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Behavioral analysis of stress controllability effects in a new swim stress paradigm

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Abstract

Previous animal stress studies have illustrated the marked impact of coping on subsequent behavior and physiology by using shock as the stressor. The current study evaluates the generality of shock stress controllability effects in a new swim stress paradigm on several dependent measures: behavioral despair, analgesia, shuttlebox escape, and alcohol reactivity. In this new paradigm, rats in the escape group are able to learn the behavioral response as evidenced by significant reduction in the acquisition of a lever press response. Both escape and yoked subjects showed "behavioral despair" in comparison to both restrained and home cage controls when tested 24 h later. In the standard shuttlebox escape task 24-h post-stress, no group differences emerged, although a trend for poorer performance in the yoked subjects was evident. No group differences were observed in pain sensitivity after the first or second forced swim exposure. Finally, stress controllability effects were observed in behavioral reactivity to alcohol 2-h post-stress as measured by rotarod performance. This effect is opposite to the previous observations with the tailshock stress controllability paradigm. These results suggest that (1) there are certain similarities, but some fundamental differences between the behavioral endpoints measured following intermittent swim stress in comparison to the well-established effects of the intermittent tailshock stress model and (2) the qualitative nature of a stressor may markedly influence the behavioral and physiological consequences of stress and coping.

Keywords: Swim stress; Triadic design; Behavioral despair; Analgesia; Shuttle escape learning; Alcohol-induced ataxia

1. Introduction

The use of tailshock or footshock stress in a triadic design (i.e., escapable shock, yoked-inescapable shock, and a non-shock control) results in a number of behavioral, physiological, and immunological deficits in the inescapably shocked but not escapably shocked animals. Among such deficits are learning deficits (Anisman et al., 1979; Glazer and Weiss, 1976; Maier and Seligman, 1976; Maier et al., 1973; Seligman and Maier, 1967; Weiss et al., 1975), reduced activity (Drugan and Maier, 1983, 1982; Jackson et al., 1978; Maier et al., 1979), reduced mobility in a swim test (Prince and Anisman, 1984; Weiss et al., 1981), reduced aggression (Maier et al., 1972), depressed immunocompetence (Laudenslager et al., 1983; Mormede et al., 1988; Sklar and Anisman, 1979; Stein et al., 1985; Visintainer et al., 1982), increased gastrointestinal lesions (Weiss, 1968), opioid stress-induced analgesia (Drugan et al., 1981, 1985a; Grau et al., 1981; Jackson et al., 1979; Maier et al., 1980), and reduced social interaction (Short and Maier, 1993). However, certain studies report no impact of stress controllability on endocrine and immune endpoints (Maier and Laudenslager, 1988; Sandi et al., 1992). Furthermore, exposure to uncontrollable but not controllable tailshock stress results in an increased sensitivity to the behavioral effects of amphetamine and cocaine (MacLennan and Maier, 1983), opiates (Grau et al., 1981; Maier et al., 1980; Sutton et al., 1997) as well as alcohol and valium (Drugan et al., 1992, 1996).

Relatively few studies have investigated whether uncontrollable stress, in general, leads to behavioral as well as physiological deficits or whether many of the effects observed are unique to shock stress. Hiroto and Seligman (1975) showed that in humans, the stress of unsolvable anagrams led to a deficiency in learning a task, which terminated a mild shock to the index finger.

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Similarly, Breier et al. (1987) found an enhanced hypothalamic–pituitary–adrenal (HPA) axis activation in human subjects exposed to uncontrollable, but not controllable, noise stress. This endocrine response is reminiscent of several reports in animals showing alterations in HPA activity associated with uncontrollable, but not controllable stress (Dess et al., 1983; Swenson and Vogel, 1983), although certain investigators find no difference (Maier et al., 1986; Mormede et al., 1988; Sandi et al., 1992). Furthermore, certain investigators show that genetic strain is an important factor for observing the differential effects of stress and coping on endocrine measures (Zhukov, 1993).

Alentor et al. (1977) developed a model that evaluated controllable and uncontrollable swim stress in rats. They found that rats exposed to uncontrollable but not controllable swim stress were unable to learn a shock avoidance task. Prince and Anisman (1990) also used swim stress controllability to investigate changes in serum corticosterone levels in mice. Mice able to escape a forced swim had lower corticosterone levels in comparison to yoked, inescapably stressed counterparts. However, both Alentor et al. and Prince and Anisman did not use a triadic design, which involves the simultaneous exposure of a third group of rats that are confined to the stress apparatus during the session without exposure to the stressor. The inclusion of such a group will allow comparison of this confined group to a naive, untreated control group.

We have developed a device that employs a triadic design using intermittent, forced swimming in ambient temperature water as the stressor. Following exposure to this paradigm, all groups were tested on several behavioral measures including: behavioral despair, stress-induced analgesia (SIA), shuttlebox escape learning, and reactivity to the ataxic effects of alcohol. These dependent measures were chosen to allow a comparison of this intermittent swim stress model with the tailshock stress controllability model in rats.

