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Research article

Two profiles in the recovery of reward devaluation in rats: Latent class growth analysis

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ABSTRACT

Consummatory successive negative contrast (cSNC) occurs when animals exposed to an unexpected downshift from a high palatable reward (e.g., 32% sucrose solution) to a less preferred one (e.g., 4% sucrose solution) show an abrupt and transient suppression of the consummatory response, compared with control animals that always had access to the less preferred one. This phenomenon constitutes an animal model of stress produced by frustrative events. To obtain information about individual differences regarding cSNC, we used Latent Class Growth Analysis (LCGA) to analyze a sample of 53 animals exposed to an incentive downshift. We found two profiles of animals, both showing the suppression of the consummatory response but diverging in the speed of the recovery. Our results are consistent with previous literature showing individual differences in cSNC and do not support the existence of a third profile.

1. Introduction

Mood disorders are pervasive in our society and studying them requires several research strategies. Studies with animal models help us to disentangle cause-effect relationships, since we can modify different environment or genetic conditions to produce depression or anxiety-like behaviors. For instance, affecting the conditions under which animals receive a reward appears to be related to these kinds of behaviors. Establishing individual differences in the way animals respond to these conditions might help us to understand the individual differences that we find in humans. One of the conditions that we want to explore is reward loss.

Reward loss refers to situations in which animals receive an unexpected reward reduction or omission. These situations appear to be aversive and stressful [1]. cSNC is one of the phenomena most commonly studied that happens as a consequence of a reward loss. cSNC occurs when animals exposed to an unexpected downshift from a high palatable reward (e.g., 32% sucrose solution) to a less preferred one (e.g., 4% sucrose solution) show an abrupt and transient suppression of the consummatory response, as compared to control animals that had always access to the less preferred one [2]. Animals experience an aversive emotional state when they find a negative discrepancy between the expected and the obtained reward. cSNC is a consequence of this particular state, also called frustration, and is closely related to fear and anxiety [1,2]. Amsel stated that the first reaction to the downshifted incentive is an unconditioned response that takes place in the first session (primary frustration), while a second reaction, a conditioned response, is present in subsequent sessions (secondary frustration) [1]. Consistent with this statement, the administration of benzodiacepines reduces the size of cSNC [3,4]; the increased hypothalamic-pituitary-adrenal activation level correlates with stronger suppression of the consummatory responses [5,6]; and lesions in the lateral amygdala attenuate these responses, while lesions in the corticomedial and central amygdaloidal nuclei eliminate them [7].

Most studies have addressed this topic based on the analysis of mean-level responses. However, the animals' responses to a reward devaluation event reflect a range of individual differences that indicate the lack of an homogenous response. Selective breeding studies also suggest important individual differences [8,9]. Several additional studies have indicated that anxiety-related behaviors such as high avoidance are susceptible to be genetically selected as a trait, suggesting important variations across individuals [10–12]. As previously stated, selective breeding is important to understand individual differences; however, since they are artificial, variations may be magnified and may

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not reflect natural variations in a particular behavior.

Another way of evaluating the individual differences consists of examining the correlations between the cSNC measures and several tests of emotional behaviors. For instance, Flaherty et al. found that the rats' first reaction to reward devaluation correlated with the entry frequency to an open arm in an elevated plus maze and the latency to emerge in an emergence test [13]. Nevertheless, other studies have attempted to replicate these correlations, but they have found contradictory and inconsistent results [14,15]. In fact, there are documented difficulties in finding inter-correlations in the measurements of different tests that evaluate stress and anxiety in rodents [16]. This suggests that simple correlational approaches have serious limitations to address the individual differences expressed in a particular situation.

Recently Papini et al. identified several profiles of cSNC in rats using a more complex approach [17]. Specifically, the authors analyzed through latent growth mixture modeling (GMM) the data from 21 experiments in both male and female Long Evans and Wistar rats, and found three profiles: animals without expression of negative contrast, animals showing negative contrast but no recovery, and animals expressing both negative contrast and recovery of the consummatory response. GMM is a statistical technique derived from Structural Equation Modeling. It identifies unobserved classes or profiles across a pool of observations across time. Each profile has its own longitudinal change with a particular slope (indicative of the increasing or decreasing of the measurements across time) and intercept (indicative of the magnitude of the measurement of the initial responses). Under GMM each profile has its own estimate of mean and variance [18].

The fact that a previous study used GMM to identify different profiles of cSNC response poses specific problems. First, GMM does not work well with small samples [19,20]; second, although the authors try to homogenize those responses by comparing experimental with control ones, several important variations (sex of the animals, strains, and experiments) made the analysis even more difficult. As a consequence, entropy, an important index of a good classification, was less than 0.8; one of the profiles (i.e., animals without expression of negative contrast) comprised less than 10% of the animals, which made the existence of the profile less likely to be correctly identified [21]. Finally, the profile of rats that comprised less than 10% of the animals (rats with no contrast) had a very distinctive and lower consummatory response during the entire experiment. We believe that this does not reflect an absence of cSNC, but a low response to any reward.

