CONDITIONED INHIBITORY CHANGES IN HEART RATE WITH AND WITHOUT ETHANOL

by

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INTRODUCTION

The broad objective of the present investigation was to provide information on excitatory and inhibitory changes in heart rate (HR) that occur in excitatory and inhibitory conditioning paradigms. At the present time, considerable emphasis is being placed on the study of the effects of conditioned-inhibitory stimuli on behavior (Boakes & Halliday, 1972; Hearst et al, 1970; Gray, 1975; Rescorla, 1969; Rescorla & Wagner, 1972) in a wide variety of learning situations. This interest in the study of inhibition at the behavioral level represents a sharp break with traditional classical conditioning investigations reported by Western investigators (Hearst, 1972; Rescorla, 1969, 1975a). While Eastern European as well as Russian researchers have long been active in the study of conditioned inhibitory phenomena (Pavlov, 1927; Konorski, 1948) little interest in this field was expressed by Western investigators prior to 1960. Thus, although substantial information is available in this country concerning the parameters of excitatory conditioning relatively little is known about the determinants of inhibitory control of behavior. In view of this imbalance of information, some authors have suggested that the study of inhibitory conditioning should be given equivalent or perhaps even greater priority than research on excitatory conditioning (Hearst, 1972; Rescorla, 1969).

Historical Overview of the Concepts of Excitation And Inhibition in Classical Conditioning

During the latter part of the 19th century, a number of experimental observations were made that prompted the suggestion that the peripheral nervous system was organized into distinct excitatory and inhibitory pathways (Fearing, 1930). The primary basis for this assumption was the finding of separate peripheral nerves which appeared to subserve either excitatory or inhibitory functions. A logical extension of the conceptual separation of the peripheral nervous system into excitatory and inhibitory segments was the proposal that the central nervous system (CNS) was also organized along excitatory and inhibitory lines (Fearing, 1930; Pavlov, 1927).

Early empirical support for the latter hypothesis was provided by Weber and Weber in the 1840's and Sechenov in the 1860's (Fearing, 1930; Sechenov, 1965). The Webers extended the concept of inhibition to cover observations of increased activity of spinal reflexes in frogs after decebration. Sechenov also gave detailed consideration to problems of central inhibition. In a series of investigations, he demonstrated that the brain was responsible for inhibitory control over spinal reflexes. Through ablation techniques and physical and chemical stimulation of brain areas, he was able to selectively suppress or inhibit spinal reflex excitability. On the basis of his findings, Sechenov proposed a theory of CNS function based on the concept of centers. He suggested that discrete centers of excitation and inhibition existed in the CNS. Further, these sites were assumed to be functionally interactive and their coordination was thought

to be the basis for the integrative activity of the CNS. Sechenov's views had a major impact on later developments in classical conditioning largely through the writing of Pavlov (1927).

Pavlov's theory of nervous system activity and the conceptual basis for his studies of conditioned behavior were derived largely from the earlier work of Sechenov. He accepted Sechenov's basic assumption that excitation and inhibition were separate physiological processes with discrete loci in the CNS. Likewise, he emphasized the basic functional antagonism or reciprocity of the processes. In the context of classical-conditioning studies, Pavlov maintained that a process of excitation was responsible for all reflex increases while a process of inhibition was responsible for all reflex decreases. He also suggested that potentially identifiable processes of excitation and inhibition were necessary precursors to and isomorphic with overt behavioral responses.

Pavlov (1927) assumed that an excitatory process was largely responsible for the appearence of orienting or investigatory responses, the evocation of unconditioned responses and the establishment of conditioned responses. In general he maintained that excitation was responsible for the more gross and undifferentiated aspects of behavior e.g., components of orienting and unconditioned responses. However, excitation was also felt to be critical in the development of conditioned responses (CRs) where it was assumed to act in an integrated and complementary manner with the process of inhibition. In contrast to excitation, inhibition was assumed to be responsible for the diminuition or disappearance of responses observed in adaptation, habituation, and extinction. Overall, Pavlov and his

colleagues placed much greater emphasis on the concept of inhibition than did their Western counterparts.

Beyond his categorical use of the term inhibition, Pavlov established a classification scheme of types of inhibition. A basic distinction was made between external and internal inhibition. The term external inhibition was applied when an established CR was disrupted by the introduction of a novel stimulus or distracter into the experimental setting. Often, novel or intense stimuli introduced near the presentation of an excitatory CS+ interrupted or prevented the performance of the CR (Pavlov, 1927; Konorski, 1948). An inference sometimes drawn from such observations was that the extraneous stimulus had suppressed or inhibited the CR. While the term external inhibition was often used descriptively, the disruption of excitatory CRs by novel or intense stimuli was not felt to provide a firm basis for making inferences about a CNS process of inhibition (Pavlov, 1927; Konorski, 1948). Typically, novel or intense stimuli produced marked skeletal and autonomic responses which could interfere directly with the performance of the CR through a mechanism of peripheral response competition.

In contrast to external inhibition, internal inhibition was assumed by early Russian investigators to develop gradually and only as the result of repeated non-reinforced CS presentations (Pavlov, 1928; Konorski, 1948). Furthermore, internal inhibition was considered to be a central process rather than a peripheral process involving competing or antagonsitic responses (Konorski, 1948; Pavlov, 1927; Rescorla, 1969, 1975b). Pavlov cited the habituation of orienting responses, extinction of CRs, and the

suppression of responding to a nonreinforced CS (CS-) in a differential conditioning paradigm as behavioral evidence for the presence of internal inhibition. It was also thought to be the basis for conditioned inhibition, positive induction, and inhibition of delay.

Pavlov made several important assumptions about the underlying basis of internal inhibition. One of the most controversial of these was that internal inhibition developed at the primary afferent site of the CS or CS "center" in the CNS. He also suggested that the presence of inhibition at an afferent center made that center temporarily refractory to further activation. These assumptions were not challenged by Western investigators working in the classical conditioning area until quite recently (Boakes & Halliday, 1972; Gray, 1975; Rescorla, 1969, 1975a). Prior to this work, several Russian and Eastern European investigators began to critically question Pavlov's basic theory of inhibition (Anokhin, 1974; Beritoff, 1965; Konorski, 1948, 1967). These authors suggested that the basis for the extinction of excitatory CRs and the occurrence of other type of response decrements was the presence of inhibition at US sites or motivation centers rather than at CS centers.

Konorski (1948,1967) argued that the traditional extinction procedure of presenting the CS alone following conditioning training may not be the most effective way of reducing response strength. He proposed that the removal of CRs might be facilitated by directly reducing the strength of the US and he suggested several ways that this could be accomplished. These included giving a series of US-alone presentations, decreasing the magnitude or intensity of the US, and presenting the US immediately before

the CS in a backward order. Konorski (1948) argued that responses controlled by a CS presented in a backward relationship with a US should be opposite to those controlled by a CS presented in a forward relationship with the same US. The backward procedure was therefore considered the most direct method of extinguishing excitatory CRs and establishing internal inhibition.

Current Issues in the Study of Behavioral Inhibition

Consistent with Konorski's suggestions, contemporary views of inhibition also emphasize the importance of the relationship between a CS and US in the generation of conditioned inhibition. Rescorla (1969, 1975a) and Rescorla and Wagner (1972) have proposed that conditioned inhibition is a process that is symmetrical to that of conditioned excitation. They have maintained further that conditioned excitation develops from a positive contingency or correlation between a CS and a US, whereas conditioned inhibition develops from a negative contingency or negative correlation between a CS and US.

Procedures such as explicitly-unpaired CS and US presentations, backward conditioning, discrimination conditioning, and conditioned inhibition all appear to meet Rescorla's operational definition regarding the necessary conditions for the establishment of a conditioned inhibitor. In each case, the CS is consistently presented in the absence of the US such that there is a negative correlation between the two events. Habituation and experimental extinction procedures typically result in complete loss of responding to a CS and this loss has often been attributed

to the development of internal inhibition (Rescorla, 1969, 1975a; Rescorla & Holland, 1976). However, such procedures would not be expected to generate a conditioned inhibitor by Rescorla's definition because they do not involve US presentations.

Whether the occurrence of conditioned inhbition is dependent on the presence of an explicit negative correlation between a CS and US remains an important issue in the field of classical conditioning. Work on this issue has had considerable impact on the problem of selecting appropriate control groups in studies of classical conditioning. The explicitly-unpaired control procedure has been widely used in studies of classical conditioning to provide an estimate of nonassociative changes in behavior. It has the advantage of equating groups for number of CS and US presentations while at the same time preventing the CS from becoming positively associated with the US. In the past, it has also typically produced a near-zero baseline of responding in classical conditioning (Jensen, 1961; Prokasy, 1965; Rescorla, 1967).

Despite its apparent advantages, complete dependence upon the explicitly-unpaired control procedure has been criticized (Prokasy, 1965; Rescorla, 1967). Prokasy argued that it was an unsatisfactory control paradigm because it provided a negative correlation between the CS and US. He suggested that it should be supplemented by a procedure in which the CS and US were presented randomly with no particular relationship, either positive or negative being allowed to develop. In the truly-random procedure, the probability of occurrence of the US in the presence of the CS is equal to the probability of its occurrence in the absence of the CS. More recently,

Rescorla ((1967,1969) has extended this line of reasoning and proposed a rather comprehensive theoretical system to account for excitatory and inhibitory modification of behavior that occurs in classical conditioning. On the basis of this theory, a CS employed in a truly-random arrangement with a US should have relatively neutral response eliciting properties.

According to most contemporary views, CSs having inhibitory properties should have specific measurable behavioral consequences (Hearst,1972; Gray, 1975; Rescorla, 1969,1975a). It has been suggested (Rescorla, 1969), that the inhibitor should control response tendencies that are opposite to those controlled by a conditioned excitor. A second consequence is that excitatory conditioning to such a CS should be retarded as measured in a reversal conditioning test. Similarly, the presence of the CS should decrement the responses to an excitatory CS in a summation or combined-cue test. Generally, it has been argued that a CS should meet the requirements of two or more of these conditions before it is concluded that it is inhibitory (Hearst, 1972; Gray, 1975; Rescorla, 1975a). The two recommended empirical tests have been reversal conditioning and combined cue (Hearst, 1972; Rescorla, 1975a).

Although examined infrequently in contemporary research, procedures other than those mentioned above appear to have utility in the study of excitatory and inhibitory changes in behavior. Paradigms such as positive and negative induction and inhibition of delay were frequently used in early classical conditioning studies of excitatory and inhibitory phenomena (Konorski, 1948; Pavlov, 1927; Rescorla, 1969). In induction paradigms,

CS- and CS+ are presented in sequence, with marked changes in behavior to the second stimulus supposedly reflecting either excitatory or inhibitory properties of the first stimulus. In the inhibition of delay procedure, evidence of inhibition is provided if subjects learn to withhold responding during the early part of a long CS-US interval. In addition to procedural manipulations, there is also some evidence that pharmacological agents such as ethanol may be useful in evaluating and characterizing various kinds of classically conditioned changes in responding. Although the findings vary widely in terms of the conditions under which they were obtained, there is nevertheless evidence available which suggests that ethanol may have specific effects on inhibitory processes.

The following sections are concerned with each of the major strategies that have been used to examine inhibitory phenomena in classical conditioning. The first section deals with studies in which potential inhibitory effects of pretest CS-alone exposures were examined. The next three sections pertain to studies involving the use of different types of "unpaired" procedures, of Pavlovian induction, and inhibition of delay, respectively. The final section is concerned with investigations bearing on the question of the effects of ethanol on inhibitory processes.

Pre-conditioning CS-alone Experiments

A number of studies have been conducted to evaluate the effects of pretest CS-alone exposures on subsequent excitatory conditioning to that CS. The findings of many of these experiments have suggested that this procedure made the CS inhibitory (Lubow & Moore, 1959; Lubow, 1973; Weiss &

Brown, 1974). The critical observation in the investigations was that excitatory conditioning to the CS was retarded or impaired following as few as one or as many as several hundred preconditioning presentations of the CS. This effect was labeled "latent inhibition" (Lubow & Mooore, 1959) presumably because evidence about the presence or absence of inhibition was provided by the outcomes of later conditioning performance.

In the initial study of this phenomenon, Lubow and Moore (1959) observed that pretest trials with the CS retarded the acquisition of a leg-flexion CR in dogs. Following this observation, the latent-inhibition effect was documented in a considerable number of studies involving a variety of skeletal responses such as tail movement (Chacto & Lubow,1967) and eyelid closure (Siegel, 1969). However, for unknown reasons the effect has been much more difficult to obtain for autonomically mediated responses.

For example, Ray and Brener (1973) reported that a group of restrained rats given 120 pretest CS exposures prior to conditioning actually showed more rapid HR conditioning to the CS than did comparison groups including one given random CS and US exposures. They suggested that the failure to observe "latent inhibition" may have resulted from possible differences between skeletal-motor and autonomic responses.

Fitzgerald and Hoffman (1976) also failed to find the effect in a study involving separate groups of rats given either 0, 10, or 50 CS-alone trials prior to HR conditioning. Instead, the group given 50 CS-alone trials conditioned more rapidly than any of the other groups. Also, findings obtained in classical to instrumental transfer studies have

suggested that pretest CS exposures may not establish a CS an an inhibitor.

Rescorla (1971) examined possible inhibitory effects resulting from CS preexposures in two separate experiments. In the first experiment, inhibition was assessed with both reversal learning and summation procedures. After rats were trained to lever press for food, they were assigned to either one of two experimental or two control groups. The experimental groups received 80 CS exposures while the control groups were merely exposed to the test chamber. In the reversal test the experimental subjects showed retarded excitatory conditioning, indexed by a conditioned suppression. However, in the summation test the experimentals did not differ from the controls.

In a second experiment, Rescorla examined the effect of CS preexposures on the development of conditioned inhibition. After appetitive bar press responses were learned, half of the subjects were exposed to 80 nonreinforced tone presentations while the other half were only exposed to the test environment. Next subjects were given eight light-shock pairings superimposed on the bar-press responding. Finally, subjects were tested for the development of conditioning to the tone. In this test, subjects were given reinforced light-alone presentations and overlapping light-tone presentations which were not reinforced. The experimental group was retarded in the development of discrimination to the light. In brief summary, CS preexposures resulted in retardation of both excitatory and inhibitory conditioning but had no effect on summation outcomes. On the basis of these outcomes, Rescorla suggested that pretest exposures did not make the CS inhibitory but instead reduced its salience so subjects did not attend to it.

Results similar to those of Rescorla were obtained by Reiss and Wagner (1972). They examined the effects of CS preexposures using a conditioned suppression paradigm and a summation test. First, half of the rats received 1,380 presentations of a stimulus (A), and the other half received 12 presentations of a second stimulus (B). Next, all animals were given 120 presentations of a third stimulus (C) paired with a shock. In a summation test the groups received stimulus A with C or stimulus B with C. While both stimuli interfered with responding to C, stimulus B had the greatest effect. Thus number of pretest exposures was not positively related to interference with excitatory responding in the summation test. Finally, each group was given excitatory conditioning to all of the CSs. The development of CRs was most retarded to stimulus (A), the most frequently preexposed stimulus. Reiss and Wagner proposed that taken together the outcomes of the summation and reversal test were better explained by a loss of CS salience or attentional deficit in subjects rather than to conditioned inhibition.

