Open-field exposure facilitates consummatory extinction

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During extinction, the organism learns that a conditioned stimulus or a conditioned response is no longer associated with an unconditioned stimulus, and as a consequence, a decrement in the response is presented. The exposure to novel situations (e.g. exploration of a novel open field) has been used widely to modulate (i.e. either enhance or deteriorate) learning and memory. The aim of the present study was to test whether open-field exposure could modulate consummatory extinction. The results indicated that open-field exposure accelerated the extinction response (i.e. experimental animals provided novelty exposure had lower consummatory behavior than control animals) when applied before – but not after – the first extinction trial, or when applied before the second extinction trial. The results suggest that environmental treatments such as novelty exposure provide a valuable, nonpharmacological alternative to potentially modulate extinction processes. *NeuroReport* **00:000–000**

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Introduction

A surprising reward omission (SRO) occurs when an expected reward is not presented or it is reduced in quality [1], leading to frustration and emotional arousal [2]. Consummatory extinction (cE) is an example of SRO, where rats are repeatedly exposed to an appetitive sucrose solution, which is then suddenly removed [3].

Anxiolytic pharmacological treatments can accelerate cE, that is, the animals extinguish their consummatory response more rapidly than their controls [4,5], and yet, they can induce undesirable side effects (e.g. drug abuse or dependence [6]). Environmental treatments provide a nonpharmacological alternative to alter extinction processes. The exposure to novel situations [e.g. exploration of a novel open field (OF)] has been used to modulate (i.e. either enhance or deteriorate) learning and memory in humans [7] and animals [8,9].

OF exposure exerted opposite effects when applied before the first or the second trial in a consummatory successive negative contrast (cSNC, another e.g. of SRO [10,11]). This provided the background for one of the aims of the present study. We tested the effects of OF exposure in the first and second trial of a cE paradigm, and expected opposite results from these treatments. The specific direction of these effects was difficult to predict. There are drugs that enhance cSNC and accelerate cE [10–12], but there are treatments that attenuate cSNC and yet accelerate cE [4,5,13–15]. Because timing is a critical factor determining the effects of novelty exposure [16,17], we provided OF exposure before or after extinction.

Animals and methods

Animals

Forty-seven male Wistar rats, born and reared at the vivarium of IDIM (CONICET, Buenos Aires, Argentina), were used. The animals, 120 days old at the start of the experiment, were individually housed at a constant temperature with ad-libitum access to water. Food was gradually reduced over 7 days until the animals reached 85% of their ad-libitum weight (mean = 348 g). This level of deprivation was maintained throughout the experiment.

Apparatus

The rats were provided access to sucrose in five boxes (24 × 29 × 21 cm; MED Associates, St Albans, Vermont, USA) enclosed in a sound-attenuating and light-attenuating cubicle and equipped with a sipper tube that protruded 2 cm into the box. Time in contact with the sipper (measured in 0.01 s increments) was recorded by a computer that measured the cumulative amount of time that a photocell located in front of the tip of the sipper tube was activated. Previous studies that used the sucrose concentrations used in the present experiments indicated that time in contact with the sipper shows a significant correlation with fluid intake [3]. Moreover, several studies have concurrently used time in contact with the sipper and fluid intake and yielded comparable results with either dependent variable [18–20]. Sucrose

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solutions (w/v) were prepared by mixing 320 or 40 g of commercial sugar in 1 l of tap water to obtain the final 32 and 4% sucrose solutions, respectively. The open field was made of gray acrylic (50 × 50 × 50 cm) and divided into nine equal squares. A light bulb (100 W) was suspended on top of the apparatus to provide illumination.

Behavioral procedures

A 40-min habituation session was conducted to attenuate taste neophobia. During the habituation, the water bottle was filled with 20 ml of a 32% sucrose solution. Three experimental phases, in which responses to sucrose (or the empty sipper tube) were tested in daily 5-min trials, were then conducted. Each trial began the first time the photocell was activated. (i) Acquisition phase: the animals were exposed to the 32% sucrose solution for five trials (i.e. trials 1–5). (ii) Downshift phase: 24 h after the last acquisition trial, the rats had access to a 4% sucrose solution for three trials (i.e. trials 6–8). (iii) Extinction phase: the animals were exposed to the empty sipper tube for two trials (i.e. trials 9 and 10).

OF exposure (duration: 5 min) was performed 1 h before (pre-T9 group) or immediately after (post-T9 group) the first extinction trial (trial 9), or 1 h before the second extinction trial (trial 10; pre-T10 group). The rationale for this time frame is that, in previous studies [21], we observed that OF exposure 1 h before the downshift affected the expression of consummatory successive negative contrast. This effect was not observed when the OF was applied 3 h before or immediately before the test. Exposure to the OF after the first extinction trial (i.e. post-T9 group, in the present study) was meant to modulate the consolidation of extinction.

