75 min (0.75 R/min); it is not known if the onset
of the noxious period would be a function of the previous
radiation exposure rate. (2) In the Smith and Schaeffer
study the rats were given a choice between saccharin
and water whereas in the Garcia study only saccharin was
available. It is possible that Smith and Schaeffer observed
the decrement in saccharin drinking merely because the rats
had water to drink as an alternative.

In the present investigation rats’ drinking behavior on a
single saccharin bottle was observed for several hours after
either a 100 R or a sham radiation exposure. From these
data it is possible to describe when the effects of the radia-
tion produce a physiological disturbance or become
noxious to the rat, i.e., at what time the maximum taste
aversion conditioning will occur.

METHOD

Animals

One hundred and sixty-two male, naive albino rats of the
Sprague Dawley strain from the Charles River Breeding
laboratory were used. The animals weighed between
350–400 g. They were randomly assigned to 19 treatment
groups of 8 rats each. Animals were individually housed in
Hoelge cages where Purina lab chow was always available
and tap water was available ad lib prior to the experiment.
Laboratory temperature, lighting and humidity were auto-
matically controlled with the lights on from 7:30 a.m. to
7:30 p.m.

Apparatus

The radiation source was Cobalt-60 (60Co) (Gamma
Beam 150, Atomic Energy of Canada, Ltd.). Eight animals
at a time were irradiated or sham-irradiated in individual
Plexiglas boxes (20 x 9 x 9 cm) mounted on a motor
driven Ferris wheel rotating at 1.5 rpm. The Ferris wheel
was constructed of 3/4 in. plywood, 1.2 m in diameter,
mounted upright on a metal frame, and was friction driven
by a variable speed 5 h.p. motor via a system of pulleys and
belts. Rotation in front of the source insured an equal
exposure of 100 R in 10 min as measured by a Victoreen R
meter for all animals. Sham-irradiation was accomplished
according to the procedure described here except the 60Co
source was not raised. Drinking tests were carried on in the
animals’ home cages which were in an adjoining room.
Single-bottle drinking measures were taken with 100 ml
glass graduated cylinders fitted with Girton tubes. The
accuracy of measurement was within ± 0.5 ml.

Procedure

All groups were habituated to the laboratory at least 4
weeks prior to treatment. For all groups the treatment
procedure began with 2 consecutive days of 23.5 hr water
deprivation: each followed by 30 min access to tap water.
After a third consecutive 23.5 hr water deprivation period,
the rats were irradiated or sham-irradiated (US). They were
then allowed 24 hr of access to a 0.1% (w/vol) sodium
saccharin solution (CS) after a given delay time between
offset of the radiation and the beginning of the 24 hr of
saccharin availability.

The first experimental condition (no delay) consisted of
2 groups of 8 rats each. One was irradiated and the other
sham-irradiated; then they were allowed access to the
saccharin solution immediately upon return to the home
cage. The next two groups (0.5 hr) were treated identically
except a 0.5 hr delay was imposed between offset of irradi-
ation and onset of 24 hr saccharin availability. There were
eight delay conditions in all (no delay, 0.5 hr, 1.0 hr, 1.5
hr, 2.0 hr, 4.0 hr, 6.0 hr, and 24.0 hr), and for each condi-
tion, both an irradiated and sham group were run. (See
Fig. 1.)

The 24 hr saccharin drinking test consisted of 10 mea-
ures of cumulative intake taken at 5, 10, 15, 20, 25, 30,
60, 120, 180 and 1440 min (24 hr) after the graduated
cylinders were attached to the cages. There was one excep-
tion to the deprivation procedure which occurred in the 24
hr US-CS delay groups. These groups received a 30 min
access to water prior to irradiation to avoid excessive
deprivation.

Three water control groups were run to determine
whether or not there is a radiation-produced decrement in
fluid intake. For two groups the procedure was identical to
that described above for the no delay groups except that
tap water instead of saccharin was available during the 24
hr test. The third water control group consisted of 8 rats
which were irradiated then given 24 hr access to tap water
1.5 hr after offset of irradiation.