2. Materials and methods

2.1. Subjects

Male Sprague–Dawley rats purchased from Charles River Laboratories (Stoneridge, NY) weighing 180–200 g upon arrival served as subjects. Rats were 6 weeks old at the time of arrival and were allowed 1 week to acclimate to the vivarium before experimentation. Rats were maintained in the vivarium with 12/12-h light:dark cycle with lights on at 0700 h. Rats were housed in polyethylene tub cages (four per cage) prior to experimentation and were given free access to food and water. All experiments were conducted between 0700 and 1400 h.

2.2. Apparatus

2.2.1. Swim stress controllability

The escape/yoke/restrained or confined swim device consists of three Plexiglas cylinders (two: 21×45 cm, diameter $\times$ height; one: 21×15 cm, diameter $\times$ height) each with thirty-seven 1.2-cm holes drilled in the bottom and open at the top. These cylinders are attached to a motor pulley system and suspended above a black fish tank $76 \times 30 \times 45$ cm ($L \times W \times H$) filled to a height of 29 cm with ambient (23°C) water. These cylinders can be lowered and raised out of the water at the same time. Because the middle cylinder (restrained/confined group) is shorter, it never enters the water. In each of the large cylinders is an omnidirectional lever (Med Associates) coated with a thin film of vaseline. The movement of this lever in any direction closes a switch. One of these levers (escape group) is connected to an Omron Programmable Controller Model S6 (Omron Electronics, Schaumburg, IL). The movement of this lever by the escape rat activates a relay system activating a motor that lifts the two cylinders (escape and yoked rats) out of the water. The action of the motor lifting the Plexiglas cylinders out of the water produces a noise that raises the background level from 55 to 63 dB. Responses on the yoked lever are recorded, but do not activate the motor. Above each of the cylinders is a space heater, which blows (36°C) warm air into the large cylinders and unheated air into the middle (restrained/confined group) cylinder during the intertrial interval (ITI). This continuous flow of warm air during the experiment is employed to minimize loss of body temperature in the two swim subjects, while the unheated air over the smaller cylinder controls for forced air exposure. The water in the aquarium was changed after each triad of animals and the aquarium was cleaned with antibacterial spray.

2.2.2. Behavioral despair

The behavioral despair test was conducted in Plexiglas cylinders (height: 36.4 cm, diameter: 19.5 cm) with a solid Plexiglas floor containing 29 cm of ambient (23°C) water. The tubes were placed on a counter in a room separate from where the stress pretreatment occurred. In a subsequent study, the Plexiglas cylinders were placed adjacent to the swim stress controllability apparatus.

2.2.3. Pain sensitivity/tail-flick test

Pain sensitivity was evaluated using a warm water tail immersion test. This procedure was conducted in a similar fashion to other methods previously described (Janssen et al., 1963; Tazi et al., 1987). A Precision Instruments Dubnoff Shaking Incubator/Bath (Model # 66799) was used to heat the water and maintain it at $52 + 1$°C.

2.2.4. Shuttlebox escape test

All rats were tested for shuttle-escape performance in a two-way shuttlebox (BRS/LVE Model RSC-044). The

gridshock to the shuttlebox floor was produced by a BRS/LVE (Model # SGS-004) shock generator/scrambler. The shuttlebox escape program was controlled by an IBM-PC.

2.2.5. Alcohol-induced motor ataxia

All rats were tested for alcohol-induced incoordination using a rotarod treadmill 6 cm in diameter and 35-cm long (UGO Basile Biological Research Apparatus-Model # 7700, 21025 Comerio, Varese, Italy). The rotarod has four equal areas that are partitioned off from one another and the rod rotated at a speed of 10 rpm (Drugan et al., 1996).

3. Procedure

3.1. Acquisition and behavioral despair

On the day of stress pretreatment, rats were randomly assigned to one of four groups: escape, yoked, restrained/confined, and naive. Rats were then weighed and for the remainder of the study were individually housed in polyethylene tub cages. Naive rats remained in their home cages in the vivarium until testing. Escape, yoked, and restrained/confined rats were then transported to the treatment room. Escape and yoked rats were placed in the large Plexiglas cylinders, while the restrained/confined rats were placed in the smaller, middle cylinder. Fig. 1 provides an illustration of the swim stress controllability device. Note the restrained rat is confined to the small Plexiglas cylinder with a wire mesh covering and without exposure to the water.

Rats were exposed to 100, unsignaled, forced swim trials with an average ITI of 45 s. In a typical trial, the rats were lowered into the water and the rats were raised out when the escape rat fulfilled the response requirement on the omnidirectional lever. If the response requirement was not achieved within 60 s, the trial was automatically terminated and the rats were raised from the water. For the first 20 trials, the response requirement was FR-1. Starting on trial 21, if the escape rat performed the response requirement in under 10 s on four of the previous five trials, the response requirement was increased to FR-2. The response requirement was again increased to FR-3 on trial 51. However, in the event that an escape rat was performing the response in less than 3 s of four of the five previous trials, the FR requirements were increased to ensure that both rats were exposed to at least 3 s of swim stress on each trial. Rats were removed from the experiment as "poor learners" if (a) the first 10 FR-1 trials were performed significantly faster than the last FR-1 trials, or (b) the rat failed to fulfill the response requirement in under 30 s for four out of five consecutive trials on FR-2 and/or FR-3 schedule. This is similar to the criterion used for the wheel-turn response in the tailshock stress controllability model (Drugan et al., 1996). Under this criterion, 2 out of 14 escape rats (and their yoked, restrained, and naive counterparts) were dropped from the analysis. At the end of the 100 trial sessions, rats were towel dried and placed under an incandescent heat lamp for 30 min to ensure that they were dry before being placed back in individual cages in the vivarium.