Control animals were transported to the experimental rooms in the homecage, but did not experience OF exposure. Experimental animals were allowed free OF exploration for 5 min. A significantly reduced amount of time in contact with the sipper, in comparison with the control group, was taken as an indication of greater, treatment-induced, extinction.

Experimental design

A 2 [treatment (animals exposed or not to OF, experimental, EXP, and control groups, CTRL, respectively] × 3 [timing of treatment: experimental or control exposure 1 h before (pre-T9 group) or immediately after (post-T9 group) the first extinction trial (ninth trial), or 1 h before the second extinction trial (10th trial, pre-T10 group)] factorial design was used. Therefore, six groups were formed: CTRL pre-T9 ($n = 8$); CTRL post-T9 ($n = 8$); CTRL pre-T10 ($n = 7$); EXP pre-T9 ($n = 8$); EXP post-T9 ($n = 9$); and EXP pre-T10 ($n = 7$).

Data analysis

Time in contact with the sipper during acquisition, downshift, and extinction phases was analyzed independently by repeated-measures (RM) analysis of variance (ANOVA). Treatments (OF and CTRL) were the between factors, whereas trials (i.e. 1–5 in the acquisition, 6–8 in the downshift, 9–10 in extinction) were the RM. Least significant difference pairwise comparisons were performed to analyze significant main effects and significant interactions ($\alpha = 0.05$). AQ5

Results

Analysis of contact with the sipper tube during acquisition and downshift phases

The ANOVA for the acquisition yielded significant main effect of trials. As shown in Fig. 1 all groups gradually increased their time in contact with the sipper tube (s), $F(1,40) = 148.23$, $P < 0.0001$ ($\eta_p^2 = 0.787$). In the downshift phase, there was a main effect of trials, $F(2,82) = 50.53$, $P < 0.0001$ ($\eta_p^2 = 0.552$).

Analysis of contact with the sipper tube during the extinction phase

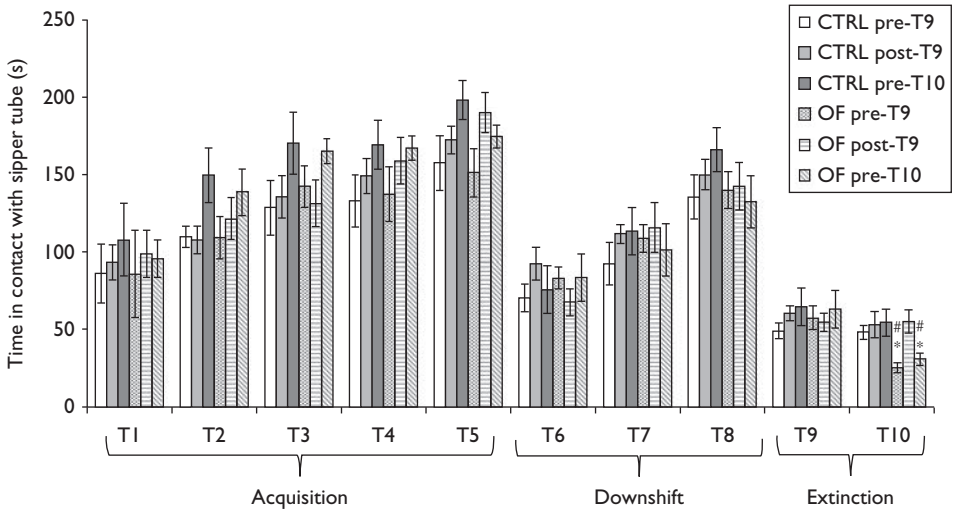
As shown in Figs 1 and 2, time in contact with the sipper (s) in trial 9 was similar across control and experimental rats. In the 10th session, those rats that explored the OF either before the first or the second extinction trial (i.e. EXP pre-T9 and EXP pre-T10 groups, respectively) showed greater extinction than CTRL counterparts. Rats exposed to the OF after termination of the first extinction trial (i.e. EXP post-T9 group) showed similar goal-tracking time as the controls. These qualitative impressions were corroborated by the statistical analysis. The RM ANOVA yielded significant main effects of trials $F(1,40) = 9.87$, $P < 0.004$ ($\eta_p^2 = 0.21$)], and the treatment × trials interaction also achieved significance [$F(1,40) = 2.71$, $P < 0.04$ ($\eta_p^2 = 0.255$)]. The post-hoc tests indicated similar levels of time in contact with the sipper tube (s) during trial 9 in all groups. The post-hoc tests also indicated that, in trial 10, time in contact with the sipper in EXP pre-T9 and EXP pre-T10 groups was significantly lower than that in all the other groups [$F(5,39) = 4.11$, $P < 0.004$]. Moreover, in trial 10, the EXP pre-T9 and the EXP pre-T10 group had – as indicated by the corresponding post-hoc tests – significantly lower time in contact with the sipper tube in comparison with trial 9 [EXP pre-T9 $F(1,39) = 11.19$, $P < 0.002$; EXP pre-T10 $F(1,39) = 9.83$, $P < 0.003$], but the other groups had a similar time in contact between trials.