RESULTS

Cumulative saccharin intakes for all groups are presented
for the first 3 hr of the 24 hr test in Fig. 1. It can be
observed from the top graph in Fig. 1 (no delay) that the
irradiated group stopped drinking with respect to the sham
group after 1.5 hr. This difference in cumulative intake was
statistically significant at 2 hrs (Mann-Whitney, p < 0.05).
The next groups (0.5 hr) received the saccharin solution
one half hour after the offset of irradiation or sham-
irradiation and were found to significantly differ from
each other at 1 hr. It is obvious from Fig. 1 that as the US-CS
delay increased up to 1.5 hr the times at which the irradi-
ated and sham groups became significantly different from
each other decreased from 1 hr in the 0.5 hr delay condi-
tion to 10 min in the 1.5 hr condition.

Weaker taste aversions were found in the 2 hr, 4-hr and 6
hr delay conditions, defined in terms of the time span
before irradiated sham groups’ drinking rates resulted in
significant differences in cumulative intake. The irradiated
24 hr delay group showed no decrement saccharin drinking
rate with respect to its sham control (Mann-Whitney,
p > 0.05).

The cumulative water intakes for the no delay sham
and irradiated water control groups are plotted in Fig. 2. There
was no significant decrement in water intake among the
The data presented in this experiment represent an attempt to characterize the nature of the unconditioned response to radiation by defining the onset and the peak of the aversion-sensitive period following irradiation. Time was found to be a crucial variable in conditioning a radiation-induced taste aversion. It is obvious from the top four graphs in Fig. 1 that it is not necessarily important for rats to consume a given quantity of the CS (15–20 ml in the no delay group), but that it takes 1.5 hr for the taste aversion to develop. In fact, the irradiated 1.5 hr delay group had consumed only about 4.5 ml of saccharin by the time their cumulative intake differed significantly from their sham controls.

It appears from these data that the effects of radiation with 100 R do not reach a threshold for conditioning a taste aversion until 1.5 hr. This is also the time when a taste aversion can be most readily conditioned; in these terms it is the peak of the aversion-sensitive period. It was also indicated by this procedure that this period lasts at least six hours; however, by 24 hr it is over. We were unable to explore delay intervals between 6 and 24 hr without seriously confounding the results. The stimulation of drinking brought about by onset of the dark cycle might compete with the formation of a taste aversion.

In the Garcia et al. [4] study they found no depression in drinking either in rats which received water or in rats which received saccharin for 20 min on exposure day. They attribute these results to the fact that no aversive response (CR or UR) was obvious during the conditional pairing of the saccharin and X-ray. They refer to the procedure whereby the noxious agent is delayed long after drinking as a non-associative procedure. In the present study, however, it was clearly shown that if the drinking test was extended to 1.5 hr there would have been significant differences between irradiated and sham groups’ saccharin drinking rates on exposure day in the Garcia study. It is possible that this difference would have occurred even sooner than 1.5 hr with the 200 R of radiation that they used.

The depression in saccharin drinking described in this study appears to be the result of an associative conditioning process, whereby animals in the experimental groups learned to reject the saccharin solution because it was conditionally associated with the effects of radiation. Evidence for the learning interpretation comes from the fact that the irradiated water control groups showed no decrement in water drinking rate with respect to the sham
controls. In other words the water control groups showed that the rats were not too sick to drink. Thus the saccharin aversion found in irradiated experimental groups was not explained by purely physiological, or non-associative factors, such as pseudo-conditioning.
These findings have demonstrated that it is possible to observe a subtle and otherwise invisible physiological disturbance such as the response to sublethal doses of radiation by monitoring the development and time course of a conditioned taste aversion. The behavioral technique described here may be useful for defining the time course and depicting the peak sensitivity of animals to other agents such as slow acting drugs. This method allows one to measure the latency of onset of subtle physiological effects.

REFERENCES