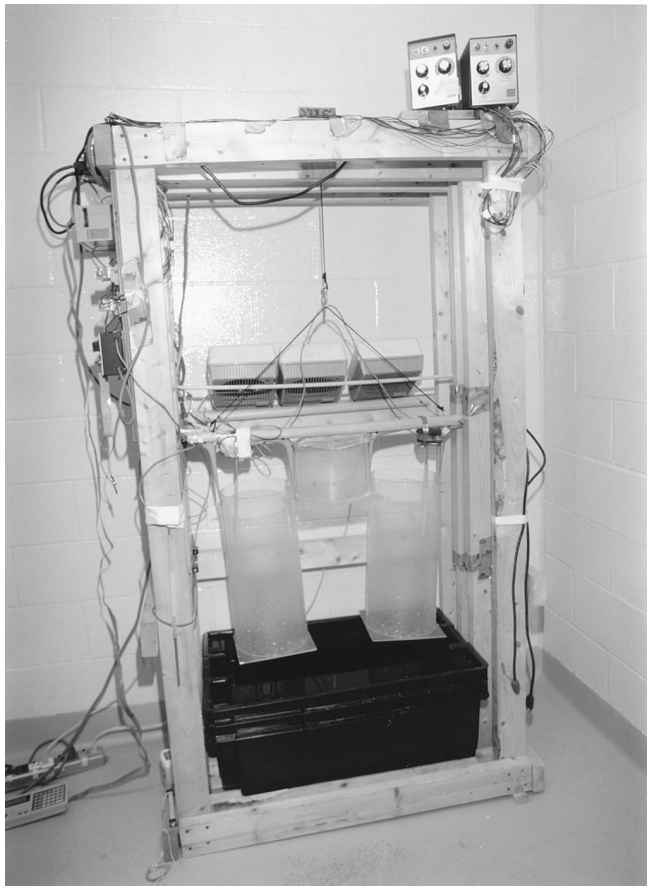

Fig. 1. A picture of the swim stress controllability apparatus. There is an escape rat (left cylinder) that can terminate the forced swim by pressing an omnidirectional lever, a yoked rat (right cylinder) that has no control over the forced swim and a restrained/confined rat (middle cylinder), which is in the apparatus for the same period of time, is exposed to the same movement, but not exposed to the forced swim. A fourth, naive rat remains in its home cage until testing.

Twenty-four hours following the swim stress controllability pretreatment, all four groups of rats were evaluated for immobility (i.e., behavioral despair) during a 5-min forced swim test. Rats were taken to a separate room or to the same room as the stress pretreatment (two separate experiments) and tested one at a time. The experimenter scoring the rats was blind to group membership. During a 5-min forced swim test, immobility was defined as the absence of vigorous activity such that the forepaws did not break the surface of the water. This procedure is similar to the methods described by Porsolt et al. (1977) and Drugan et al. (1989). At the end of the 5-min forced swim, rats were towel dried and placed under an incandescent heat lamp for 30 min.

3.2. Pain sensitivity testing

Prior to being placed in the swim stress paradigm or back in the home cage vivarium (naive control), all rats were randomly assigned to groups and tested for baseline pain sensitivity. The rats were gently wrapped in a towel and held vertically and 1/2 of an inch of the caudal portion of the tail was lowered into the warm water bath. The latency to tail-flick was measured by an investigator blind to group membership. If the rat did not perform the response within 10 s, the trial was terminated and a latency of 10 s was recorded. This cut-off was used to prevent tissue damage (Tazi et al., 1987). The average of two tail-flick tests (separated by 1 min) was taken for both baseline and post-stress tests. Immediately following the baseline tail-flick test, rats in the escape, yoked, and restrained/confined groups were exposed to the swim stress controllability paradigm. Immediately post-stress, all four groups were administered two tail-flick tests.

Twenty-four hours later, all subjects were returned to the stress treatment room where two more baseline tail-flick tests were performed. Immediately following these tests, all rats were placed in the water-filled Plexiglas cylinder for the behavioral despair test. Immediately following the 5-min swim, all rats were tested for pain sensitivity and then placed under heat lamps for 30 min before being returned to the vivarium.

3.3. Shuttlebox escape performance

Twenty-four hours following the swim stress controllability paradigm all four groups of rats were tested for escape performance in a two-way shuttlebox as previously described (Drugan et al., 1985b, 1987, 1989; Maier and Seligman, 1976). Briefly, each trial began with a warning tone (80 dB, 2.8 kHz) followed by a 1.0-mA gridshock 5 s later. The first five trials required a single crossing of the shuttlebox in order to terminate the gridshock. These trials (FR-1) are unaffected by prior experience with tailshock stress exposure and test for nonspecific effects such as sedation (Maier and Seligman, 1976). The subsequent 25 trials require two crossings to terminate the gridshock (FR-2). If the escape response does not occur within 30 s of shock onset, the trial is automatically terminated and a 30-s latency is recorded. The order of testing of the four groups is counterbalanced and the experimenter testing shuttle-escape performance is blind to group membership. The latency to shuttle was recorded on an IBM-PC.