Discussion

The aim of this study was to explore new treatments that facilitate extinction of unadaptive responses. Specifically, we tested the modulatory effect of OF on cE when the extinction phase is preceded by a nonabrupt change (i.e. a decrease in sucrose concentration from 32 to 4%) in the magnitude of the reinforcer. The rats explored the OF either before or after the first extinction trial or before the second encounter with the empty sipper. Very little was

Fig. 1

Groups	Trials 1–5 (%)	Trials 6–8 (%)	Trial 9	Trial 10
CTRL pre-T9	32	4	CTRL → EST	EST
CTRL post-T9	32	4	CTRL → EST	EST
CTRL pre-T10	32	4	CTRL → EST	EST
EXP pre-T9	32	4	OF → EST	EST
EXP post-T9	32	4	EST → OF	EST
EXP pre-T10	32	4	EST	OF → EST



Time in contact with the sipper tube (s) during acquisition (trials 1–5), downshift (trials 6–8) and extinction (trials 9 and 10). Animals were subjected to a single open-field (OF) exposure, 1 h before (EXP pre-T9 group) or immediately after (EXP post-T9 group) the first extinction trial, or 1 h before the second extinction trial (EXP pre-T10 group), or were left untreated (CTRL pre-T9, CTRL post-T9 and CTRL pre-T10 groups). Vertical lines represent SEM. The asterisk sign denotes a significant difference between a given group and the control group. The hash sign indicates a significant within-group difference between extinction trials 9 and 10 (T9 and T10). CTRL, control; EST, empty sipper tube; EXP, experimental.

known on the modulation of cE occurring after gradual changes in the quantity of the reinforcer. Instead, the vast majority of research had assessed the effects of different treatments on cE after an abrupt decrease in the magnitude of the reward (i.e. from 32 to 0% or 4 to 0% [5, 23]). Such swift changes in the magnitude of expected reinforcers are, however, uncommon in clinical settings. For instance, the contingency management approach to drug disorders differentially reinforces behaviors likely to compete with drug seeking, with the objective of first reducing and ultimately eliminating drug use [22]. The 32-4-0 procedure in the present study was aimed at modeling situations in which the magnitude of the reward loss is more gradual.

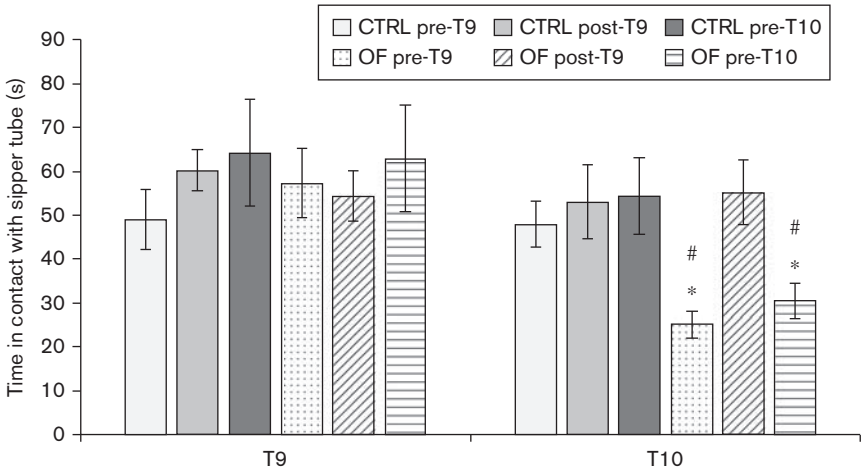
On the basis of our previous work, we had hypothesized differential effects of OF on cE during the first or the second extinction trial [21,23]. Here, exploration of OF before the first or the second encounter with the empty sipper tube had the same results. Specifically, these animals showed a lower consummatory behavior than control animals and a significant decrease in goal-tracking times across trials. A corollary is that, although cSNC and cE can be deemed as frustration or SRO procedures, functional differences seem to exist between them. Moreover, some research suggested that treatments that accelerate cE (i.e. induce less consummatory behavior [23]) enhance cSNC [24], and yet others proposed that when a treatment facilitates cE [4,5,14], it also diminishes frustration in cSNC, that is, induced more consummatory behavior in cSNC [4,5,14]. Our results add information in favor of the second possibility.