Overall, little firm support exists that CS preexposures make a CS a conditioned inhibitor. Positive support has only been provided from the outcomes of isolated tests of excitatory conditioning. Where both reversal and summation tests have been used positive outcomes have not been obtained in both tests. This suggests that apparent latent inhibition effects may have been due to reduced CS salience rather than to conditioned inhibition. An objective of the present study was to examine the effect of CS preexposures compared to those of explicitly-unpaired and truly-random CS exposured in multiple tests of conditioned inhibition.

Negative relationships between the CS and US: Studies in which single tests of inhibition were made

Inhibitory stimulus effects of different CS-US relationships were examined in a series of studies by Rescorla and LoLordo (1965). In one study, dogs were first trained to perform avoidance responses using a Sidman avoidance paradigm (Sidman, 1955). Next, an experimental group was given discrimination training to reinforced (CS+) and nonreinforced (CS-) cues. A control group received an equivalent number of presentations of both CSs. In the test phase, the CSs were delivered while the dogs were actively avoiding shock. It was noted that the CS+ increased the avoidance rate of the experimental group and that CS- decreased the rate. In contrast, the control group did not change their rate of responding in the presence of either CS. The authors suggested that CS- had developed inhibitory properties (the reduction of avoidance responding was attributed to inhibition of fear) because of its negative relationship with the US.

In a subsequent study, Rescorla (1966) extended his investigation of inhibitory stimulus effects resulting from negative CS and US contingencies. After learning Sidman avoidance responses, dogs were assigned to one of three treatment groups. One group was given CS-US pairings, a second group received explicitly-unpaired CS-US presentations, while a third group received completely random CS and US presentations. In the test phase, the CSs were delivered while the dogs were avoiding shock. It was found that the group given CS-US pairings displayed increased avoidance to the CS, whereas the explicitly-unpaired group showed decreased avoidance to the CS. The truly-random group displayed no change in responding when the CS

was given. These findings were considered supportive of the assumption that the contingency between a CS and US is a critical determinant of the type of response controlling properties that a CS develops. More specifically, a CS negatively correlated (i.e., explicitly-unpaired) with a US was felt to develop inhibitory properties while a CS presented in a contingent (paired) relationship with a US was felt to develop excitatory properties. Finally, the results obtained with the truly-random CS were thought to indicate that this CS had developed balanced excitatory and inhibitory properties.

Bull and Overmier (1968) also studied the properties of CSs presented in contingent or non-contingent relationships to a US. After reliable avoidance responding was established, separate groups of dogs were given differential conditioning with CS+ or CS- or exposed to random CS and US presentations. In a transfer test, the CSs were presented while subjects performed avoidance responses. The CS+ given the differential conditioning group increased avoidance while the CS- decreased avoidance. Avoidance responding in the truly-random group was not affected by the unpaired CS. These results were consistent with the assumption that CSs positively correlated with USs become excitatory, while those negatively correlated with USs become inhibitory. Furthermore, assumptions about the neutrality of a truly-random CS were supported.

A number of investigators have examined the inhibitory stimulus effects resulting from the backward presentation of CSs and USs. It might be recalled that Konorski (1948) suggested that the backward procedure was the most expedient for extinguishing excitatory CRs and establishing stable inhibitory potential to a CS.

Moscovitch and LoLordo (1968) initially trained three groups of dogs in a backward conditioning design. In one group each CS followed termination of the shock US by 1.0 sec and was itself followed by intervals of 2.0, 2.5, or 3.0 min until the next US. A second group received CSs 15.0 sec after US termination and the CSs were again followed by intervals of 2.0, 2.5, or 3.0 min until the next US. The final group received CSs 1.0 sec after the US, but the CS was followed by a randomly varying US free interval averaging 2.5 min.

In the test phase, the CSs were presented while subjects performed avoidance responses on a Sidman schedule. The first two groups showed showed marked response reduction to the CS but were not reliably different. The third group showed little decrement in responding during the CS. Moscovitch and LoLordo concluded that conditioned inhibition was established in backward conditioning but was not influenced by the backward temporal relationship between the CS and the preceeding US (the US-CS interval). They felt instead that it was determined by the forward relationship between the CS and the subsequent interval free from the US.

The role of temporal factors in backward conditioning in the establishment of conditioned inhibition was also investigated by Maier, Rapaport, and

Wheatley (1976). Different groups of rats received CSs at intervals of either 3 or 30 sec following US offset. A control group received random CS and US presentations. In the test phase, the CSs were superimposed on Sidman-avoidance responding. Only the CS of the 3-sec group reliably depressed avoidance. Based on their findings these authors emphasized that the timing of the US-CS intervals likely played an important role in the development of conditioned inhibition with a backward paradigm. They proposed that a complete theory of conditioned inhibition should focus not only on the correlative aspects of the CSs and USs but also on their precise temporal arrangement with each other.

The inhibitory effects of backward US and CS conditioning were also examined by Siegel and Domjan (1971). Two different types of reversal tests with different species of subjects were used to index inhibitory effects. In one case, an experimental group of rats was given 50 backward trials while control groups were given either CS-alone, US-alone, or truly-random CS and US presentations. In another case, an experimental group of rabbits was given 550 backward trials while controls received either CS-alone, US-alone, or truly-random CS and US presentations. In the test phase, rats were given conditioned-emotional-response training while the rabbits were given classical conditioning. Both of the experimental groups were retarded during reversal conditioning relative to controls. These findings provided support for the view that the backward procedure can generate a CS with apparent inhibitory properties and extended the phenomena to an additional species (rabbits).

In a later study, Siegel and Domjan (1974) examined the effects of

different numbers of backward conditioning trials on the acquisition of inhibition. Again, both conditioned-emotional-response training of rats and classical-eyelid conditioning of rabbits were used. Prior to testing, all subjects were exposed to either 0, 5, 10, 25, or 50 backward US-CS presentations. In the conditioning tests, a reliable difference was found between the 0 and the 50 trial group for both types of animals.

Plotkin and Oakley (1975) examined the effects of the length of the interval separating the US and CS on backward conditioning trials using eyelid reactions in rabbits as the index of inhibition. One experimental group received 125 trials with an ISI of 200 ms while a second group received 125 trials with an ISI of 500 ms. Controls included a passively restrained group, a CS-alone group, a forward trace conditioning group, and a safety-signal group. It was observed that the development of conditioned eyelid closures was retarded in both backward groups and equally so.

The findings of the above studies generally support the assumption that CSs presented in a negatively correlated manner with USs will have different effects than CSs presented alone or in a truly-random pattern with USs. Differential conditioning, explicitly-unpaired procedures, and backward conditiong techniques have all been observed to establish CSs with inhibitory response properties that can be distinguished from CSs generated through CS-alone and truly-random procedures. A number of authors have suggested that results reflecting response decrements in tests of reversal, summation, as well as in other procedures were due to the CSs having developed inhibitory characteristics. Further, the failure of subjects

given truly-random CS and US exposures to be retarded in reversal learning or show response decrements in summation tests to the CS have been considered evidence that the associative values of the CSs were relatively neutral. In the prior studies the strength of inferences about conditioned inhibition was limited by the fact that only one independent test of the stimulus characteristics was made. In the following section experiments are reviewed in which more than a single assessment of inhibition was reported.

Negative relationships between the CS and US: Studies in which multiple tests of inhibition were made

While the use of multiple tests of conditioned inhibition has been emphasized (Gray, 1975; Hearst, 1972; Rescorla, 1969, 1975a) only a limited number of studies have been reported in which two or more measures of inhibition were made. As noted earlier, in general, studies using more than one measure of inhibition, preferably the combined use of reversal and summation tests, have an increased likelihood of correctly assessing the inhibitory potential of stimulus events.

Hammond (1968) examined the inhibitory stimulus effects established in a differential conditioning paradigm. The presence of inhibition was indexed both by observation of direct response changes during differential conditioning and by means of a reversal test. Initially rats were trained to bar press for food on a variable interval schedule. Next one group was given differential classical conditioning to a reinforced stimulus (CS+) and a nonreinforced stimulus (CS-). One control group was given CS-alone presentations while a second received truly-random CS and US

exposures. During discrimination training which was superimposed on the baseline of bar-press responding, the response rate was observed to increase in the presence of the CS+ but did not change during the presentation of CS-. The CS-alone and truly-random groups displayed no change in responding to their respective CSs. In reversal conditioning, the CS- of the discrimination group was more difficult to establish as an excitor than either the CS of the CS-alone or truly-random group. Hammond suggested that the CS- had developed inhibitory properties.

The effects of negative CS and US contingency was examined by Rescorla (1969) in two different experiments. In one experiment a reversal conditioning test was used and in a second experiment a summation test was employed. In the first experiment rats were initially trained to lever press for food reinforcement. They were then randomly assigned to one of four experimental groups which differed in the extent of negative CS and US contingency or to one of four control groups. Controls received either truly-random CS and US presentations or USs with a CS different than the one that would be tested in reversal. The experimental groups were more retarded in reversal. In the second experiment after lever pressing was established, subjects were assigned to one of four experimental groups differing in extent of negative CS and US relationships. CER training was conducted after the inhibitory phase. In the summation test the group previously exposed to the most negative CS and US contingency showed the greatest response decrement. The combined reversal and summation results were considered to demonstrate that conditioned inhibition was determined largely by the extent of negative contingencies between CSs and USs.

Cunningham, Fitzgerald, and Francisco (1977) examined the inhibitory

consequences of explicitly-unpaired and truly-random procedures on the HR responses of restrained rats. All animals were first given 24 excitatory conditioning trials with the CS consistently being paired with the US. Following this treatment, the animals were divided into two groups. One of these groups was given explicitly-unpaired CS and US presentations. The other received the same number of CSs and USs except that the US occurred randomly with respect to CS. For both groups, the CS employed during this unpaired phase was different from the one used during excitatory conditioning. Subsequent to the unpaired trials, both groups received combined-cue and reversal conditioning tests of inhibition. The directions of the conditioned responses during excitatory conditioning were uniformly decelerative. During the unpaired phase, the response of the truly-random group was a small deceleration. For the explicitly-unpaired group HR changed from cardiodeceleration to cardioacceleration over the course of the unpaired trials. The opposing directions of the HR reactions of the explicitly-unpaired group to the excitatory CS+ (HR deceleration) and to the unpaired CS- (HR acceleration) suggested that CS- was inhibitory. This possibility was also supported by the fact that the acquistion of the HR CR to CS- was retarded in the explicitly-unpaired group during reversal conditioning. However, the combined-cue test in which CS+ was combined with the other CS failed to show a difference between the explicitly-unpaired and truly-random groups. In discussing their findings, Cunningham et al (1977) noted that since the HR acceleration established to CS- was opposite in direction to the HR deceleration normally occurring as the CR, a competing response interpretation of the observed retardation of conditioning to CS- could not be completely ruled out.

In general, the results of the above studies were in agreement with those covered in the earlier section in that explicitly-unpaired CSs were found to have response properties different than those of CSs employed in CS-alone and truly-random procedures. It should be noted, however, that rarely was positive evidence of an inhibitory effect clearly demonstrated in two different tests (e.g., summation and reversal, etc.). Most of the positive results have been obtained using reversal tests, while summation tests have yielded somewhat inconsistent and ambiguous results.

Positive and Negative Pavlovian Induction

The concept of induction was introduced into the field of classical conditioning by Pavlov (1927) to explain apparent irregularities or anomalies regarding the occurrence of salivary CRs. Pavlov (1927) reported that dogs receiving differential classical conditioning sometimes displayed augmented salivary CRs to CS+ if the delivery of CS+ was immediately preceded by the occurrence of CS-. Pavlov labeled this phenomenon positive induction and attributed the increased responding to an intensification of excitation to CS+ following a release of inhibition that was assumed to be attached to CS-. However, because salivary reactions to CS- were usually quite low or nonexistent, it was not possible to use the reverse procedure of presenting CS+ shortly before CS- to see if CS+ would augment the putative inhibitory characteristics of CS-. Instead, evidence of intensified inhibition to a CS- was provided by noting that the development of a salivary CR to a previous CS- was retarded if reinforced trials with CS+ were presented in between reinforced trials with CS-.

Pavlov viewed the retardation of conditioning under these circumstances as an example of negative induction and like its counterpart, positive induction, explained the effect on the basis of a rebound from an opposing state of the central nervous system. In this case, the controlling process was thought to be amplified inhibition to CS- following a release from excitation to CS+.

Although Pavlovian induction procedures have the potential of producing useful information regarding the excitatory and inhibitory capabilities of stimuli (Rescorla, 1969), they have been used infrequently for this purpose. In fact, only a limited number of examples of positive induction are available in the contemporary classical conditioning literature with the presence of negative induction still depending upon indirect measures of a performance decrement (Mackintosh, 1974). Moreover, those experiments involving induction that have been reported have rarely included appropriate control conditions.

The earliest examples of induction like effects were cited by Pavlov (1927). Kogan, a colleague of Pavlov's initially established salivary CRs in dogs to tactile stimulation of different points on the dogs' body. After the CRs were well learned, the CR at the first site was extinguished through repeated nonreinforced presentations of the tactile stimulation. It was generally noted that subsequent to this treatment stimulation of other CS sites resulted in the performance of CRs of reduced magnitude. This outcome was attributed to generalization of inhibition. However, in some cases it was found that stimulation of the initial site was followed by an enhancement of the CR elicited at another

site. Kogan's observations were not consistent with Pavlov's views about conditioning and they were not given serious consideration.

In a different study, Furosikov used a differential conditioning procedure to establish a salivary CR to tactile stimulation of a front paw (CS+) and nonresponding to stimulation of a hind paw (CS-). He then examined the effects of presenting the CS- immediately prior to CS+. He reported that the latency to onset of the first drops of saliva to CS+ was reduced and the total amount of salivation to the CS+ increased by about 50%.

In a similar experiment, Kalmykov used a discrimination training procedure and conditioned a salivary response to a strong light (CS+) and non-responding to a weak light (CS-). In the test of positive induction, the CS- was presented prior to CS+ and found to reduce the latency of the CR and to increase its magnitude by about 40%. Kalmykov therefore essentially replicated the earlier finding of Furosikov.

More recent investigations of induction have primarily been concerned with demonstrating the phenomenon rather than systematically exploring the parameters controlling its occurrence.Senf and Miller (1967) carried out three separate experiments to examine positive induction. In all of the studies, a previously non-reinforced stimulus (CS-) was presented prior to a reinforced stimulus (CS+) during extinction. It was assumed on the basis of Pavlov's (1927) theory, that if the CS- retarded the extinction of the CR to CS+ it might indicate the presence of excitatory rebound or positive induction. In the initial study, a discrimination procedure was used to establish conditioned motor activity to the CS+ that was paired

with a food US. The non-reinforced CS- was presented alone. Next, the animals were randomly assigned to one of three extinction groups. The experimental group was given closely spaced presentations of CS- and CS+. Two control groups were given only CS+ trials. As expected, extinction of the CR to CS+ was found to be retarded in the group given both CS- and CS+ presentations.

In the second experiment, rats were first trained to run for food to CS+ but not to CS- in a straight alley. The experimental group was extinguished with CS- and CS+ being given in sequence. One control group received only CS+ and a second received CS+ alternated with a neutral CS. As in the previous case, extinction of the CR was slowest in the experimental group given the CS+ and CS- during extinction.