When the sample size is relatively small, a useful alternative statistical technique is Latent Class Growth Analysis (LCGA), which is also derived from SEM; and like GLM, each identified profile has a particular slope and intercept. The distinctive characteristic is that the variance in each profile is fixed at zero. This requirement allows the sample size to be relatively small [22].

The purpose of this study was to identify the number of profiles of cSNC, but by using a more conservative approach and a more homogenous sample of rats. In this regard, the all-male Wistar rats underwent the same training protocol (four different groups, each at a different time). We used the LCGA to conduct the statistical analysis; this kind of technique is particularly relevant for analyzing longitudinal analysis in small samples.

2. Method

2.1. Subjects and apparatus

The subjects were 83 male Wistar rats bred at the Medical Research Institute vivarium (Universidad de Buenos Aires), coming from four different experiments as controls, and housed individually when they had reached the age of approximately 90 days. At this moment they began food restriction until they were 81% to 85% of their *ad libitum* body weight (250–506 g). For their housing conditions, the 12 h light-dark cycle (on 07:00) and the temperature (21–22 °C) had a controlled variation. Polycarbonate tubs measuring 40 × 22 × 20 cm housed seven rats, and stainless-steel wire-bottom cages measuring 27 × 25 × 22 cm (length × width × height) housed the remaining animals. Previous data of our laboratory showed no differences in cSNC as a function of caging design [23]. In both cases we provided sawdust bedding, placed either in a tray below the wire-bottom cages or directly into the tubs, and replaced it weekly. For their training, we enclosed them in boxes with a diffuse house light, located inside a cubicle with a source of white noise. All procedures were approved by the Institutional Laboratory Animal Care and Use Committee of the Medical Research Institute (IDIM-Universidad de Buenos Aires-CONICET).

2.2. Procedure

Fifty-three animals from the whole set of animals received a 32% sucrose solution (32 g of sugar per 68 g of water) for ten sessions, one each day, and then downshifted to a 4% sucrose solution (4 g of sugar per 96 g of water) for additional five sessions. Thirty animals received the 4% sucrose solution throughout the entire experiment (15 sessions). Each five-minute session commenced after the animal had its first contact with the solution. Five conditioning boxes were used to train the animals, which measured 24.1 cm in length, 29.2 cm in width, and 21 cm in height. Aluminum bars formed the floor of the box (0.4 cm in diameter, 1.1 cm apart from center to center). In the center of one of the lateral walls there was a 5 cm hole, 3.5 cm deep, 1 cm above the floor level, through which a sipper tube could protrude from the outside. When fully inserted, the sipper tube protruded 2 cm into the box. The animals activated photocells when they had contact with the sipper tube and the cumulative amount of time the photocell was activated in a particular session was the main dependent variable in this experiment (goal tracking time, GTT). Data were transferred to a computer running MED-PC software (Med Associates Inc.).

3. Results and partial discussion

3.1. Statistical analysis

A first step in the statistical analysis was to test significant differences among animals across the 4 different experimental groups from which these animals were obtained. We ran this statistical analysis using IBM SPSS (version 23). Among experimental animals, we did not find significant differences across experiments, $F(3, 47) = 0.52$, $p = .66$, partial $\eta^2 = 0.03$; or in the postshift sessions, $F(3, 49) = 1.02$, $p = .39$, partial $\eta^2 = 0.03$. A second step in the analysis was to compare experimental animals ($n = 53$) with control animals ($n = 30$). As can be observed in Fig. 1, we found a significant difference between control

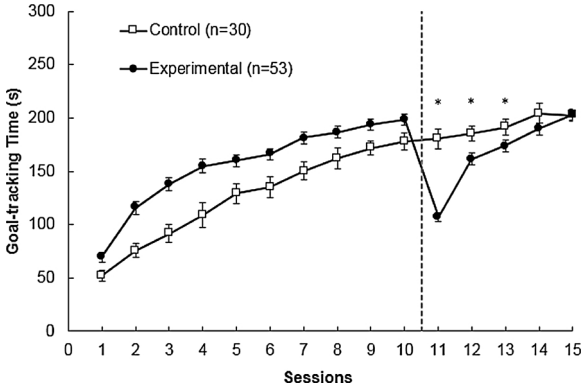

Fig. 1. Mean (± *SEM*) goal-tracking time (GTT) during ten sessions of the preshift and five additional sessions in the postshift. * Indicates statistically significant differences between experimental and control animals during the postshift.