3.4. Alcohol-induced motor ataxia

Prior to exposure to the swim stress controllability paradigm, all rats were trained to a criterion on the rotarod. The criterion test involved training the rats to run continuously on the rotarod for 2 min. If the rat fell off, it was immediately placed back on the rotarod until 2 min of continuous running was achieved. Escape, yoked, and restrained/confined rats were then placed in the swim stress controllability apparatus and exposed to 100 trials as previously described. The naive controls were placed back in the vivarium during this time. Immediately following the stress session, escape and yoked rats were placed under heat lamps for 30 min and than placed back in the vivarium in separate cages. At 1 h 45 min following the stress session, all rats were retested on the rotarod criterion. Shortly thereafter, all rats were injected with an effective dose of alcohol (0.6 g/kg) as previously determined (Austin et al., 1999; Drugan et al., 1996) or saline and 10 min were allowed for drug absorption (Drugan et al., 1996). The rats were individually housed following injection and then tested on the rotarod to determine the level of motor intoxication. A maximum of three successive trials were conducted. If a rat reached a maximum time of 300 s on the second trial after running for greater than 180 s on the first trial, no further testing was conducted. The average of the two or three trials taken was taken as the rotarod score for each subject.

The rotarod procedure is similar to those reported in the literature to measure drug-induced motor ataxia (Dar, 1990; Drugan et al., 1996; Miller et al., 1987; Morato and Rosas, 1991). The 300-s cut-off was established to allow for testing of rats in all four groups at or near the 2-h post-stress time point. All groups were run in a counterbalanced fashion, and the experimenter testing the rats was blind to group membership.

3.5. Statistical analyses

Analyses on all measures were conducted with *t* tests or one-way analysis of variance (ANOVA) unless stated otherwise. When significant main effects were found with ANOVA, Newman–Keuls post hoc comparisons ($P < .05$) were used to determine group differences.

4. Results

4.1. Swim stress controllability and behavioral despair

Fig. 2 shows the acquisition function for a mean of 10 escape subjects in the forced swim paradigm. As the figure indicates, there is a reduction in the latency required for the rats to perform the escape response, even in light of the increased fixed ratio demand. These observations were confirmed with a repeated measures ANOVA. The ANOVA revealed a significant block effect (10 trials per block) [$F(9,99) = 8.96$, $P < .001$], thereby indicating a significant acquisition function. Furthermore, the escape rats pressed the lever significantly more than the yoked rats during the stress pretreatment [$t(18) = 8.83$, $P < .001$].

The results of the behavioral despair test 24 h following swim stress controllability pretreatment are shown in Fig.

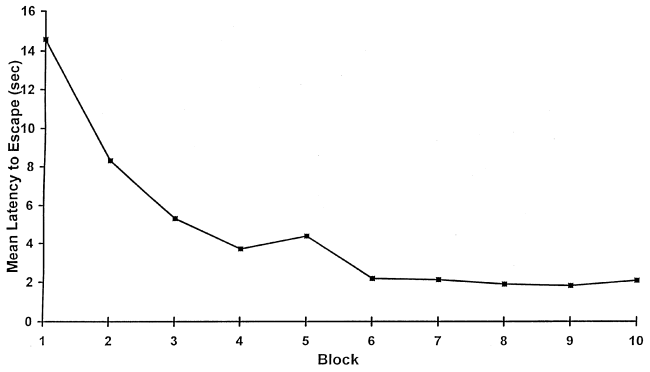

Fig. 2. Mean latency to escape from the forced swim exposure by pressing an omnidirectional lever. The acquisition function represents an average of eight escape subjects to perform the lever press escape response over the intermittent swim stress paradigm. Each block represents 10 trials.

3. As can be seen, both escape and yoked groups show an increased immobility compared to the restrained/confined and naive groups. A one-way ANOVA confirmed a treatment group main effect [$F(3,44) = 6.73$, $P < .001$]. Post hoc analysis indicated that escape and yoked groups exhibited significantly more floating behavior in comparison to both restrained/confined and naive controls ($P < .05$). In order to test the importance of context, we conducted an additional study with the immobility test being conducted in the same room as the stress pretreatment and observed the same results [$F(3,36) = 7.01$, $P < .01$]. Subsequent Newman–Keuls post hoc comparisons again indicated that the escape and yoked swim stress groups were significantly different from both the restrained/confined and naive groups, which did not differ from one another (data not shown).