Finally, in the third experiment rats were initially trained to perform bar-press responses to a food reinforced CS+ and not to respond to a non-reinforced CS-. During the test phase, one experimental group was given CS- and CS+ exposures at 10-sec intertrial intervals while a second group received CS- and CS+ at 20-sec intertrial intervals. A control group was given 20 CS+ presentations. Consistent with the findings obtained in the two prior experiments, the groups given alternated CS- and CS+ presentations extinguished more slowly than the group given only CS+ exposures. Senf and Miller suggested that CS- may have had excitatory effects since it retarded extinction of the excitatory CR. However, an alternative explanation involving stimulus generalization decrement should be considered. On this view, since the amount of stimulus change experienced by the single CS group that was extinguished with just CS+ was greater than that

experienced by the two groups given both CS- and CS+, more rapid extinction in the single group would be expected.

Pavlovian positive and negative induction were investigated by Frey and Ross (1967). In their study, rabbits were first given discriminated eyelid conditioning with the CS+ being paired with shock and CS- being presented alone. In the test of positive induction, the effects of varying the interval between CS- and CS+ was examined in each of four different groups. Interstimulus intervals of either 10, 30, 60, or 250 sec were used. In the test of negative induction, the experimental group was given CS+ followed by reinforced CS- presentations. One control group was continued on the same schedule that had been given during discrimination training, while a second received only reinforced CS- presentations. Response rates during positive induction were not affected by the spacing of CS- and CS+ with all of the groups showing comparable responses during the test for induction. Thus, evidence of a positive induction effect was not observed. In contrast, conditioning to CS- was slower when it was presented in the context of CS+ than when it was given alone. While this result suggests the possible presence of a negative induction effect, Frey and Ross felt it could also be explained in terms of stimulus generalization decrement. Once again, the basic problem was that the amount of stimulus change experienced by the group that was switched to just CS+ trials during testing was greater than that experienced by the group that received both CS- and CS+ trials.

Finally, tests of positive and negative induction were carried out by Leonard, Weimer, and Albin (1968). They first trained rats to run in a

distinctive alley (CS+) for food reinforcement and to refrain from running in an alley (CS-) associated with non-reinforcement. As a test for positive induction, the experimental group was extinguished with CS- alternating with CS+ while a control group was given CS+ trials alternating with placements in a neutral goal box. For negative induction, the experimental group was given reinforced CS- trials mixed with CS+ trials while the control group received CS- presentations alternated with placements in a neutral goal box. Negative induction was not observed. That is, conditioning in the experimental group given CS- and CS+ trials was not significantly different from that shown by the control groups. However, during the positive induction procedure, the experimental group given CS- trials alternated with CS+ trials extinguished more slowly than the group given only CS+ exposures. Like Frey and Ross (1967) these authors attributed this outcome to the occurrence of stimulus generalization decrement in the control group rather than to positive induction.

Overall, the above studies provide little evidence of the presence of Pavlovian positive and negative induction. The findings of the early Russian studies cited by Pavlov (1927) and Konorski (1948) must be considered only suggestive as controls for stimulus generalization and stimulus similarity were typically not used. Though better controls have been used in recent studies, they have not been completely satisfactory. Some findings have been consistent with the presence of an induction-type effect (Senf & Miller, 1967) but the results could just as easily be explained in terms of stimulus generalization decrement factors (Frey & Ross, 1967; Leonard et al., 1968).

Inhibition of Delay in Classical Conditioning

As is true of most of the terminology used currently by investigators of classical conditioning, the term inhibition of delay was introduced by Pavlov (1927). Pavlov noted that when long CS-US intervals were used, the occurrence of the first drops of saliva shifted progressively away from the onset of the CS. After extended training, little salivation was observed to occur during the first half of the CS-US interval with most of the salivation being located close to the onset of the US (Pavlov, 1927).

Modern studies of classical conditioning have focused primarily on the study of skeletal-motor responses (Kimble, 1961). An apparent outcome of this emphasis has been the use of relatively short CS-US intervals since it was generally agreed that if the interval were extended much beyond .5 sec classical conditioning of skeletal-motor responses was difficult to obtain. This has meant that there are relatively few experiments dealing specifically with the phenomenon of inhibition of delay.

Church and Black (1958) examined the effects of trace versus delayed conditioning and CS-US interval (5-sec versus 20-sec) on the development of classically conditioned HR responses in separate groups of dogs. The direction of the HR CR was accelerative. Differences were not found among the groups in rate of conditioning, percentage of CRs, or magnitude of CRs. However, the latency of the peak HR change of the 5-sec groups (approximately 4 sec) was different from the latency of the 20-sec groups (approximately 10 sec). The authors concluded that this result could be explained on the basis of Pavlovian inhibition of delay.

The effects of varying the CS-US interval on HR conditioning in rats were examined by Black and Black (1967). There were four groups of animals receiving 30 delayed-conditioning trials with CS-US intervals of either .5, 2.5, 5.0, or 10.0 sec. Terminal HR responses of the 2.5-and 5.0-sec groups were greater than those of the .5-sec and 10.0-sec groups. Therefore, within limits, CS-US interval length was positively associated with the magnitude of the maximum HR changes as would be expected if inhibition of delay were operating.

Further information pertinent to the occurrence of inhibition of delay during HR conditioning in rats was provided by Fitzgerald and Martin (1971). They examined the effects of CS-US intervals of 0, .1, .3, .5, 1.0, and 6.0 sec using both trace and delayed procedures. A major finding was that maximum decelerative HR responses shifted away from CS onset as the CS-US interval was increased. Thus, the largest responses occurred in the 6.0 sec group during the last 2-sec counting period of the CS-US interval. This result was considered consistent with the temporal gradient of reinforcement interpretation of CS-US interval effects (Hilgard & Marquis, 1940). According to this position, conditioning should be maximal when the CS-US interval is slightly longer than the latency of the CR. This would allow the CR to occur immediately prior to the US and be maximally strengthened by its application.

Lynch (1973) compared the development of inhibition of delay during heart-rate and leg-flexion conditioning in dogs. The animals were given 300 trials using a delayed-conditioning paradigm with a 42-sec tone CS and a 1-sec shock US. Several potentially important observations were made.

First, though HR CRs developed more rapidly than leg-flexion CRs, inhibition of delay was more difficult to achieve for HR. By the end of conditioning, the latency of leg-flexion CRs had shifted to within 10 sec of the US, whereas for HR the latency of the peak change was much shorter. Lynch noted that Gantt (1960) reported divergences in the rates of development of cardiac and motor components of CRs in dogs and labeled this effect "schizokinesis". Lynch felt his findings demonstrated that a similar difference between skeletal and autonomic CRs may occur for inhibition of delay.

Most statements about inhibition of delay have been made on the basis of observation of response diminuition or loss during the early part of relatively long CS-US intervals. In only a few cases have special tests such as combined-cue or reversal conditioning been used to evaluate the presence or absence of inhibition. In one study of this type, Rescorla (1967a) used a combined-cue test to examine the inhibitory effects of a long CS-US interval. First, dogs were trained to perform hurdle-jumping-avoidance responses. Next, an experimental group was given 24 delayed-conditioning trials with a 30-sec tone CS and a 5-sec shock US. A control group was given 24 random CS and US presentations. The two groups were tested in the hurdle-jumping situation by presenting the CSs. The major findings were that the experimental group responded less often than controls during the first 5 sec of the CS-US interval and more often during the last 5 sec of the CS-US interval. The reduction of early interval responding and the relative confinement of the CR to the latter part or the CS-US interval suggested the presence of an inhibition-of-delay gradient.

In a second experiment, Rescorla (1967a) examined inibition of delay by superimposing fear-conditioning trials on Sidman-avoidance responding. The dogs received 300 tone-shock pairings using a 30-sec CS-US interval. During the latter part of testing, CS-onset depressed the avoidance rate while maximum responding was observed during the final 5 sec of the interval. These results were consistent with those of the first experiment in showing a gradient of responding within the CS-US interval.

In summary, surprisingly few studies have been carried out to investigate inhibition of delay in classical conditioning. However, in those experiments that do exist the results have generally been consistent. In general, over the course of conditioning, levels of responding have been observed to shift away from early or intermediate periods of the CS-US interval to later segments of the interval. Thus, the results of recent studies have been in agreement with those of early Russian authors (Pavlov, 1927).

Effects of Ethanol on "Inhibitory" Control of Behavior

There has been a longstanding assumption that ethanol exhibits selective effects on suppressed or inhibited behaviors. The experimental study of these effects appears to have been initiated by Russian investigators (Pavlov, 1927; Sechenov, 1965). One of the first of these studies was carried out by Zavadski (1908). He compared the effects of either a .2-g/kg or a 1.6-g/kg dose of ethanol on conditioned salivary responses in dogs. The low dose briefly, appx. 15 min, attenuated CR magnitude while the high dose markedly reduced the magnitude of both the CR and UR. The time required for full recovery of the UR ranged from

30-60 min. Recovery of the CR on the other hand ranged from 2-4 hours. Zavadski felt that the major effect of ethanol was that of depressing CNS activity. The amount and duration of the depression appeared to be positively related to the dose of ethanol employed.

In another study carried out in Pavlov's laboratory, Nikiforovski (1910) looked at the actions of ethanol on excitatory and inhibitory conditioned salivary responses in dogs. Stable differential responding to CS- and CS+ was first established and then the animals were given either a 2.5-g/kg or a 6-g/kg dose of ethanol. Approximately 15 min after being administered, the low dose disrupted discriminated responding. Specifically, prior response suppression to CS- was lost as salivation again occurred to this stimulus. In contrast, the high dose eliminated all responding to both CS+ and CS-. On the subsequent test day without ethanol, animals previously given a large dose of ethanol displayed CRs of larger magnitude than they did while under the influence of the drug. On the basis of his results, Nikiforovski suggested that inhibitory processes, namely those controlling response suppression, were more sensitive to ethanol that were excitatory processes. He also felt that ethanol could have important after effects on the balance between excitatory and inhibitory processes that could persist for up to 24 hours.

An examination of differential salivary responding in a single dog receiving multiple doses of ethanol was carried out by Andreyev (1934). The doses ranged from 1.0 g/kg to 5.0 g/kg. Low doses produced marked agitation and restlessness usually lasting for 30 min. Low doses also increased responding to CS- but did not affect responding to CS+, suggesting

a selective effect on inhibitory as opposed to excitatory processes. The highest doses initially increased responding to CS-, but after approximately 15 min depressed responding to both CS+ and CS- was observed. Andreyev concluded that low doses of ethanol had excitatory effects while high doses had primarily depressant effects. However, he also pointed out that response increases to CS- could have been due either to increased excitation or decreased inhibition.

Gantt (1935) looked at the influence of ethanol on established salivary and motor conditioned responses in dogs. The dogs were given doses of ethanol measuring either .4 g/kg, 1.2 g/kg, or 3.0 g/kg. All doses increased the latency and decreased the magnitude of the salivary and motor responses. The effects were found to be dose dependent with higher doses producing greater effects. Gantt also observed that high doses produced a transient recovery of habituated orienting responses. This effect was attributed to a disruption of an inhibitory process underlying the suppression of the orienting responses.

A test of the effects of ethanol on skeletal-motor responses was made by Dworkin, Bourne, and Raginsky (1937). Dogs were trained to respond for food to one stimulus (CS+) and to withhold responding to a second stimulus (CS-). Next, ethanol doses of either 2.0, 2.5, or 4.0 g/kg were given. Ethanol was observed to have dose related effects on behavior. At 2.0 g/kg dogs displayed ataxia and loss of response suppression during CS- and the interstimulus interval. The 2.5-g/kg dose increased the ataxia and further disrupted discrimination to the extent that the animals responded equivalently to CS- and CS+. Finally, the 4.0-g/kg dose depressed all

responding. While the results that were obtained with low doses were attributed to ethanol's disruption of inhibition, they could also be interpreted as being due to a general excitatory effect of ethanol.

During the 1940's and 1950's, few studies involving the effects of ethanol on conditioned behaviors were conducted. However, recently there has been renewed interest in this area. While operant procedures have been used in most contemporary studies, their design has been very similar to that employed in the early classical conditioning studies. Methodologically, nearly all recent investigations have involved initially establishing discriminated active (excitatory) and passive (inhibitory) responding and then testing the effects of ethanol on the maintenance of this performance.

Laties and Weiss (1962) tested the effects of ethanol on discriminated responding in humans and in rats. In both cases, a procedure was used to establish active responding to a food reinforced CS+ and no responding to a non-reinforced CS-. Next, subjects were given either a .5-g/kg or a 1.0-g/kg dose of ethanol. The low dose did not affect responding to either CS. However, the high dose reduced the rate of responding to CS+. Similar results were observed for both humans and rats. The loss of responding to CS+ was attributed to the depressant effects of ethanol.

A conditioned suppression procedure was used by Goldman and Doctor (1964) to study ethanol. Cats were first trained to discriminate shock free (CS-) from shock reinforced (CS+) time periods. A dose of 1.0 g/kg of ethanol was then given. An overall increase in responding during both the non-shock and shock intervals was observed. It was concluded that the ethanol produced a general excitatory effect.

Sanders and Pilley (1973) used discriminated bar-press responding in rats to investigate the effects of several doses of ethanol. First, differential responding was developed to food reinforced CS+ and non-reinforced CS-. Subsequently, separate groups of rats were given doses of ethanol measuring .5, 1.0, or 1.5 g/kg. The main findings were that the groups given the two lowest doses showed no change in responding to either CS+ or CS-. However, the high-dose group displayed increased responding to CS- without a corresponding increase in responding to CS+. The authors felt that these results indicated that response suppression, and inferentially inhibition, were more sensitive to ethanol than were excitatory processes.

The behavioral consequences of several doses of ethanol were examined by Holloway and Vardiman (1971). After reliable bar pressing to food reinforced CS+ and response suppression to non-reinforced CS- were established, ethanol was administered. Different groups of rats received either .2, .4, .8, 1.2, or 1.8 g/kg of ethanol. All doses except the 1.8 g/kg increased the rate of responding to CS-. However, these increases were not paralleled by increases to CS+ or by increases in activity between trials. It was concluded that low and moderate doses of ethanol acted to selectively disrupt inhibitory control of behavior to CS-. The fact that ethanol neither increased responding to CS+ nor increased general activity were felt to support the assertion that ethanol's effects were specific to inhibition and not due to a more general excitatory effect.

In a subsequent study, Holloway and Wansley (1973) attempted to extend the findings of the prior study. After reliable responses to

CS+ and response suppression to CS- were established, rats were given one of four ethanol injections; .5, 1.0, 1.5, or 2.5 g/kg. They found that the .5-g/kg dose increased responding to both CS- and CS+ while the 1.0-g/kg dose had no effect. Both the 1.5 and 2.5-g/kg doses depressed responding during the intertrial intervals and to the CS+. These results suggested that ethanol had dose-related effects on responding with low doses facilitating responding in a non-selective fashion and high doses uniformly depressing responding. No evidence was provided that ethanol had selective effects on behavioral suppression or response-inhibitory mechanisms.

A study by Fitzgerald and Stainbrook (1977) also provided information bearing on the potential effects of ethanol on excitatory and inhibitory control of behavior. It has been widely assumed that orienting-response habituation and inhibition of delay are due to an inhibitory process. Their study was designed to evaluate the effects of two doses of ethanol (.8 and 2.4 g/kg) on the habituation of HR orienting responses and the development of conditioned HR responses. A delayed conditioning procedure was used in which the US followed the CS at an interval of 6 sec. The length of this interval was felt to be sufficient for the development of inhibition of delay. The .8 g/kg dose decreased the magnitude of the orienting response but had no effect on the HR CR. On the other hand, the 2.4-g/kg dose completely suppressed both the orienting response and the CR. The latter outcomes suggested that the high dose of ethanol may have produced generalized depression of central nervous system activity.

