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Peripheral vasopressin accelerates extinction of conditioned taste avoidance

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Abstract

Both peripheral and central administration of vasopressin improves retention and delays extinction when given before or after acquisition of shock avoidance learning. For conditioned taste avoidance, however, vasopressin prolongs extinction when injected peripherally before acquisition tests and accelerates extinction when infused intracerebroventricularly after acquisition. The following experiments were designed to determine whether this inconsistency is based on the route of administration or timing of vasopressin treatment. Because acquisition of conditioned taste avoidance is strengthened when an agent that is capable of inducing avoidance is administered after LiCl injection, it was determined in experiment 1 that a 6 μg/kg dose of vasopressin did not induce conditioned taste avoidance when administered 50 min after consumption of a sucrose solution. In experiment 2, it was determined that this dose of vasopressin accelerated extinction of a LiCl-induced conditioned taste avoidance when given 50 min after LiCl injection. These results suggest that the inconsistency is not based on route of administration. In experiment 3, it was determined that there was a tendency for animals to show prolonged extinction when vasopressin was administered 20 min before access to a sucrose solution. All of the results taken together suggest that the differential effects of vasopressin on extinction are due to the timing of administration. It was suggested that vasopressin accelerates extinction when given after acquisition by reducing the effectiveness of LiCl and it prolongs extinction when given before acquisition by altering neural responsiveness in areas mediating conditioned taste avoidance.

Keywords: Arginine vasopressin; Conditioned taste aversion

1. Introduction

The neuropeptide, arginine vasopressin, has been shown to facilitate the retention and prolong the display of learned behaviors (see Refs. [1,2]). Although a variety of tasks have been used to study the effects of vasopressin on memory (e.g., sexually and appetitively motivated tasks), shock avoidance has been used most frequently. The enhancing effect of vasopressin in shock avoidance has been demonstrated despite variations within certain parameters, such as route of administration and timing of the injection. Firstly, peripheral, as well as, central administration of vasopressin results in a prolonged display of learned behaviors. Animals treated with subcutaneous injections, intracerebroventricular infusions, or intracerebral infusions of vasopressin continue to exhibit shock avoidance behaviors when such a display is no longer seen by their saline-injected controls [3–17]. Secondly, the timing of the treatment with respect to before or after acquisition or extinction trials does not appear to be critical. Animals receiving injections before or after acquisition or the first post-acquisition testing session of a one-trial step-through passive shock avoidance task retain the learned behavior longer than controls [3–8]. In shuttle box and pole-jumping shock avoidance tasks, animals maintain a higher level of response during

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extinction testing when vasopressin is administered before or after the first or last acquisition trial, after the first extinction trial, or throughout extinction testing [6,10,12–15].

Although most of the studies have focused on shock avoidance tasks, the effects of vasopressin on conditioned taste avoidance also have been examined. Some of the results for conditioned taste avoidance have been similar to what has been found for shock avoidance. Vawter and Green [18] reported that the vasopressin analogue, desglycinamide lysine vasopressin (DG-LVP) increases resistance to the extinction of the avoidance behavior when given subcutaneously 1 h before each of the three acquisition or eight extinction trials, or before all of the acquisition and extinction trials. In a study by Cooper et al. [19], lysine vasopressin prolonged extinction in both old and young animals when subcutaneous injections occurred shortly before every fourth extinction test. However, a recent study using central injections of vasopressin reported contradictory results. In this study, infusion of arginine vasopressin into the lateral ventricle shortly after the acquisition test produced an accelerated extinction [20].

A number of suggestions focusing on the differences in methodologies used in the studies finding prolonged extinction and that finding accelerated extinction have been made [20]. Two notable differences are the route of administration and the timing of administration. The studies finding prolonged extinction used peripheral administration of vasopressin before the acquisition and/or extinction tests while the study finding accelerated extinction used central administration after the acquisition test. Peripheral administration of vasopressin increases blood pressure, decreases heart rate, inhibits gastric emptying, disrupts spontaneous locomotor activity, and suppresses eating in food-deprived animals [4,21–25]. Central administration of vasopressin also increases peripheral blood pressure [25–31]. However, the effects of central administration of vasopressin on more extensive peripheral changes have not been consistently reported, possibly reflecting a sensitivity to location of infusion [32–34]. Thus, it is conceivable that peripheral and intracerebroventricular administration of vasopressin produce a different array of physiological changes, which in turn differentially alters extinction.

Although the presence of vasopressin before as opposed to after a learning session does not differentially affect behavior in a shock avoidance learning situation, there is some evidence that it does in other learning paradigms. In the learned submission paradigm, peripheral administration of vasopressin produced either impairment or enhancement of a submissive behavior (i.e., defensive upright posture upon contact) depending on when during acquisition training treatment occurred. Peripheral injections of vasopressin before training resulted in the display of less submissive behavior during retention testing than saline injections. However, when peripheral treatment occurred immediately after training, vasopressin-treated animals displayed an increase in the frequency of the submissive behavior compared to their saline-treated counterparts [35]. This raises the possibility that the differential effect of vasopressin on extinction of conditioned taste avoidance is due to timing of administration.

The following experiments were designed to determine whether the route and/or timing of administration influences the type of effect vasopressin has on extinction of conditioned taste avoidance. To test whether these factors would accelerate or prolong extinction of taste avoidance, experiments were conducted to compliment previous findings by using peripheral administration of vasopressin shortly after the acquisition test (experiment 2) and central administration before the acquisition test (experiment 3). If route of administration is the critical factor, then one would expect to find prolonged extinction in experiment 2 and accelerated extinction in experiment 3. On the other hand, if timing of administration is the critical factor, then one would expect to find accelerated extinction in experiment 2 and prolonged extinction in experiment 3. Before conducting these experiments, it was important to verify that the dose of vasopressin used could not itself induce a conditioned taste avoidance. Agents that are capable of inducing a conditioned taste avoidance can weaken acquisition of a conditioned taste avoidance induced by another agent when administered before acquisition and strengthen acquisition when administered after acquisition [36–38]. An intracerebroventricular dose of vasopressin that does not induce conditioned taste avoidance has already been identified [20]. Therefore, experiment 1 was designed to identify a peripheral dose of vasopressin that does not induce a conditioned taste avoidance.

2. General methods

2.1. Subjects

Male Sprague–Dawley rats (Simonsen Laboratory, Gilroy, CA), which weighed approximately 300 g at the beginning of the experiments, were used in this study. They were housed in pairs in cages that measured 58×38 cm and had a solid bottom covered with wood chips. A stainless steel divider was placed in the middle of each cage to separate each pair of rats. The vivarium in which the rats were housed was temperature- (21–22 °C), humidity- (51%), and light-controlled (a 12:12-h light:dark cycle with lights on at 1000 h and lights off at 2200 h). The rats were allowed at least 1 week to adapt to their living conditions before the experiments were initiated. Rats had ad libitum access to rat chow and tap water before behavioral testing was initiated. During conditioned taste avoidance testing, water was available 23 h a day. In previous studies, we found that rats given similar drinking schedules are essentially nondeprived [39–42]. The experiments were conducted according to the standards set by the National