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Research report

Conditioned place preferences in humans using virtual reality

Robert S. Astur*, Andrew W. Carew, Bonnie E. Deaton

Department of Psychology, University of Connecticut, United States

HIGHLIGHTS

- We created a virtual reality conditioned place preference task to use with humans.
- A strong place preference exists for a room previously paired with food reward.
- Additionally, participants explicitly prefer the room previously paired with food.
- These preferences are not evident if participants are not food-restricted.

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ABSTRACT

To extend a standard paradigm of conditioning in nonhumans to humans, we created a virtual reality (VR) conditioned place preference task, with real-life food rewards. Undergraduates were placed into a VR environment consisting of 2 visually distinct rooms. On Day 1, participants underwent 6 pairing sessions in which they were confined into one of the two rooms and explored the VR environment. Room A was paired with real-life M&Ms for 3 sessions, and Room B was paired with no food for 3 sessions. Day 2 was the test day, administered the next day, and participants were given free access to the entire VR environment for 5 min. In experiment 1, participants were food restricted, and we observed that on the test day, participants display a significant conditioned place preference for the VR room previously paired with food ($p < 0.001$). Additionally, they display a significant explicit preference for the M&M-paired room in a forced-choice of "Which room do you like best?". In experiment 2, when participants were not food restricted, there was no evidence of a place preference, either implicitly (e.g. dwell time) or explicitly. Hence, we show that we can reliably establish a place preference in humans, but that the preference is contingent on the participants' hunger state. Future research will examine the extent to which these preferences can be blocked or extinguished as well as whether these preferences are evident using other reinforcers.

The conditioned place preference task (CPP) is widely used in nonhuman research as a hallmark task to assess drug abuse liability and reward. Generically, the task involves two compartments that are joined by a connecting compartment or tunnel. These compartments are distinct across many modalities, including visual, auditory, tactile, and olfactory cues. Procedurally, an animal is given a rewarding substance and confined in one of the two compartments for a fixed amount of time. Later, the animal is given a placebo substance and is confined in the other distinct compartment for the same amount of time. These pairings are often repeated multiple times to strengthen the relationship between the context and the presence or absence of reward. Following these pairings is a "test" session in which the animal is given free access to both chambers on a reward-free day, and it is observed that the animal typically shows a strong preference to dwell in the chamber where the reward was paired, even though that reward is no longer present [24]. This effect can be seen with a variety of drugs including amphetamine, cocaine, nicotine, caffeine, morphine, heroin, ethanol, and diazepam [14]. Additionally, this effect is seen with more natural reinforcers such as food, water, social play, and copulation [22]. Pavlovian conditioning is the most widely accepted explanation for the CPP. Essentially, the context paired with the reinforcer becomes a conditioned stimulus that predicts the presence of the reinforcer (CS+). As a whole, these studies demonstrate that animals can be conditioned to prefer a previously neutral environment by pairings with reward.

Despite the myriad of studies utilizing the CPP in nonhumans, it remains unclear how strongly this phenomenon translates to

* Corresponding author at: Department of Psychology, 406 Babbidge Road, Unit 1020, Storrs, CT 06269-1020, United States. Tel.: +1 2032369938; fax: +1 2032369828.
E-mail address: robert.astur@uconn.edu (R.S. Astur).

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humans. Recently, there have been a few attempts to extend the CPP to humans. In a study by Childs and de Wit [4], healthy participants repeatedly were given *d*-amphetamine in a unique context or a placebo in a different context. On a separate day, participants were asked to rate the rooms that they were exposed to previously, and participants displayed a significant preference for the room that was paired with the *d*-amphetamine. This is one of the first published studies that reveal a CPP in humans. However, the dependent variable of preference rating is different than what is typically used with nonhumans, which is time spent in each of the rooms during the test day. Childs and de Wit [5] have since replicated their findings, again using explicit verbal preference. In a related study, Molet and colleagues [16] report a CPP for a virtual reality (VR) environment paired with consonant music (relative to white noise), and report a conditioned aversion for a VR environment paired with dissonant music. In this study, the dependent variable is analogous to that used with nonhumans: time spent in each of the rooms. However, the training and testing sessions were all run in the same 30 min session, and the environments had vastly different geometries and stimuli. Ideally, the test session would be on a separate day, or at least separated from the training session by a significant amount of time, so that long-term memory effects can be assessed, and carry-over effects can be minimized. Additionally, testing on a separate day provides a better comparison to the nonhuman literature and generalizes more strongly to understanding behavior during a day free of reinforcers.