In brief summary, although some support exists that ethanol may exhibit selective effects on inhibitory control of behavior, the evidence is not convincing. In early classical conditioning studies carried out in the Russian laboratories, control groups were generally lacking and independent use of supplemental tests, e.g., reversal, summation, etc., to strengthen inferences about inhibition were not provided. While the design and methodology of more recent studies have been improved, special tests to evaluate the presence of inhibition have not usually been used.

A final point to be made is that in most of the available studies the effects of ethanol were examined on well established responses. There is some evidence that ethanol and other drugs may have greater effects on incompletely or newly developed responses than on well established responses (Gantt, 1935; Overton, 1967). Very few attempts have been made to investigate systematically the effects of ethanol on the acquisition of inhibitory response control.

STUDY RATIONALE

While parameters for the establishment of excitatory classical conditioning have been extensively examined, the determinants of inhibitory conditioning are less well known. Also, at present relatively little information exists on the empirical characteristics of conditioned inhibitors. Though research on inhibition has increased recently, many questions remain unclarified. Part of this problem has been due to some general weaknesses in many of the prior studies.

In order to distinguish conditioned inhibition from other possible processes it has been proposed that conditioned inhibitors have some specific empirical consequences. (Gray, 1975; Hearst, 1972; Rescorla, 1969, 1975a). The suggestion has been made that a conditioned inhibitor should control response tendencies opposite those of a conditioned excitor, that reversal conditioning to an inhibitor should be retarded, and that presentation of an inhibitor should decrement the responses to an excitor in a summation test. It has been recognized that outcomes from a single test procedure such as reversal or summation can often be explained by processes other than conditioned inhibition (Hearst, 1972; Rescorla, 1969). Findings of either procedure if used in isolation can often be attributed to attentional deficits and may in some cases be explained by the presence of antagonistic or competing peripheral responses. To rule out interpretations alternative to that of conditioned inhibition, especially various attentional hypotheses, the corroborative use of both reversal and summation tests has been recommended (Hearst, 1972; Rescorla, 1969, 1975a).

Hearst (1972) and Rescorla (1969, 1975a) have proposed the following basic rationale for the ability of the combined use of reversal and summation tests to rule out attentional explanations. If an attentional deficit were responsible for retardation of reversal learning, evidence of inhibition during a summation test would not be expected. Failure to attend to the inhibitor should not affect responding to the excitor. Similarly, while attention loss might explain positive summation outcomes, it could not at the same time easily account for retarded reversal learning. It might be argued that the inhibitor attracted the subjects' attention during the summation test, decreasing its attention to the excitor, and thereby producing a loss in response strength. However, if the inhibitor were readily noticed, it would be expected to facilitate rather than retard reversal conditioning. While obtaining positive results in both reversal and summation tests is generally considered satisfactory for ruling out attentional interpretations, it is important to recognize that these outcomes do not necessarily rule out peripheral competing response interpretations. The failure to examine systematically the development of peripheral responses during training phases and to rule out the presence of competing responses in test phases have been pointed to as important flaws in many studies of conditioned inhibition (Black, 1971; Gormezano & Kehoe, 1975; Trapold & Overmier, 1972).

Another possible constraint on the generality of conclusions that have been made about conditioned inhibition arises from the fact that most positive outcomes have involved the measurement of only skeletal-motor responses. The potential therefore exists that some of the general assumptions

that have been made about conditioned inhibitors may not apply to autonomic-nervous-system responses. Along the same line, a general failure of investigators to concurrently monitor both skeletal and autonomic responses has precluded the analysis of potentially important differential response development and/or response interactions in the training and testing phases of conditioned inhibition studies.

In view of the prior considerations, the present investigation was conducted to provide new information on the determinants and empirical characteristics of conditioned inhibitors. Measurements of both cardiac and skeletal-motor responses were made during both the "unpaired" or inhibitory training phase and all subsequent testing phases of the study. This allowed an examination of possible differential response changes in the autonomic and skeletal-response systems and analysis of potentially important response interactions.

The response eliciting properties of CSs employed in explicitly-unpaired, CS-alone, and truly-random procedures were compared in a single integrated experimental design. Recall that it has been assumed that procedures which establish a negative contingency between a CS and US such as the explicitly-unpaired procedure are uniquely capable of establishing conditioned inhibition. The CS-alone procedure provided an important comparison condition since its abiltity to generate conditioned inhibition is both an important theoretical and empirical issue. Finally, the truly-random group was included since, in principle, it is capable of preventing the development of positive or negative CS and US contingencies, and

could potentially provide a near-zero response baseline against which to measure response development in the explicitly-unpaired and CS-alone groups.

The overall design of the experiment allowed several specific tests of conditioned inhibition to be made. Excitatory conditioning was conducted prior to the "unpaired" or inhibitory training phase. Establishment of the excitatory conditioned response allowed a comparison of its detailed characteristics with those of potential inhibitors which might develop in the subsequent "unpaired" phase. The use of heart rate as the primary response measure allowed a trial-by-trial comparison of the development and characteristics of responses in the explicitly-unpaired, CS-alone, and truly-random groups in the "unpaired" phase. The possible development of differential responses in the groups during the "unpaired" phase provided an additional opportunity for making inferences about the relative ability of the training procedures to establish conditioned inhibition.

Two basic test procedures were employed to index possible inhibitory stimuli developed in the "unpaired" phase. These procedures were the Pavlovian positive induction procedure and the re-learning or reversal test. While infrequently used, it was felt that the induction procedure when used in combination with the reversal test would provide a good basis for making inferences about conditioned inhibition. Since the induction procedure allowed the direct assessment of responding to both the potential inhibitory stimuli and the conditioned excitatory stimulus, it was felt to permit a more thorough examination of competing response interpretations than the summation procedure while still providing a basis for indexing inhibitory

stimulus effects. Additionally, in principle, positive results in both the positive induction test and the reversal test should be nearly as effective as combined summation and reversal outcomes in ruling out attentional hypotheses. An ancillary procedure, inhibition of delay, was also included to examine possible inhibitory factors present in long CS-US intervals.

The potential selective action of ethanol on inhibitory response control was also explored. Effects of two doses of ethanol (.8 g/kg and 1.6 g/kg of body weight) were examined on the development of inhibitory responding in the "unpaired" phase and during all test phases. A balanced cross over design was used to index direct effects of ethanol on responding in both the "unpaired" phase of day 2 and the tests of inhibition on day 3 and to allow examination of possible transfer or carry over effects of day 2 treatment on day 3 performance. Ethanol was only given to subjects in the explicitly-unpaired group since in theory it was only in this group that conditioned inhibition was expected to develop.

METHOD

Subjects

The subjects were 88 experimentally naive, female, Long-Evans hooded rats, 90-120 days of age, that ranged in weight from 250-300 g. The animals were purchased from the Department of Animal Care of the University of Oregon Health Sciences Center and housed under a 12-hr light-dark cycle with free access to food and water.

Apparatus

During the experimental sessions the rats were restrained in adjustable animal holders manufactured by Narco Bio-Systems Company. The holder consisted of a 19-cm long x 4-cm wide x 5-cm high inverted U-shaped plastic housing contoured to fit snugly around the rat's body. The housing was mounted on a plastic base that had a removable plate under the rear section that allowed intraperitoneal injections to be made while the animal was restrained. Slots at both ends of the housing permitted the insertion of guillotine-type plastic inserts that were adjusted to hold the rats securely.

To minimize unwanted extraneous auditory signals, the animals were placed in a small-animal Industrial Acoustics sound isolation chamber, equipped with a ventilating fan and a 60-W house light recessed in the ceiling. To further mask undesired auditory stimuli, white noise measuring approximately 75 dB sound pressure level (re .0002 dyne/cm^2) was presented continuously through a 23-cm speaker mounted approximately 7.5 cm from the wall facing the rat. Two 9-cm speakers, mounted in a

15-cm deep x 25-cm high x 31-cm wide plywood cabinet were used for delivery of the tone CS. The cabinet was positioned directly in front of the rat.

Skeletal-motor activity was measured using an on-line recording system that provided a punched-paper-tape output of general movement. Briefly, the system consisted of an Astatic (#24) phono-cartridge that was attached to the underside of a spring-mounted 23-cm long x 28-cm wide x .5-cm thick plastic plate supporting the rat. An 8-cm long x 1-mm diameter rod was fitted into the needle housing of the cartridge. Movement-produced displacement of this rod generated a voltage which was amplified by means of a Grass model 5-p preamplifier set at a sensitivity of .10 mv/cm. The output of the preamplifier was fed to a Massey Dickinson resistive shift trigger that converted the voltage to discrete pulses, the frequency of which was proportional to the input voltage. The pulses were collected in a transistorized counting network and the totals punched out on paper tape. The movement-detection system was periodically calibrated during the course of the experiment by repeatedly dropping 1.0-, 3.0-, and 5.0-g clay balls onto the plastic plate from a 10-cm height. The average number of pulses that each weight produced was 2, 7, and 12, respectively. At this sensitivity, the recording system was capable of detecting minute changes in skeletal-motor activity.

The electrocardiogram (EKG) was monitored on a Grass polygraph from two 20-gauge hypodermic needles inserted subcutaneously, one on each side of the rat's thoracic cavity. Heart rate was recorded by

means of an automated on-line system which provided a punched-paper-tape tabulation of the number of heart beats occurring in successive time intervals within each trial. The characteristics of this system have been described in detail by Fitzgerald, Vardaris, and Teyler (1968). In brief, the EKG was amplified by a solid-state differential amplifier and then written out on one channel of the polygraph. A lever-type Microswitch was positioned so that a switch closure was produced when the polygraph pen was deflected by the R-wave of the QRS complex. The Microswitch closure triggered a pulse shaper that supplied a pulse to a transistorized counting network consisting of AND gates, OR gates and flip-flop memory devices. At the end of each counting period, the contents of the counter were punched out on an eight-bit Tally high-speed paper-tape punch.

To provide a visual check on the reliability and accuracy of the system, the output of the pulse shaper was also used to operate a relay whose contacts switched a small voltage onto a second polygraph pen. These spikes represented the heart beats that were actually counted and could therefore be compared with the EKG polygraph records and the punched heart-beat totals. The accuracy of the counting circuit was periodically checked by substituting a 10-Hz signal for the incoming EKG signal.

The conditioned stimuli (CSs) were either 4- or 8-kHz tones, 6.3 sec in duration, generated by an audio-oscillator. The intensities of the tones measured 85 dB(sound pressure level re. .0002 dyne/cm^2). The unconditioned stimulus (US) was a .3-sec train of 100V dc, .5-ms

pulses at a frequency of 50 Hz produced by a Massey Dickinson constant wattage shocker. The US was delivered to the base of the rat's tail through two #6 round head machine screws spaced 1-cm apart and held in place by a piece of elastic rubber tubing. The area of the rat's tail under the electrode was scrubbed with a moist gauze pad and electrode paste was applied to help maintain constant electrode resistance throughout conditioning. After the electrode was put in place, a resistance measurement was taken with a voltmeter. If the resistance measured more than 20-k ohms, additional electrode paste was applied and the electrodes were repositioned. During experimental sessions, the shock level was monitored at regular intervals with an oscilloscope by measuring the voltage drop across a 100-ohm resistor in series with the shock electrode.

Two animals were conditioned concurrently through the use of separate identically-equipped chambers, with trials alternating between animals. Trials were initiated automatically by a film-tape programmer while events within a trial were programmed and timed using Massey Dickinson transistorized logic modules.

Procedure

The investigation required three days for training and testing each animal.

Day 1. The training consisted of three successive phases. During the first phase, the animals were permitted 30 min to adapt to the restrainer. Phase 2 included the random presentation of 24 CS-alone

trials (i.e., 12 each of the 4-kHz and 8-kHz tones) at intertrial intervals of 60, 90, or 120 sec (M = 90 sec). In Phase 3 each rat received 30 excitatory classical conditioning trials with either the 4 or 8KHz tone being paired with the US. A delayed conditioning procedure was used in which the .3-sec US overlapped the final .3 sec of the 6.3-sec CS. Intertrial intervals varied randomly among 120, 150, and 180 sec values (M = 150).

Day 2. There were two phases on day 2. Prior to the beginning of the first phase, each rat was given an intraperitoneal (i.p.) injection of either saline, .8 g/kg of body weight of ethanol (10% v/v), or 1.6 g/kg of body weight of ethanol (20% v/v). The doses were prepared from a base of 95% ethanol. Following the injection, the rats were allowed a 30-min adaptation period just as on Day 1. Phase 2 followed immediately and consisted of "unpaired" trials that differed on the basis of the relationship between the CS and US. There were three groups in this phase labelled explicitly-unpaired, truly random, and CS alone. In the case of all of the groups, the CS that was used during Phase 2 was different from that employed during excitatory classical conditioning on Day 1. Thus, for example, if the 4-kHz tone was used as CS+ during excitatory conditioning, then the 8-kHz stimulus was selected as the "unpaired" CS (i.e., CS-) on Day 2.

The rats in the explicitly-unpaired group during Phase 2 received 54 unpaired presentations of the CS alone and of the US alone in a semi-randomized order at intervals of 120, 150, or 180 sec (M=150). No more than three CSs

or three USs were allowed to occur consecutively. Twenty-four animals (one third) of those in this group received training in Phase 2 following an i.p. injection of saline, one third received .8 g/kg of ethanol and one third 1.6 g/kg of ethanol.

The truly-random group (n = 8) was given the same sequence of CSs as that presented to the explicitly-unpaired group, except that for this group the occurrence of shock was programmed randomly with respect to the CS. This was accomplished by dividing the session into 270 60-sec intervals and fixing the probability that the shock would occur in a given interval at 54/270 = 0.2. Thus, the probability of shock during CS and the 60-sec interval following CS onset was equal to the probability of the shock during all other 60-sec intervals (i.e., PR (US/CS = Pr (US/$\overline{CS}$) = .2). The location of the shock within a given 60-sec interval was determined by a random sequence that closely equated the truly-random group for the density of shocks received by the explicitly-unpaired group. All animals in the truly-random group received an injection of saline prior to the beginning of Phase 2.

The CS-alone group (n = 8) received the same sequence of CSs as that used in the explicitly-unpaired and truly-random protocols. However, the animals in this group received no shock. As was true of the truly-random group, all animals in the CS-alone group received an injection of saline prior to the beginning of Phase 1.

Day 3. Day 3 consisted of six consecutive phases. Prior to the beginning of Phase 1, the animals in each of the three explicitly-unpaired subgroups of Day 2 were further divided and randomly assigned

to one of three groups forming a balanced cross-over design with respect to drug treatment. Thus, for example one third of the 24 animals (n=8) in the Day 2 saline group was again given saline on Day 3, one third was switched to the .8-g/kg dose of ethanol and one third was switched to the 1.6-g/kg ethanol dose. All of the rats in the truly-random and CS-alone groups were given saline.