4.2. Swim stress controllability and pain sensitivity

The results of the analgesia tests are shown in Fig. 4 (day 1) and Fig. 5 (day 2). The mean tail-flick latencies do not appear to differ among the four groups at baseline or immediately following swim stress controllability on day 1. These observations were confirmed by a one-way repeated measures ANOVA. The split-plot ANOVA revealed a nonsignificant group effect [$F(3,36) = 1.05$, $P = .38$], a nonsignificant repeated measures effect [$F(1,36) = 2.48$, $P = .12$], and a nonsignificant Treatment × Repeated Measures interaction [$F(3,36) = 1.17$, $P = .34$]

The results of the analgesia tests on day 2 following a 5-min forced swim are shown in Fig. 5. A split-plot ANOVA indicated a nonsignificant group treatment effect [$F(3,36) = .62$, $P = .61$], a significant repeated measures effect [$F(1,36) = 52.65$, $P < .001$], and a nonsignificant Group × Repeated Measures interaction [$F(3,36) = 1.62$, $P = .20$]. Post hoc Newman–Keuls mean comparisons indicated that all groups in the post-stress tail-flick test differed significantly from their pre-stress baseline scores. No other comparisons were significant.

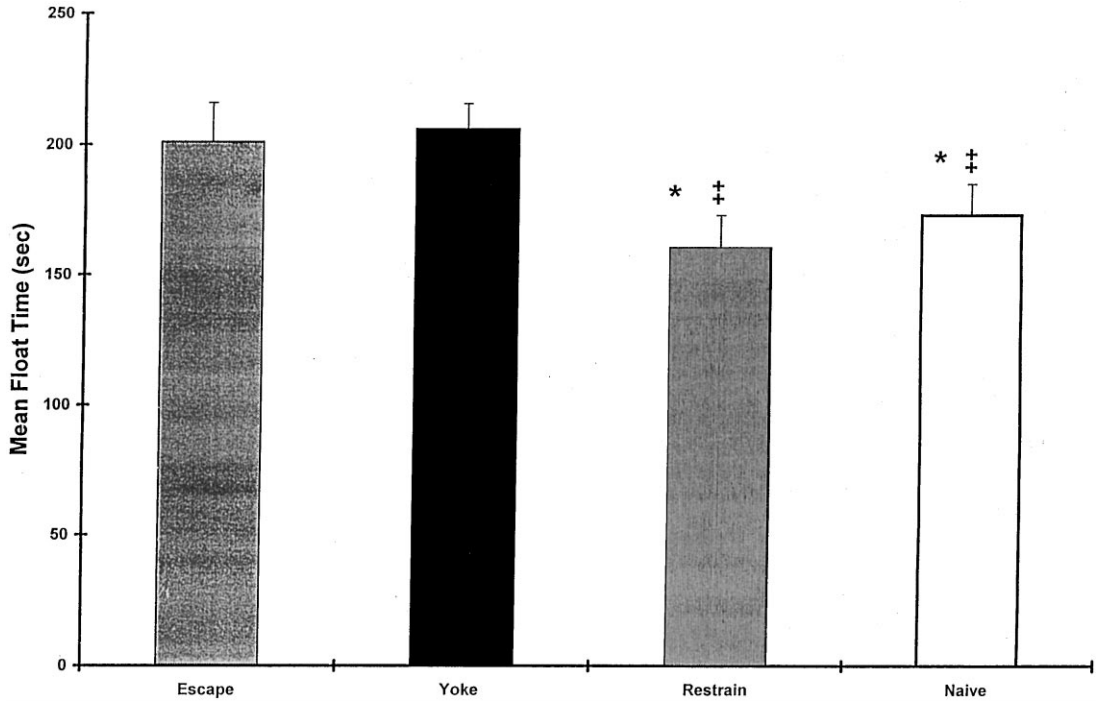

Fig. 3. Mean (+S.E.M.) float time for all groups during a 5-min swim test in a different context from pre-stress swim controllability. * Indicates significantly different from yoke group and + indicates significantly different from escape group by Newman–Keuls post hoc mean comparisons after ANOVA ($P < .05$).