In the current paper, we created a direct VR analog of the rodent CPP model by using a VR environment with similar geometry, procedures, and dependent variables as used in rodent tasks. Additionally, we also implemented human-only variables used by Childs and de Wit [4] such as explicit room preference ratings and room choice. We used chocolate as a reward, given that food is a primary reinforcer, and it easy to administer. Place preferences have been demonstrated with both food and various drugs as the reinforcers, and the brain mechanisms underlying exposure to either nicotine-associated or chocolate-associated cues are similar [1,18]. Moreover, basic learning phenomena such as extinction and reinstatement are similar when using either food or drug rewards [13]. Hence, using a food reward allows us the simplicity of using it with healthy undergraduates without the experimental complexities of drug studies. We hypothesized that on the test day, food-deprived participants would prefer a room previously paired with chocolate M&Ms, and that they would rate this room as more enjoyable, and they would choose this room more often in a forced-choice test.

1. Method

1.1. Participants

21 University of Connecticut undergraduates (12 males; avg. age = 20.5 yrs.) were recruited from Introductory Psychology classes for this experiment via the university participant pool. Participants were required to attend both days of this two-part experiment. They were required to abstain from eating for 6 h prior to their session each day. It was also required that participants be able to eat chocolate for the purposes of this experiment. Participants received class credit for their participation. Approval for this study was obtained from the University of Connecticut Institutional Review Board.

1.2. Apparatus

An IBM-compatible computer with a SVGA color monitor was used for testing. Participants navigated through the virtual environments by manipulating a joystick. A speaker connected to the computer was used to provide auditory feedback to the participants. A Med Associates Inc. ENV-203IR pellet dispenser was used to dispense M&Ms into a tray for the participant to consume.

1.3. Procedure

This was a two-day experiment. Food-deprived participants arrived on day one at approximately 9:00 A.M. At this time, they were informed of the requirements of the experiment and signed consent was obtained. The participant was seated at a computer and was guided through a brief tutorial on how to interact with the virtual environment using a joystick. Participants received a 90 s practice session in which they were placed into an empty VR room. Throughout the practice session and in the experimental sessions, to encourage exploration, a coin appeared periodically in random locations, and participants were required to locate and collide with the coin. Additionally, an M&M was dispensed during the practice session, and participants were instructed that throughout the experiment, they are to eat the M&Ms as they are dispensed. Participants were allowed to ask questions at any time.

After finishing the practice session, each participant completed six 6-min experimental pairing sessions in a virtual environment. A 5-min break followed each session. During the first break, participants were asked to complete a short survey containing questions about their age, sex, and what and when they last ate. The environment consisted of two visually distinct rooms connected by a neutral hallway (see Fig. 1). In each of the six experimental sessions, the participants were confined into one of the two rooms and were to explore the environment using the joystick. Throughout the experiment, to encourage exploration, a coin appeared periodically in random locations, and participants were required to locate and collide with the coin. One room was paired with real M&Ms for three sessions while the opposite room was paired with no food for three sessions. The room paired with M&Ms and the orders of the pairing sessions were counterbalanced. One M&M was dispensed periodically into a cup next to the participant during the M&M sessions, and the participant was instructed to eat the M&Ms as they were dispensed. Specifically, an M&M was dispensed every 21 s ± 5 s. Between 50 and 60 M&Ms total were dispensed on day one, which is approximately the amount in a regular 47.9 g single size bag of M&Ms. After all six sessions were completed, participants were offered snacks and then dismissed.

Participants returned approximately 24 h later for the test day of the experiment. They were placed in the same virtual environment from day one and started in the neutral hallway. They had access to both rooms for the entire 6-min session. M&Ms were not dispensed on the test day. After the test, participants were given a survey. Questions asked which of the two rooms they preferred, how much they enjoyed each room on a scale of 0–100, and how much they enjoy chocolate on a scale of 0–100. Participants were also asked what and when they last ate. Participants were then offered snacks, debriefed, and dismissed.

2. Results

On the conditioning day, the last time that participants ate was 11.7 h previously (SD = 1.8). On the test day, the last time that participants ate was 12.0 h previously (SD = 1.7). On the test day, participants displayed significantly more dwell time in the room previously paired with M&Ms compared to the No Food room, $t(20) = 3.53$, $p < 0.01$. Specifically, participants spent 49% of their time in the M&M room compared to 20% of their time in the no food room (see Fig. 2). The remainder of the time was spent in the neutral hallway. After the experiment, participants were explicitly asked, “Which room did you prefer spending time in more?” and were to