During the first phase of Day 3, the animals were allowed 30 min to habituate to the restrainer. Phase 2 was comprised of six additional "unpaired" trials of the same type as those given the various groups during the "unpaired" phase of Day 2. All experimental parameters were the same as those employed in the groups on the previous day. During Phase 3, all animals were given six paired excitatory conditioning trials using the same CS and parameters i.e., ISI's ITI's etc., as those employed during original excitatory conditioning on Day 1. Phase 4 was a test phase and consisted of 12 induction trials in which the CS- was presented 6 sec prior to the delivery of CS+. Both CSs were of 6 sec duration and the ITI's were 120, 150, and 180 sec (M=150). Subjects did not receive any shocks during this phase. Phase 5 was reversal conditioning in which CS- was now paired with the shock US on 24 trials. All experimental parameters were the same as those used during excitatory conditioning on Day 1. Phases 6 & 7 were a continuation of the reversal phase. In these phases the CS-US interval was lengthened from 6 sec to 10 sec and then from 10 sec to 20 sec. Subjects were given 6 trials at the 10 sec interval and 6 trials at the 20 sec interval. Other than interval length experimental variables were identical to those in the reversal phase.

Heart rate and skeletal-motor activity were measured in consecutive time intervals on each of the trials of the various phases of the study. The first interval was 6 sec in length and was located immediately prior to the onset of the CS. Heart rate and motor activity in this pre-CS interval served as a measure of baseline responding in the two systems. The remaining time intervals were 2 sec in length and they occurred during and following the presentation of the CSs. For purposes of generating measures of conditioning, mean HR and motor activity in the pre-CS interval were subtracted from HR and motor activity in each of the 2-sec CS-US intervals, forming a series of difference scores.

For convenience of reference a schematic diagram of the experimental design has been included in Appendix A.

RESULTS

Although all animals were treated the same on day 1, analyses of variance were carried out on the findings of this day using treatments that were to be introduced on day 2 as dummy variables. The same procedure was employed in analyses of day 2 data with prospective day 3 treatments included as dummy variables. Frequency of the CSs was also included as a factor in all preliminary analyses of variance. This procedure was followed to check on the presence of chance differences among groups prior to the use of differential treatments. The results of preliminary analyses were not reported unless differences among prospective groups were found. Since reliable differences were routinely not found, nearly all reported analyses were performed on data collapsed across dummy factors and auditory frequency of the CSs.

Day 1

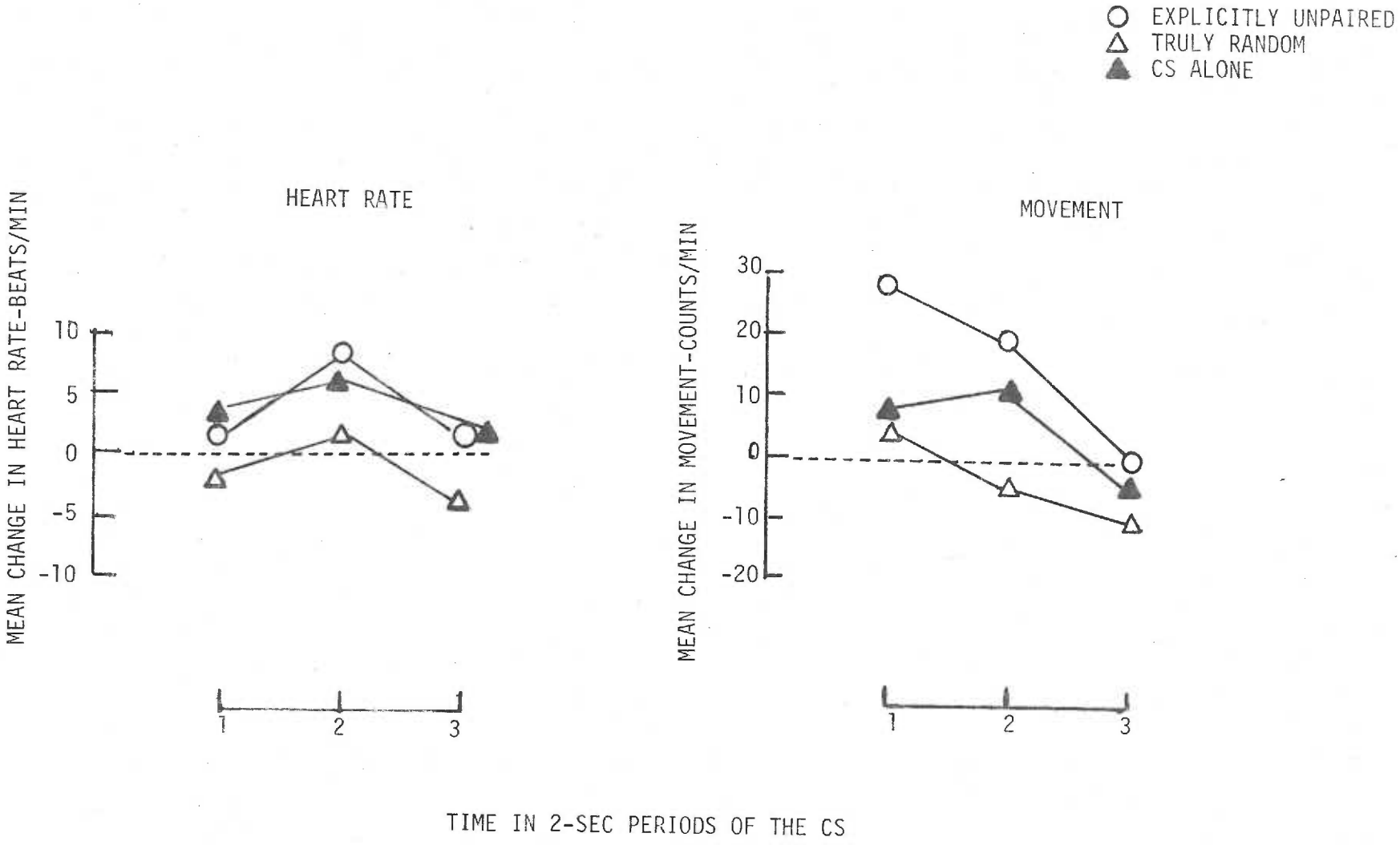
It should be recalled that day 1 consisted of three basic phases. These phases, which were identical for all animals, were adaptation, pretest CS-alone presentations of the two CSs, and excitatory conditioning. It will also be noted that all data from the phases of day 1 were plotted on the basis of the three principal prospective groups, namely the explicitly-unpaired, truly-random, and CS-alone.

HR and movement responses on pretest CS-alone trials

In Figure 1, the HR and movement responses of the explicitly-unpaired, truly-random and CS-alone groups averaged over the 24 pretest CS-alone trials are plotted as a function of 2-sec periods of the CS. Inspection of the left side of the figure reveals that the HR responses of all three groups were relatively small in magnitude. For the explicitly-unpaired and CS-alone groups there was a tendency for the direction of the

Figure 1. Mean heart-rate and movement responses of the explicitly-unpaired, truly-random, and CS-alone groups averaged over the 24 pretest CS-alone trials and plotted as a function of 2-sec periods of the CS.

FIGURE 1


EXPLICITLY UNPAIRED
TRULY RANDOM
CS ALONE
HEART RATE
MEAN CHANGE IN HEART RATE-BEATS/MIN
10
5
0
-5
-10
1
2
3
MOVEMENT
MEAN CHANGE IN MOVEMENT-COUNTS/MIN
30
20
10
0
-10
-20
1
2
3
TIME IN 2-SEC PERIODS OF THE CS

responses to be accelerative, whereas for the truly-random group the overall direction was slightly decelerative. A 2 by 2 by 3 (CS frequency by trial blocks by counting periods) analysis of variance was conducted on the data of each group. For the explicitly-unpaired group the mean HR response to the 8 kHz stimulus (+3.74 bpm) was reliably larger than the response to the 4 kHz stimulus (-.29 bpm), F (1,71)= 16.74, $p<.001$. In addition, the HR change across counting periods was significant, F (2,142)= 9.33, $p<.01$, as was the CS frequency by counting periods interaction, F (2,142)= 3.34, $p<.05$. This interaction was due to the fact that the HR responses of the explicitly-unpaired group were larger to the onset of the 8-kHz stimulus than to the 4-kHz stimulus. The same analysis performed on the data of the truly-random and CS-alone groups provided no significant outcomes.

The right side of Figure 1 indicates that all groups showed an increase in movement to the onset of the CS. Movement then decreased either back to baseline in the case of the explicitly-unpaired and CS-alone groups or slightly below baseline in the case of the truly-random group. The results of a 2 by 2 by 3 (CS frequency by trial blocks by counting periods) analysis of variance on the explicitly-unpaired group provided a significant effect of counting periods, F (2,142)= 32.07, $p<.001$, and a significant frequency by counting periods interaction, F (2,142)= 4.31, $p<.01$. This interaction was due to the fact that the 8-kHz CS tended to produce more movement than the 4-kHz CS during the first counting period. Movement during the last two counting periods was similar to the two CSs. Separate analyses of variance performed on the data of the truly-random and CS-alone groups provided no significant outcomes.

HR and Movement Responses on Excitatory Conditioning Trials

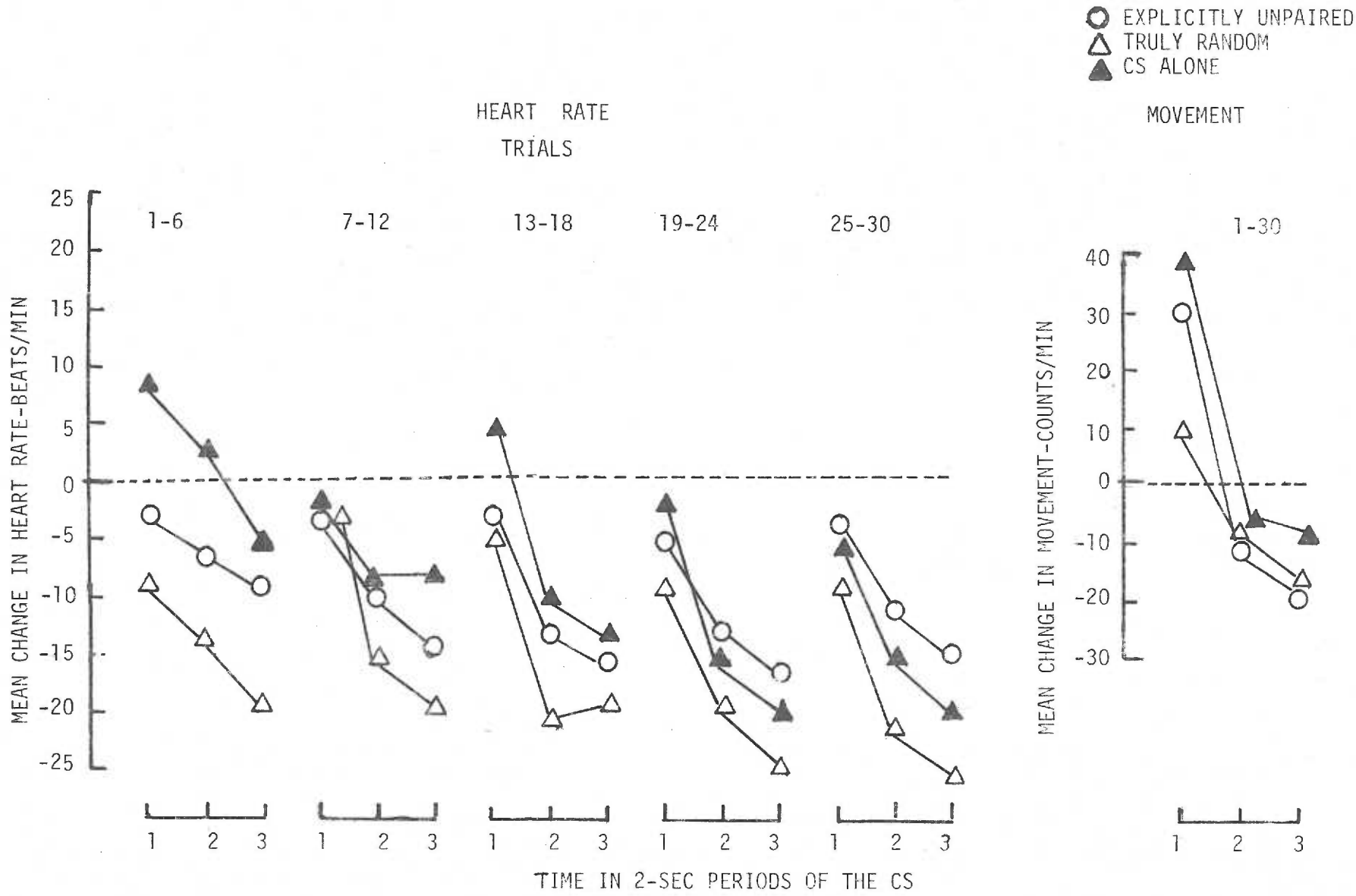
The left side of Figure 2 illustrates the mean CS-minus pre-CS HR responses of the three groups in successive 2-sec counting periods of CS+ averaged over blocks of six conditioning trials. On the far right of the figure is shown a composite of the movement activity displayed by the three groups averaged over the 30 excitatory conditioning trials. From an inspection of this figure, it is clear that the direction of the HR CR of the three groups to CS+ was basically decelerative. The topographies of the CRs were such that the groups showed maximum cardiodecelerations in the third period of CS+ or just prior to the onset of the US. In general, the overall magnitudes of the HR decelerations increased as a function of trials. A 3 by 2 by 5 by 3 (day 2 dose by CS frequency by trial blocks by counting periods) analysis of variance performed on the data of the explicitly-unpaired group provided a significant trials effect, F (4,264)= 4.24, $p<.01$; a significant counting periods effect, $F(2,132)= 68.28$, $p<.001$; and a significant trials by counting periods interaction, $F(8,528)= 3.35$, $p<.01$. A similar analysis on the CS-alone group resulted in a significant trials effect, $F(4,24)=3.85$, $p<.05$ and a significant counting periods effect, F (2,12)= 8.25 $p<.01$. For the truly-random group a reliable effect of counting periods was obtained, F (2,12)= 18.50, $p<.01$. Separate t tests comparing the mean HR CRs of the three groups failed to reach significance.

Inspection of the far right of Figure 2 reveals that all groups showed similar patterns of movement activity to CS+ during excitatory conditioning. These reactions were characterized by increases in movement

Figure 2 Left side. Mean CS minus pre-CS heart-rate responses of the explicitly-unpaired, truly-random, and CS-alone groups in successive 2-second periods of CS+ averaged over blocks of six excitatory conditioning trials

Right side. Mean CS minus pre-CS movement activity of the explicitly-unpaired, truly-random, and CS-alone groups in successive 2-second periods of CS+ averaged across all 30 conditioning trials.

FIGURE 2


EXPLICITLY UNPAIRED
TRULY RANDOM
CS ALONE
HEART RATE
TRIALS
MOVEMENT
1-6
7-12
13-18
19-24
25-30
1-30
MEAN CHANGE IN HEART RATE-BEATS/MIN
MEAN CHANGE IN MOVEMENT-COUNTS/MIN
25
20
15
10
5
0
-5
-10
-15
-20
-25
40
30
20
10
0
-10
-20
-30
1 2 3
TIME IN 2-SEC PERIODS OF THE CS

during the first counting period of the CS followed by below baseline decreases in movement during the second and third periods of the CS. A 3 by 2 by 3 (day 2 dose by CS frequency by counting periods) analysis of variance carried out on the data of the explicitly-unpaired group established that the change in movement across counting periods was reliable, F (2, 132)= 65.83, $p<.001$. None of the other factors was significant. Similar analyses performed on the movement data of the truly-random and CS-alone groups failed to provide any significant main effects or interactions. There were no reliable differences among the groups in terms of movement activity.