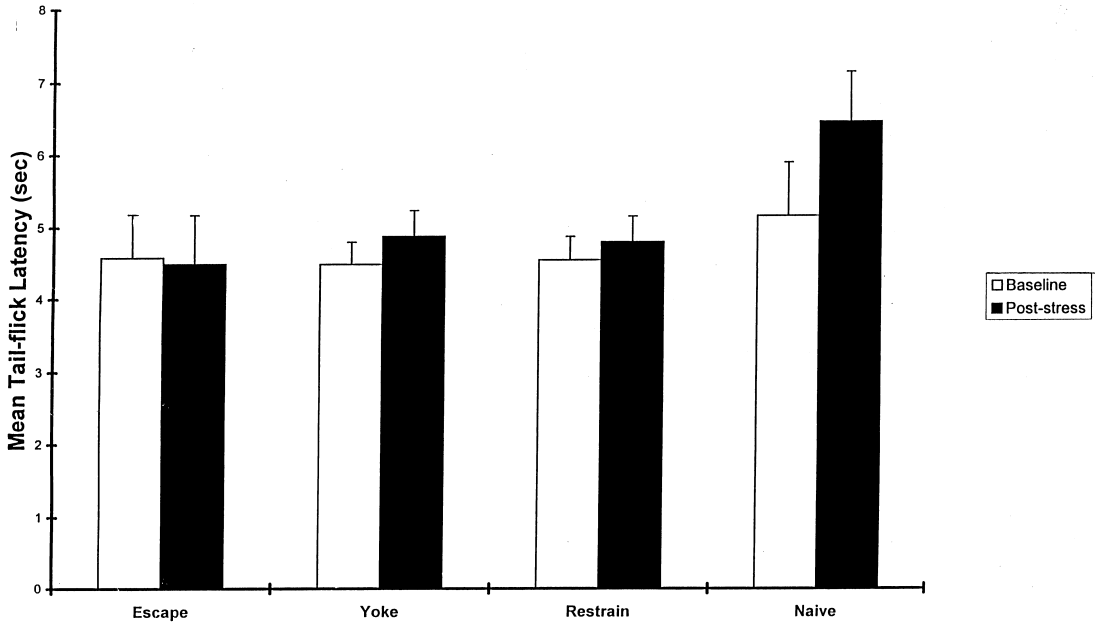

Fig. 4. Mean (+S.E.M.) tail-flick latency in seconds for all groups before (baseline) and immediately following (post) swim stress controllability, restraint, or no stress on day 1.

4.3. Swim stress controllability and shuttlebox escape learning

Fig. 6 shows the effects of swim stress controllability on shuttlebox escape performance 24 h later. A one-way ANOVA indicated no group differences on latency to perform the FR-1 response [$F(3,28)=.43$, $P>.1$]. Regarding the FR-2 performance, a split-plot ANOVA revealed a nonsignificant group main effect [$F(3,28)=1.09$, $P>.1$], a nonsignificant repeated measures (block) effect [$F(4,112)=.19$, $P>.1$], and a nonsignificant Treatment × Repeated Measures interaction [$F(12,112)=.19$, $P>.1$]. However, given the interesting trend in the data and the expectation from previous models that the yoked group would perform more poorly than the escape group, we conducted one apriori contrast: escape

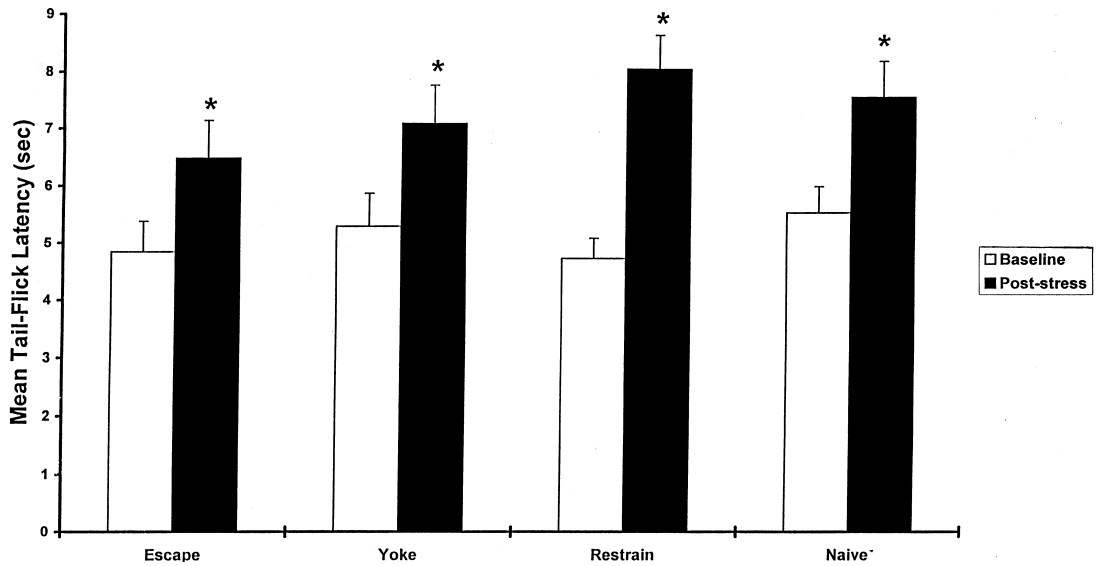

Fig. 5. Mean (+S.E.M.) tail-flick latency in seconds for all groups before (baseline) and immediately following (post) a 5-min forced swim test on day 2. * Indicates significantly different from respective baseline measure as determined by Newman–Keuls post hoc comparisons ($P<.05$) after ANOVA.