Moreover, the results of this experiment agree with previous reports in which novelty enhanced fear extinction [25]. These authors explained the effect of novelty by a process of behavioral tagging, which could also be applied to the present study. Under this framework, extinction results in a group of synapses being tagged. Novelty exposure strengthens these synapses by facilitating the synthesis of plasticity-related proteins [26].

The present study adds to a growing body of literature that indicates that OF exploration can interfere with memory formation [7–9,21,23]. Exposure to a learning task can cause proactive or retroactive interference in

Fig. 2

Groups	Trials 1–5 (%)	Trials 6–8 (%)	Trial 9	Trial 10
CTRL pre-T9	32	4	CTRL → EST	EST
CTRL post-T9	32	4	CTRL → EST	EST
CTRL pre-T10	32	4	CTRL → EST	EST
EXP pre-T9	32	4	OF → EST	EST
EXP post-T9	32	4	EST → OF	EST
EXP pre-T10	32	4	EST	OF → EST



Time in contact with the sipper tube (s) in rats exposed to consummatory extinction (cE) after a downshift procedure. During extinction, animals were subjected to two, 5-min trials (T9 and T10 trials) of access to an empty sipper tube (EST). Animals were subjected to a single open-field (OF) exposure 1 h before (EXP pre-T9 group) or immediately after (EXP post-T9 group) the first extinction trial, or 1 h before the second extinction trial (EXP pre-T10 group), or were left untreated (CTRL pre-T9, CTRL post-T9, and CTRL pre-T10 groups). Vertical lines represent SEM. The asterisk sign denotes a significant difference between a given group and the control group. The hash sign indicates a significant within-group difference between extinction trials 9 and 10 (T9 and T10). CTRL, control; EXP, experimental.

another task. Proactive interference occurs when previously acquired information modifies the storage or retrieval of new information, whereas retroactive interference occurs when newly learned information interferes with or impedes the recall of previously learned information [21,27]. In the present experiments, exposure to OF interfered with subsequent extinction training when applied before the first or the second extinction trial, but not when applied after the first extinction trial. On the basis of this pattern of results, it could be argued that OF proactively, but not retroactively, interfered with extinction training.

Several studies have involved the hippocampus in extinction responses [28,29]. For instance, low-frequency stimulation of hippocampus accelerated extinction [30], whereas lesions of this region delayed extinction [31,32]. It is also well documented that exploration of a novel environment engages the hippocampus [33–35]. Thus, a likely explanation for the present results is that OF exposure stimulated hippocampus functionality, and this activation promoted a more rapid extinction response.

The noradrenergic and cholinergic transmitters systems are involved in learning and memory processes [36,37], and alter novelty-induced arousal [38,39]. For instance, acetylcholine levels in the cortex and hippocampus have been observed to be greater in rats exposed to a novel open field than in control counterparts [40–43]. An interesting avenue of research would be to analyze the mediational role of these transmitters in the effects of OF on consummatory extinction. It would also be interesting to test the effects of other novel situations (e.g. social novelty, environmental enrichment, etc.).

Unfamiliar contexts, like the OF used in the present study, can induce anxiogenic or stress-like effects [44], which in turn can interfere with learning acquisition. Thus, it could be postulated that the effects of OF in the present study were a side-effect of stress. In a previous experiment, however, OF exposure altered behavioral

performance when presented 1 h before, but not when presented immediately before, a reward downshift. This result does not support the hypothesis of OF altering memory through anxiogenic or stress-like effects.

Successful extinction hinders treatment efficacy in clinical psychology and psychiatry [45], and this problem seems particularly pervasive in substance abuse disorders [46]. A widely used approach in addiction treatment is the avoidance of cues or contexts associated with drug-intake behaviors and effects. Yet, sometimes, this proves impossible. An alternative strategy would be to diminish the behavioral control exerted by these cues. According to the present set of results, exposure to novelty after termination of treatment may help individuals cope with spontaneous recovery of symptoms and the urge to seek drugs.

Conclusion

The main result of the present study was that, under most circumstances, novelty exposure accelerated the extinction response: a relatively lower consummatory behavior was observed in rats exposed to the novel OF before the first or the second extinction trial. The use of novelty-inducing treatment seems to be a promising, nonpharmacological approach to modulate learning and memory processes.

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Conflicts of interest

AQ6 None declared.

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