Although not shown in a figure, the HR URs of the three groups to the shock US were highly similar. In each case, the URs consisted of cardio-accelerations of approximately 40 beats per minute (bpm) above baseline during the first 4 sec after shock termination. During the next 4 sec, the HR levels decreased slightly to about 30 bpm above pre-CS levels. Movement also showed a marked increase during and shortly after shock, reaching a maximum of 350 counts-per-minute above pre-CS levels. During the second 4-sec measurement period after shock, movement decreased to about 50 counts-per-minute over baseline.

Separate t tests established that there were no group differences either in terms of HR or movement to the shock US.

Baseline HR and Movement during the three phases of Day 1

Figure 3 depicts at the top and at the bottom, respectively, mean baseline HR and movement of the explicitly-unpaired, truly-random, and CS-alone groups during the three phases of day 1. The top left-hand side

of the figure illustrates that all of the groups showed a decrease in baseline HR during the 30-min adaptation period. Although differences in the absolute HRs of the groups are visible, these were not reliable according to appropriate t tests. Moreover, in only the explicitly-unpaired group was the decrease in baseline HR reliable, F (2, 138) = 8.78, $p < .001$.

The top center of Figure 3 shows that the HR levels of all groups increased slightly across the pretest CS-alone session. Furthermore, the between-group differences evident during adaptation were also present during pretest. Separate 2 by 4 (CS frequency by trial blocks) analyses of variance revealed a significant effect of trials in the explicitly-unpaired group, F (3, 207) = 9.8 $p < .001$, and in the truly-random group, F (3, 18) = 5.12, $p < .01$. Individual t tests established that the overall difference between the explicity-unpaired and truly-random groups was significant, t (78) = 2.92, $p < .005$.

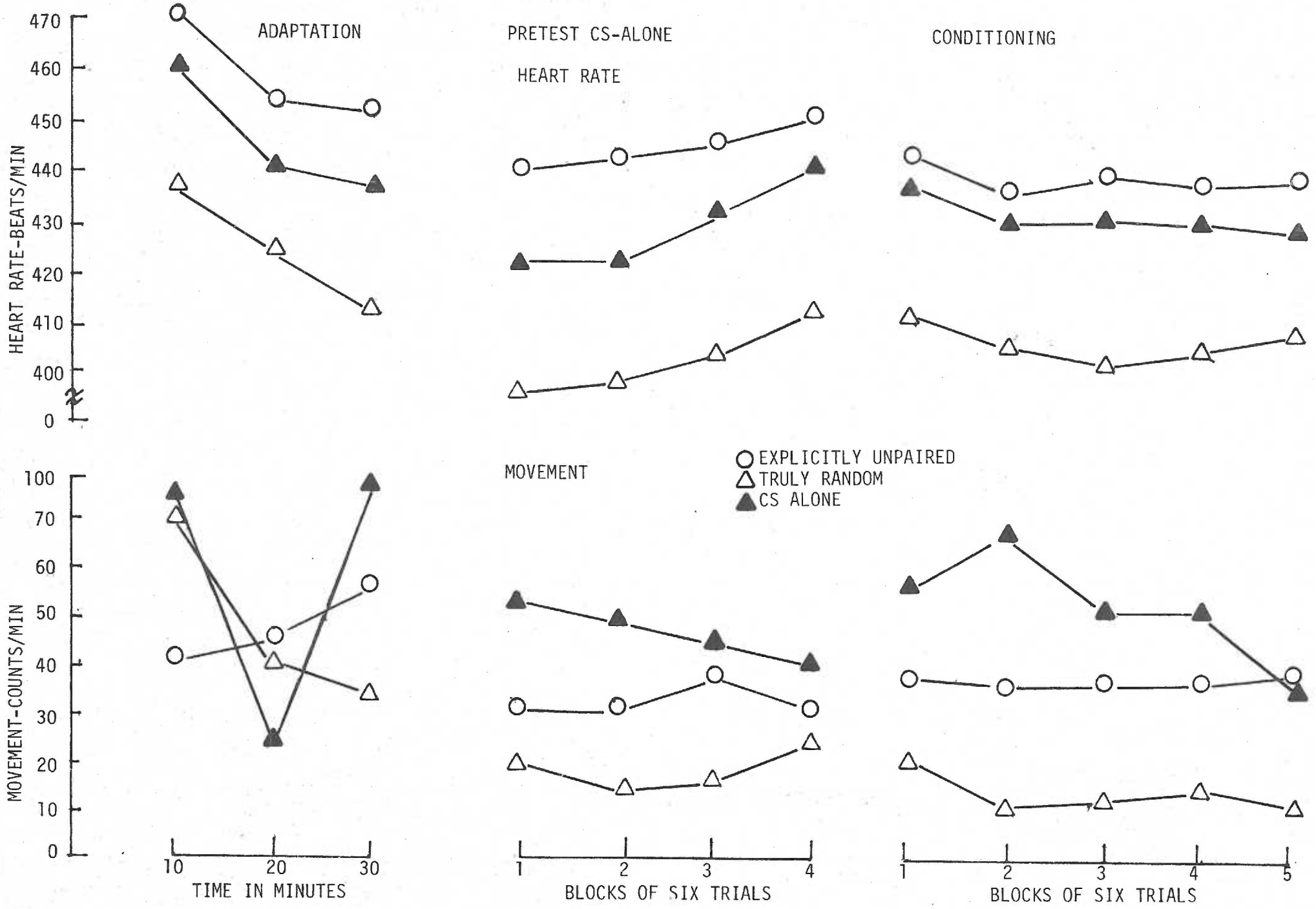
The top right side of Figure 3 reveals that there was little systematic change in the baseline HRs of the groups during the excitatory conditioning phase of the study. As in the prior phases, however, there did appear to be differences among the groups in terms of the overall levels of HR. Separate 2 by 5 (CS frequency by trial blocks) analyses of variance revealed no significant effects for any of the groups. Results of t tests indicated that the explicitly-unpaired and truly-random groups were significantly different, t (78) = 3.04, $p < .005$.

The bottom half of Figure 3 reveals that with the exception of the 30-min adaptation period, baseline movement activity in the various groups was reasonably constant across each of the phases of day 1.

Figure 3. Top. Mean baseline heart rate in beats-per-minute of the explicitly-unpaired, truly-random, and CS-alone groups in the adaptation, pretest and excitatory conditioning phases of Day 1.

Bottom. Mean baseline movement activity in counts-per-minute of the explicitly-unpaired, truly-random, and CS-alone groups during the adaptation, pretest, and excitatory conditioning phases of Day 1.

FIGURE 3


ADAPTATION
PRETEST CS-ALONE
CONDITIONING
HEART RATE
HEART RATE-BEATS/MIN
470
460
450
440
430
420
410
400
0
MOVEMENT
EXPLICITLY UNPAIRED
TRULY RANDOM
CS ALONE
MOVEMENT-COUNTS/MIN
100
70
60
50
40
30
20
10
0
10
20
30
TIME IN MINUTES
1
2
3
4
BLOCKS OF SIX TRIALS
1
2
3
4
5
BLOCKS OF SIX TRIALS

Analyses of variance comparable to those reported above for HR established that there were no significant effects for any of the groups. Moreover, t tests failed to show that any of the differences among the groups was reliable.

DAY 2

Day 2 included a 30-min period of adaptation followed by the 54 trials of the "unpaired" phase. It will be recalled that the CS on these trials (i.e., CS-) was different from the CS (i.e., CS+) used during excitatory conditioning on day 1. It should also be remembered that there were three main treatment groups during the "unpaired" phase: explicitly-unpaired (n=72), truly-random (n=8), and CS-alone (n=8). Furthermore, recall that there were actually three explicitly-unpaired subgroups with one of the groups receiving saline (n=24), the second .8 g of ethanol per kg of body weight (n=24), and the third 1.6 g of ethanol per kg of body weight (n=24). The truly-random and CS-alone groups were both given an equivalent amount by volume of saline.

HR and Movement Responses to the CS during the "unpaired" phase

Figure 4 presents the HR and movement responses of all groups to CS- during the "unpaired" phase averaged over successive blocks of six trials each. There were eight occasions in the truly-random schedule on which the US occurred within 1-min prior to the delivery of CS-. Since it is possible that on these trials the HR reactions to the CS may have been directly affected by the preceding US, the results of the truly-random group were tested with and without these trials included. These

tests showed that the presence of the eight trials did not significantly change the results for this group. Therefore, the data from these trials were included in the analyses carried out on the data from the truly-random group.

The left side of Figure 4 reveals that the directions of the HR reactions of all groups to CS- on the first block of "unpaired" trials were decelerative. Over the course of subsequent trials, the directions of the HR responses of each of the three explicitly-unpaired groups changed from cardiodeceleration to cardioacceleration. Although the magnitudes of the accelerations of the three explicitly-unpaired groups were similar by the end of the "unpaired" phase, the saline group appeared to require fewer trials for the HR response to change direction than did the two ethanol groups. In the case of the truly-random group, the original decelerative response gradually diminished in magnitude to a near-zero level with but a single sizeable accelerative change occurring on the next to last trial block. The CS-alone group, on the other hand, showed a consistent cardiodeceleration to CS- throughout the "unpaired" phase, with the magnitude of the reaction decreasing only slightly.

A 3 by 2 by 9 (day 2 dose by CS frequency by trial blocks) analysis of variance performed on the data of the three explicitly-unpaired groups provided a significant trial blocks effect, F (8,528)=33.05, $p<.001$, and a significant day 2 dose by trial blocks interaction, F (16,428)=2.56, $p<.01$, establishing that overall heart rate changed reliably as a function of trials and that the changes in the different groups were not parallel. The overall mean magnitude of the heart-rate responses displayed by the explicitly-unpaired groups were not significantly different from each other.

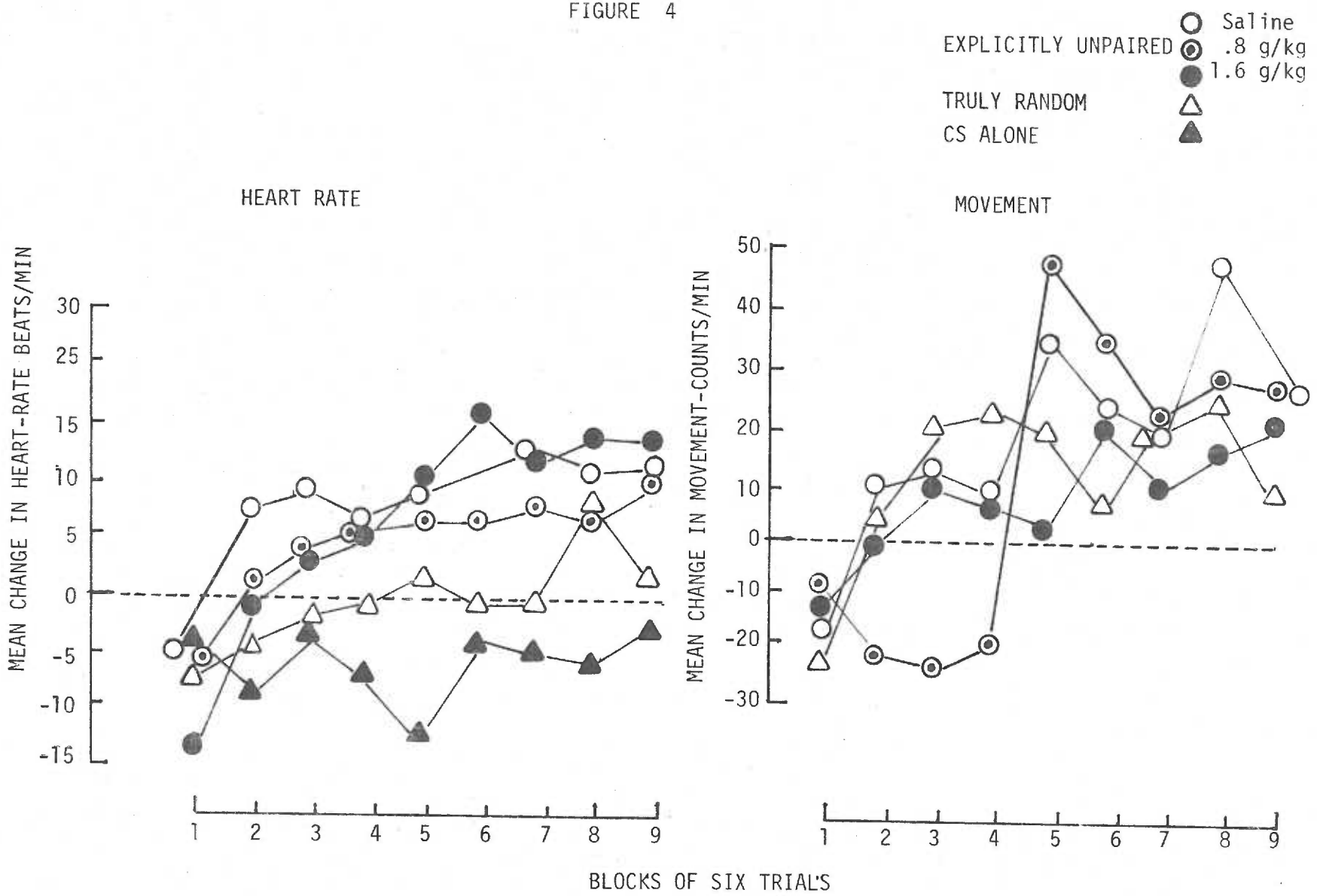
A 2 by 2 by 9 (groups by CS frequency by trial blocks) analysis of variance comparing the HR reactions of the truly-random and CS-alone groups shown in Figure 4 provided a significant effect of CS frequency, F (1, 12 = 9.36, $p < .01$, and a significant groups by CS frequency interaction, F (8, 96)= 2.32, $p < .05$. These two outcomes were due to the fact that in both groups the 4-kHz tone produced larger HR decelerations than did the 8-kHz tone with this tendency being more pronounced in the CS-alone group than in the truly-random group. In fact, the overall mean HR change of the four rats in the truly-random group to the 8-kHz tone was a small acceleration. Separate t tests established that the mean HR response of the combined explicitly-unpaired groups was significantly different from that of both the truly-random and CS-alone groups ($p < .05$, in each case).

On the right side of Figure 4 are plotted the movement responses of the explicitly-unpaired and truly-random groups during the "unpaired" phase averaged over blocks of six trials each. Due to an error in programming the electronics controlling the movement detector system, the movement reactions of ten animals in the explicitly-unpaired groups and of four animals in the CS-alone group were not recorded. Since this left only four animals in the CS-alone group, the results of this group were not included in Figure 4. To equate the explicitly-unpaired groups, twenty animals were randomly eliminated, leaving fourteen animals in each of these groups. Inspection of Figure 4 indicates that the explicitly-unpaired and truly-random groups showed progressive increases in movement to CS during the course of the "unpaired" phase. In all cases, the amount of change in motor activity increased from near zero levels at the beginning of this phase to approximately 20 to 40 counts-per-minute by the end of the phase.

Figure 4. Left side. Mean heart-rate responses of the explicitly-unpaired (saline, .8 g/kg, and 1.6 g/kg groups), and the truly-random and CS-alone groups to CS- during the unpaired phase averaged over successive blocks of six trials.

Right side. Mean movement activity of all of the above groups to CS- during the unpaired phase averaged over successive blocks of six trials.