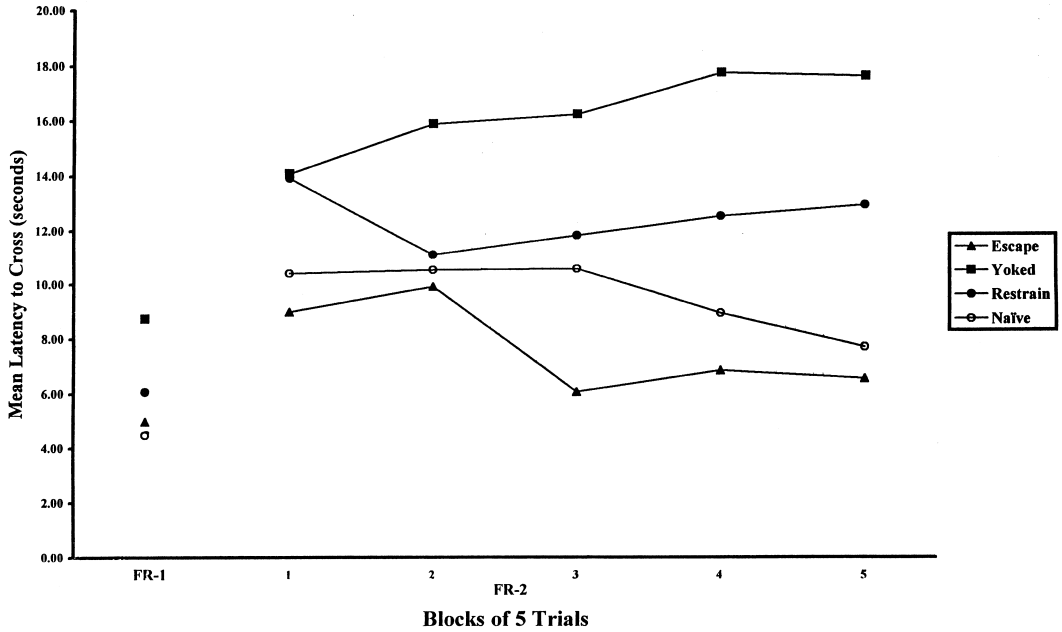

Fig. 6. Mean latency (in seconds) to escape across blocks of five shuttlebox test trials for rat exposed to escapable swim stress, inescapable swim stress, restraint or no treatment (naive) 24 h prior to testing ($n = 8$ rats/group). The standard error of the means (S.E.M.) for each group for blocks 1–5 are as follows — escape: 3.25, 3.70, 3.45, 3.35, 3.46; yoked: 3.11, 4.13, 3.78, 4.12, 4.19; restrained: 4.09, 3.81, 4.47, 4.84, 5.01; naive: 2.37, 3.47, 3.87, 3.61, 3.43.

vs. yoked (Kirk, 1995). A one-tailed t test was conducted between the escape and yoked groups and revealed a significant difference between groups collapsed across the five trial blocks [$t(28) = 1.705$, $P < .05$].

4.4. Swim stress controllability and alcohol-induced motor ataxia

The effects of swim stress controllability on alcohol-induced motor ataxia are shown in Fig. 7. A one-way

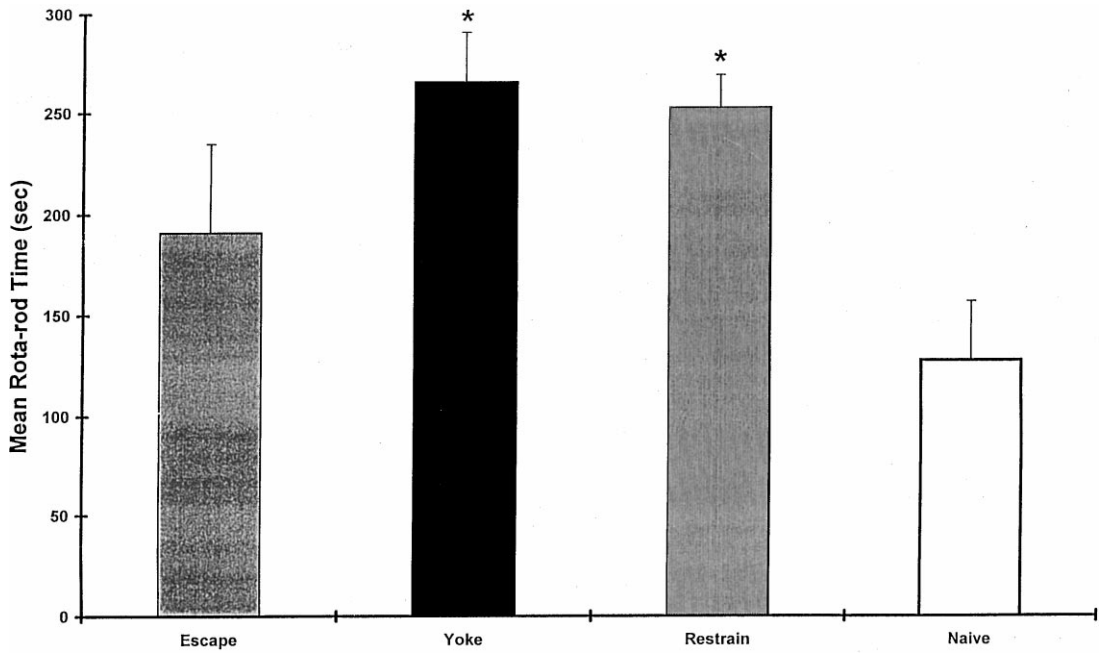

Fig. 7. Mean (+S.E.M.) time spent on rotarod in seconds for all groups 2 h following the swim stress controllability pretreatment. All subjects were administered an intraperitoneal injection of 0.6 g/kg ethanol 10 min prior to test. * Indicates significantly different from naive control by Newman–Keuls mean comparisons after ANOVA ($P < .05$).