FIGURE 4

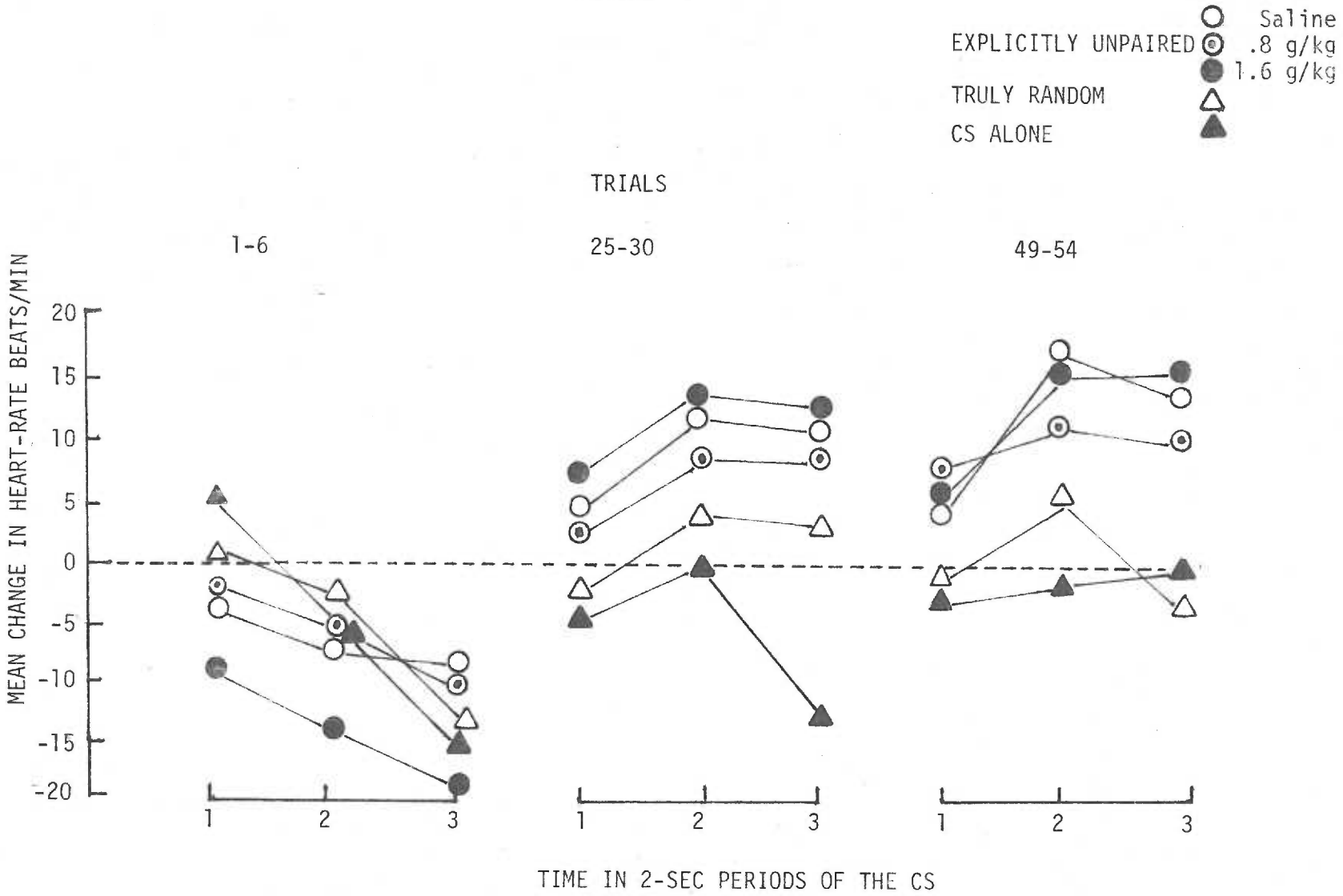

Saline
EXPLICITLY UNPAIRED .8 g/kg
1.6 g/kg
TRULY RANDOM
CS ALONE
HEART RATE
MOVEMENT
MEAN CHANGE IN HEART-RATE BEATS/MIN
MEAN CHANGE IN MOVEMENT-COUNTS/MIN
30
25
15
10
5
0
-5
-10
-15
50
40
30
20
10
0
-10
-20
-30
1 2 3 4 5 6 7 8 9
BLOCKS OF SIX TRIALS

There was no indication that ethanol either facilitated or suppressed movement activity in the two explicitly-unpaired groups. A 3 by 2 by 9 (day 2 dose by CS frequency by trial blocks) analysis of variance carried out on the data of the explicitly-unpaired groups disclosed only an effect of trial blocks, F (8, 12) = 7.50, $p < .001$. A separate analysis carried out on the data of the truly-random group provided no significant effects. In subsequent t tests comparing the movement activity of each of the explicitly-unpaired groups with that of the truly-random group none of the differences were significant.

Figure 5 provides an illustration of the detailed characteristics of the HR reactions of the groups to CS- during the "unpaired" phase of the study. In this figure are displayed the mean HR responses of each group in 2-sec periods of CS- averaged over the first six trials (1-6), the middle six trials (25-30), and the final six trials (49-54) of the "unpaired" phase. An inspection of this figure reveals that the forms or topographies of the responses of the groups on the initial block of trials were very similar to those that were established to CS+ during excitatory conditioning on day 1. For all groups, the cardiodecelerations were larger toward the end of the CS than at the beginning of the CS. As the directions of the HR responses of the explicitly-unpaired groups changed from cardiodecelerations to cardioaccelerations, the largest HR reactions still occurred toward the end of the CS, except that now the directions of the reactions were accelerative rather than decelerative. Figure 5 provides no evidence that the forms of the responses of the explicitly-unpaired groups were influenced by ethanol. In contrast to the explicitly-unpaired groups, the CS-alone group generally showed HR deceleration in each 2-sec period of the CS,

Figure 5. Mean heart-rate responses of the three explicitly-unpaired groups (saline, .8 g/kg, and 1.6 g/kg) and the truly-random and CS-alone groups averaged over the first six trials (1-6), the middle six trials (25-30), and the final six trials (49-54) of the unpaired phase.

FIGURE 5

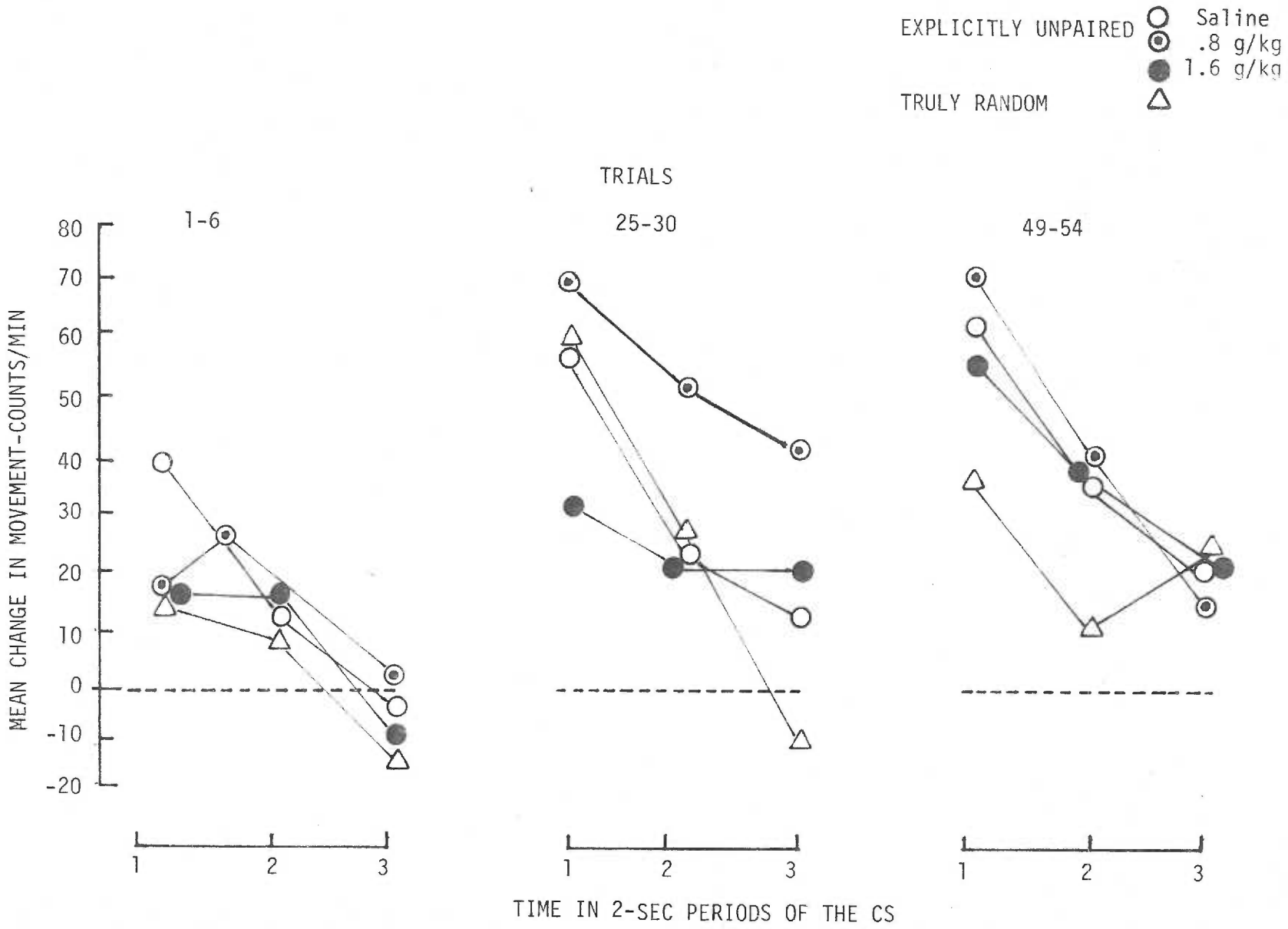

Saline
EXPLICITLY UNPAIRED .8 g/kg
1.6 g/kg
TRULY RANDOM
CS ALONE
TRIALS
1-6
25-30
49-54
MEAN CHANGE IN HEART-RATE BEATS/MIN
20
15
10
5
0
-5
-10
-15
-20
1
2
3
TIME IN 2-SEC PERIODS OF THE CS

whereas the truly-random group showed both decelerative and accelerative HR changes. A 3 x 2 x 3 x 3 (day 2 dose by CS frequency by counting periods by trial blocks) analysis of variance performed on the data of the explicitly-unpaired groups in the three blocks of trials established that the following factors were significant: Trial blocks, F (2,132)=80.95, $p<.001$, counting periods, F (2,132)=4.96, $p<.01$, and the trial blocks by counting periods interaction, F (4,264)=18.81, $p<.001$. Basically, these outcomes support a reliable effect of trials on the topographies of the responses of the groups. A similar analysis conducted on the truly-random and CS-alone groups provided a reliable counting periods effect, F (2,24)= 8.46, $p<.001$, and a reliable trial blocks by counting periods interaction, F (4,48)=4.90, $p<.001$, reflecting the loss of the original responses that were present at the beginning of the "unpaired" phase. Separate t tests showed that the explicitly-unpaired groups were significantly different from the truly-random and CS-alone group on the middle and final block of trials ($p<.05$, df=30 in each case).

Figure 6 displays the movement responses of the explicitly-unpaired and truly-random groups in the three 2-sec periods of the CS- averaged over the same trial blocks as those used for HR. An inspection of the left side of this figure indicates that during the initial block of trials, the movement responses of the groups were highly similar in form. With the onset of the CS, there was a burst of movement in the first and second counting periods followed by a return of movement to near or slightly below baselevel in the third-counting period. During the middle and final block of trials, the movement-increase reactions of the explicitly-unpaired groups grew larger in the first- and second-counting periods, with increased movement also being evident in the third-counting period. While

Figure 6. Mean movement activity of the explicitly-unpaired groups (saline, .8 g/kg, and 1.6 g/kg) and the truly-random and CS-alone groups in successive 2-second periods of the CS- averaged over the first six trials (1-6) the middle six trials (25-30) and the last six trials (49-54) of the unpaired phase.

FIGURE 6


EXPLICITLY UNPAIRED
Saline
.8 g/kg
1.6 g/kg
TRULY RANDOM
TRIALS
1-6
25-30
49-54
MEAN CHANGE IN MOVEMENT-COUNTS/MIN
80
70
60
50
40
30
20
10
0
-10
-20
1
2
3
TIME IN 2-SEC PERIODS OF THE CS

the truly-random group also exhibited an overall increase in movement in each of the three counting periods from the beginning to the end of the "unpaired" phase, the form of the reaction was more variable than that of the explicitly-unpaired groups. A four-way analysis of variance (day 2 dose by CS frequency by trials blocks by counting periods) carried out on the data of the explicitly-unpaired groups provided a significant effect of trial blocks, F (2, 78) = 12.40, $p < .01$, and a significant effect of counting periods, F (2, 78) = 14.44, $p < .01$, establishing that the increase in movement over trials was reliable, and that the pattern of movement within the trials was reliable. Statistical appraisal of the movement data of the truly-random group failed to provide any reliable effects. Individual t tests established that the mean movement responses of the explicitly-unpaired groups were not reliably different from that of the truly-random group.

Comparison of Figures 5 and 6 reveals that the accelerative HR responses of the explicitly-unpaired groups to CS were associated with increases in skeletal-motor activity. However, HR and movement did not appear to be linked firmly to each other. Thus, maximum HR accelerations occurred toward the end of the CS, whereas maximum movement occurred toward the beginning of the CS.

Baselevel HR and Movement During the Adaptation and "Unpaired" Phases of Day 2

The mean baselevel HRs of the various groups during the 30-min adaptation period following the i.p. injection of either ethanol or saline and during the subsequent "unpaired" phase of day 2 are plotted in Figure 7. Focusing first on the left side of the figure, it is clear that during the adaptation period the HR levels of the explicitly-unpaired groups receiving either the .8 g or 1.6 g dose of ethanol were elevated above those of the three groups receiving saline. An analysis of variance carried out on just the data of the three explicitly-unpaired groups provided a significant ethanol dose effect,

F (2, 169) = 14.69 $p < .001$, with both ethanol groups being significantly different from the saline group ($p < .05$, in each case) according to a Newman-Keuls test. An analysis of variance comparing the truly-random and CS-alone groups produced no significant outcomes. Individual t tests showed that both of the explicitly-unpaired ethanol groups were significantly different from the truly-random group but not from the CS-alone group.