ANOVA indicated a significant group main effect: [$F(3,44) = 3.6$, $P < .05$]. Post hoc Newman–Keuls mean comparisons indicated that the yoked and restrained/confined groups were significantly different from the naive group. The escape group did not differ from any other group. These ataxic effects were observed only in response to an injection of ethanol. A separate study analyzing the ability of all four groups to run on the rotarod following a saline injection indicated no group differences [$F(3,28) = 1.47$, $P > .1$] (data not shown).

5. Discussion

In the current set of experiments, we illustrate the feasibility of using a triadic design (escapable stress, yoked-inescapable stress, and restrained or confined control) in an intermittent swim stress paradigm. Experiment 1 indicated that the escape rats were able to learn the lever-pressing response quite effectively and maintain a latency less than 5 s even though the response contingency was increased to at least an FR-2 for all escape subjects.

Twenty-four hours following the intermittent swim stress controllability exposure, immobility was evaluated during a 5-min forced swim test. This procedure is a variation of the original behavioral despair paradigm developed by Porsolt et al. (1977, 1978), which has been used as a screen for antidepressants and evaluated by others as an animal model of depression (Henn et al., 1993; Willner, 1984). Rather than using a single, 15-min massed exposure to swim stress, we exposed rats to 100 intermittent trials of swim stress. Spaced exposure to forced swim less than one half of the total time used by Porsolt et al. (1977) (e.g., approximately 7 min) results in significant immobility in rats exposed to either escapable or inescapable swim stress.

Controllability of this stressor, therefore, has no impact on subsequent immobility. These results are different from the observations of Weiss et al. (1981) that increased floating behavior was observed in rats exposed to inescapable but not escapable tailshock stress. Our effect is observed in the same pre-stress context or in a different room, indicating context independence of this phenomenon.

The alterations observed in pain sensitivity in the current swim stress paradigm also diverge from the previous tailshock stress controllability paradigm. Immediately following the swim stress controllability procedure, we observed no change in tail-flick latencies compared to pre-stress baselines. Exposure to intermittent tailshock stress in a comparable time frame results in transient nonopioid SIA in the escape group and prolonged, opioid-mediated SIA in the yoked group (Drugan et al., 1985a; Maier et al., 1980). The qualitative differences in the stressors used in these two paradigms is probably the key difference. Tailshock stress is an example of electrical stimulation that induces a different physiological reaction to the stress (e.g., discomfort as evidenced by vocalization), whereas ambient water swim stress does not result in vocalization during the stress exposure (Drugan, unpublished observations). In fact, Bodnar et al. (1978a,b) have shown that exposure to acute, massed ambient water swim stress does not change pain sensitivity, while cold water exposure results in SIA. The pattern of stress exposure (e.g., massed vs. spaced footshock stress) has also been shown to be critical in influencing the nature of SIA (Lewis et al., 1980; Maier et al., 1983). Therefore, future experiments employing intermittent cold water swim stress controllability may result in SIA.

Twenty-four hours following the swim stress controllability paradigm and immediately following the 5-min re-exposure to swim stress (i.e., behavioral despair test), all groups showed SIA compared to their pre-stress baseline. Prior stress exposure did not alter the acute swim stress-induced SIA. These results verified that our tail immersion method was capable of detecting SIA. Perhaps exposure to cold water swim stress controllability in future experiments might potentiate the subsequent acute (5 min of continuous forced swim) SIA.

Shuttlebox escape behavior was not significantly altered by swim stress controllability when analyzed by a split-plot ANOVA. However, due to previous experimental work employing triadic designs, we expected that the yoked group would differ from the escape group. Therefore, we tested and confirmed a difference between these two groups using an apriori contrast. From this data, it is clear that the magnitude of the shuttlebox escape deficit following inescapable swim stress is quite modest in comparison to the rather robust phenomenon observed following inescapable tailshock stress. However, altering the swim stress parameters in future studies (e.g., additional trials and/or cold water) may potentiate the trend that we have observed in the current study.

Finally, the effects of swim stress controllability on alcohol-induced motor ataxia were opposite to that observed using the traditional tailshock stress controllability paradigm. Inescapable swim stress reduces rather than potentiates the ataxic effects of alcohol in comparison to naive controls. This result cautions generalizations about the molecular consequences of different forms of inescapable stress. More specifically, the nature of the stress clearly has a differential impact on the neurotransmitters thought to play a critical role in the motor incoordinating effects of alcohol (e.g., GABA, serotonin, NMDA; Grant, 1994).

Although some of the endpoints measured in the current study using intermittent swim stress parallel those found with tailshock stress controllability paradigms, others show fundamental differences. It is imperative to explore other important endpoints (e.g., immunology, neurochemistry) so as to address the legitimacy of generalist claims about the effects of stress control on subsequent behavior and physiological functioning. Before definitive statements can be made about fundamental distinctions between these two paradigms, it is necessary to obtain well-accepted measures of stress severity. Does intermittent swim stress produce a

release of neuroendocrine stress hormones such as adrenocorticotropic hormone (ACTH), corticosterone (Maier et al., 1986; Mormede et al., 1988; Swenson and Vogel, 1983) or endogenous opioids as does shock stress (Akil et al., 1976; Drugan et al., 1981; Madden et al., 1977; Maier et al., 1980)? Are the immunological consequences the same? These questions will be addressed in future studies using intermittent, cold water swim stress.

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