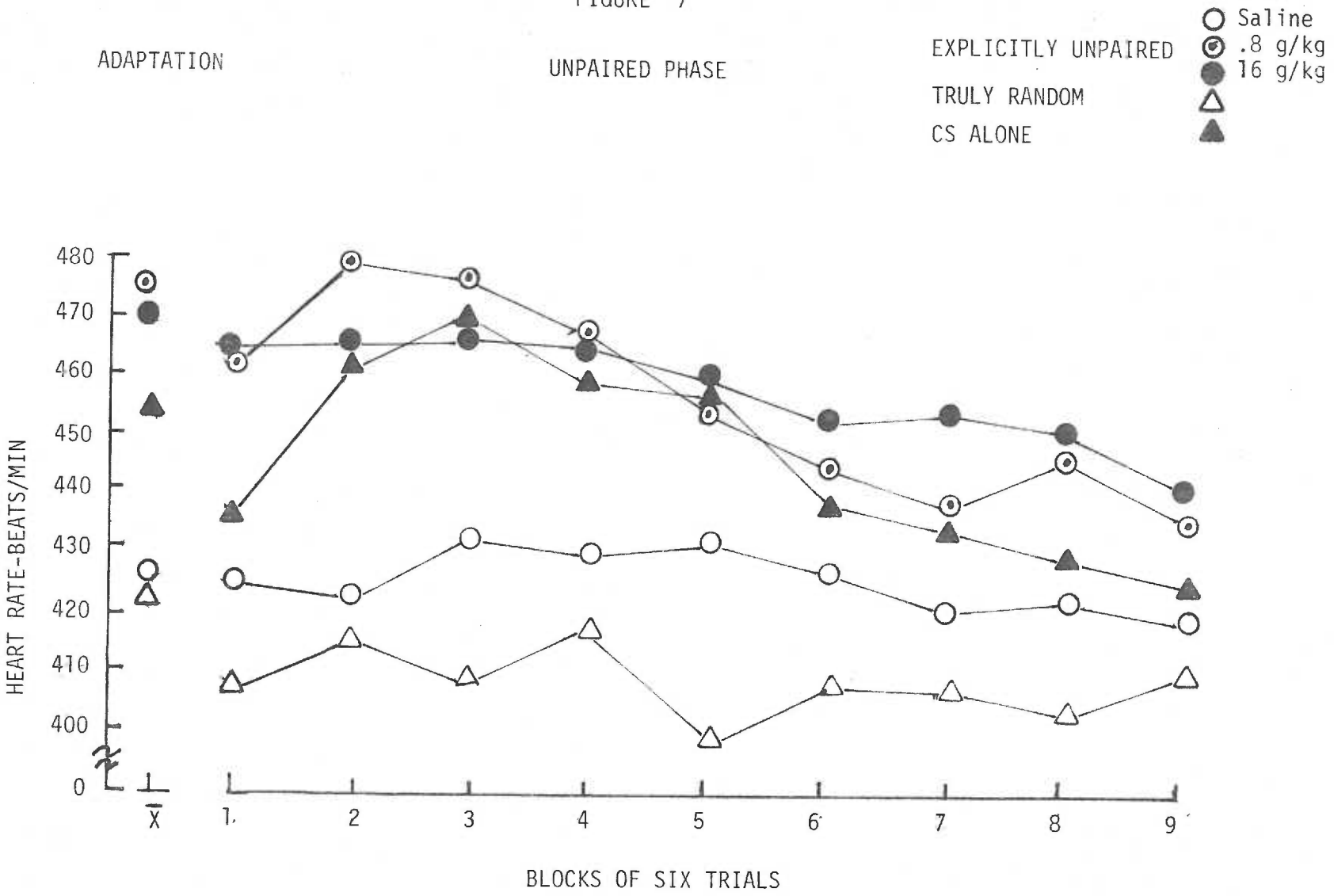
The right hand side of Figure 7 depicts the mean pre-CS HR of all groups during the "unpaired" phase averaged over successive blocks of six trials. Each block represents a temporal span of approximately 30 min. Visual inspection of these data shows that baselevel HR in the two explicitly-unpaired-ethanol and CS-alone groups was elevated above that of the explicitly-unpaired-saline and truly-random groups throughout the "unpaired" phase. A 3 by 2 by 9 (day 2 dose by CS frequency by trial blocks) analysis of variance on the data of the explicity-unpaired groups provided a significant day 2 dose effect, F (2, 66) = 8.25, $p < .001$; a significant trial blocks effect, F (8, 528) = 16.33 $p < .001$, and a significant day 2 dose by trial blocks interaction, F (16, 528) = 2.6, $p < .01$. A Newman-Keuls test established that the HR level of each of the two ethanol groups was significantly higher than that of the saline group ($p < .05$). The HR levels of the two ethanol groups were not significantly different from each other.

A comparable analysis of variance performed on the data of the truly-random and CS-alone groups provided a significant groups effect, F (1, 12) = 6.71, $p < .05$; a significant trial blocks effect, F (8, 96) = 5.21, $p < .001$; and a significant groups by trial blocks interaction, F (8, 96) = 3.33, $p < .005$. The groups by trial blocks interaction reflected the sharp initial increase and later decrease in the HR baselevel of the CS-alone group contrasted with the relative stability of the HR of the truly-random group.

Figure 7. Far left side. Mean baseline heart rate in beats-per-minute of the explicitly-unpaired groups and the truly-random and CS-alone groups during 6-second sampling periods averaged over the 30-minute post-injection adaptation period of Day 2.

Right side. Mean baseline heart rate in beats-per-minute of the explicitly-unpaired and truly-random and CS-alone groups during the 6-second pre-CS period averaged over successive blocks of six trials during the unpaired phase of Day 2.

FIGURE 7


ADAPTATION
UNPAIRED PHASE
EXPLICITLY UNPAIRED
TRULY RANDOM
CS ALONE
Saline
.8 g/kg
1.6 g/kg
HEART RATE-BEATS/MIN
480
470
460
450
440
430
420
410
400
0
X
1
2
3
4
5
6
7
8
9
BLOCKS OF SIX TRIALS

Finally, t tests were performed comparing the mean HR scores of the three explicitly-unpaired groups with those of the CS-alone and truly-random groups. Reliable differences existed between the explicitly-unpaired .8-g/kg. group and the truly-random group, t (30 = 4.21, $p < .005$, and between the explicitly-unpaired 1.6-g/kg group and the truly-random group, t (30) = 4.24, $p < .005$.

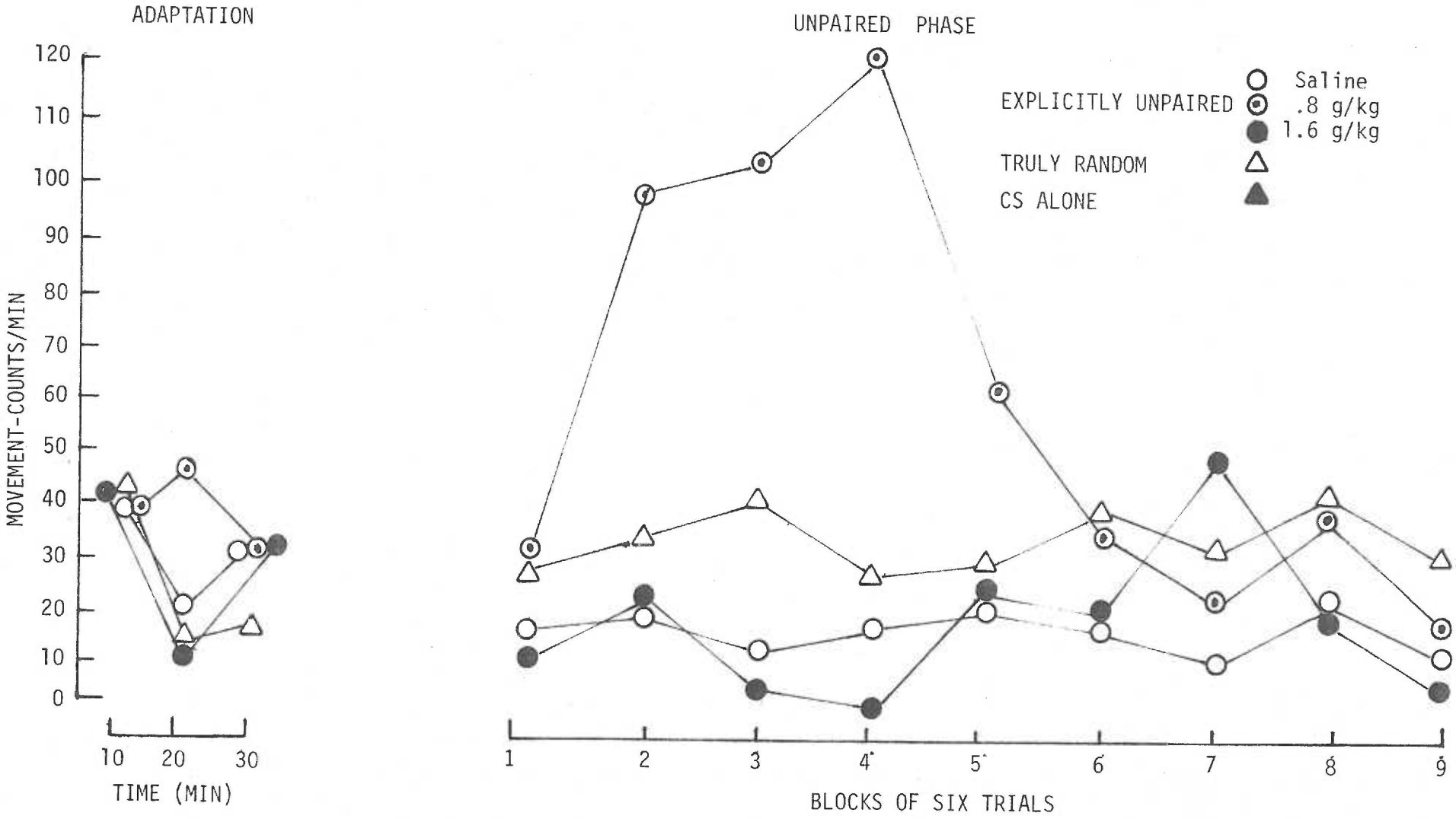
Figure 8 displays the mean baselevel movement of the explicitly-unpaired and truly-random groups during the adaptation and "unpaired" phases of day 2. The left side of the figure shows that the amount of background motor activity during the 30-min period following the injection of the alcohol or saline was generally similar in the various groups. Separate analyses of variance carried out on the results of the explicitly-unpaired and truly-random groups failed to provide any significant outcomes.

On the right side of Figure 8 is plotted the mean movement activity of the groups during the pre-CS period of the "unpaired" phase, averaged over blocks of six trials each. An examination of this part of the figure reveals that with the exception of the .8-g/kg ethanol group, the movement activity of all groups was similar and showed no systematic change across trials. The .8-g/kg group, however, demonstrated a marked increase in movement during the second trial block. This increase occurred approximately one hour after the ethanol injection. Movement activity continued to increase in this group on the third and fourth trial blocks and then returned rapidly to a level that matched the other groups. A 3 by 2 by 9 (day 2 dose by CS frequency by trial blocks) analysis of variance comparing the movement of the explicitly-unpaired groups provided a reliable day 2 dose effect, F (2, 36) = 4.4, $p < .05$, and a significant day 2 dose by trial blocks interaction, F (16, 288) = 2.54, $p < .01$. The day 2 dose by trials interaction was due mainly to the marked

Figure 8. Far left side. Mean baselevel movement activity of the explicitly-unpaired (saline, .8 g/kg, and 1.6 g/kg groups) and the truly-random group during 6-second sampling periods of the 30-minute post-injection period of Day 2.

Right side. Mean baselevel movement activity of the explicitly-unpaired and truly-random groups during the 6-second pre-CS period and averaged over successive blocks of six trials during the unpaired phase.

FIGURE 8


ADAPTATION
UNPAIRED PHASE
EXPLICITLY UNPAIRED
Saline
.8 g/kg
1.6 g/kg
TRULY RANDOM
CS ALONE
MOVEMENT-COUNTS/MIN
120
110
100
90
80
70
60
50
40
30
20
10
0
10
20
30
TIME (MIN)
1
2
3
4
5
6
7
8
9
BLOCKS OF SIX TRIALS

changes across trials in the mean response levels of the .8-g/kg group in contrast to the relatively invariant responses of the 1.6-g/kg and saline groups. Separate 2 by 9 (CS frequency by trial blocks) analyses performed on the data of the truly-random group did not produce any significant main effects or interactions. Subsequent t tests failed to establish the existence of significant differences between the explicitly-unpaired groups and the truly-random group.

Day 3

It will be recalled that day 3 consisted of six consecutive treatment phases. These included (1) 30 min. of adaptation to the restrainer, (2) six "unpaired" trials with CS-, (3) six paired excitatory conditioning trials with CS+, (4) 12 induction trials, (5) 24 reversal conditioning trials, and (6) 12 paired excitatory conditioning trials with extended CS-US intervals. The explicitly-unpaired groups of day 2 namely the saline group ($n = 24$), the .8 g/kg of ethanol group ($n = 24$), and the 1.6 g/kg of ethanol group ($n = 24$) were divided into three sub-groups of equal size ($n = 8$) on day 3. The rats within one of the subgroups received the same drug treatment that they had been given on day 2, while the animals within the other two subgroups were switched to one of the remaining drug conditions. This transfer or cross-over feature of the study made it possible to assess potential main effects and interactions of day 2 and day 3 drug treatments on the performance of the explicitly-unpaired animals during the various phases of day 3. Initially, all analyses on the data from day 3 were carried out with the drug treatment in effect on day 2 as a factor. If significant effects involving day 2 drug treatment were not obtained, the data were in some cases collapsed across the day 2 treatment factor.

HR and Movement During the "Unpaired" and Paired Phases of Day 3

The mean HR responses of all groups in the three counting periods of CS- and CS+ averaged over the six trials of the "unpaired" phase and over the six trials of the paired excitatory phase are presented in the top and bottom of Figure 9, respectively. The designations at the top of the panels for the explicitly-unpaired groups indicate the drug treatment in effect on

day 2. The drug treatments in effect on day 3 for the three functions within each panel are shown in the legend. The same general format was used on succeeding figures to designate the drug conditions employed on day 2 and day 3.

Inspection of the panels across the top of Figure 9 shows that the directions of the responses of the explicitly-unpaired groups to CS- on the "unpaired" trials were typically accelerative just as on day 2. Also in keeping with day 2, the magnitudes of the cardioaccelerations tended to be greater in the second and third periods of the CS than in the first period of the CS. Within the day 2, 1.6-g/kg condition, the group that was switched to saline on day 3 showed larger HR accelerations than did the two groups that were maintained on ethanol. This tendency was less evident on the day 2, .8-g/kg condition. A 3 x 3 x 2 x 3 (day 2 dose by day 3 dose by CS frequency by counting periods) analysis of variance carried out on the data of the explicitly-unpaired groups provided only a reliable effect of counting periods, F (2, 54) = 23.83, $p < .001$, indicating that the change in HR over successive portions of CS- was relaible. Significant effects of the day 2 and day 3 drug treatments on the accelerative HR responses to the CS- were not obtained. Focusing next on the top far-right panel in the figure, it is obvious that the truly-random and CS-alone groups displayed similar, small magnitude responses not unlike their responses to CS- on day 2. A 2 x 2 x 3 (truly-random vs CS alone by CS frequency by counting periods) analysis of variance provided a significant CS frequency effect, F (1, 12) = 5.91, $p < .05$, and a significant counting periods effect, F (2, 24) = 3.42, $p < .05$. The CS frequencey effect was due to the fact that the 4-kHz CS- tended to

produce either small cardiodecelerations, or small cardioaccelerations whereas the 8-kHz CS- tended to produce either small cardiodecelerations or relatively large cardioaccelerations.

Although not presented in a figure, the movement responses of the explicitly-unpaired, CS-alone and truly-random groups to CS- on the six "unpaired" trials were similar to those shown to CS- on day 2 and plotted in Figure 6. For each group, there was a burst of activity during the first 2-sec counting periods of the CS, followed by progressively less activity during the second and third counting periods. Analysis of variance on the movement responses of the explicitly-unpaired groups provided a significant effect of counting periods, F (2, 126) = 14.18, $p < .01$. A separate analysis carried out on the data of the truly-random and CS-alone groups provided a significant effect of counting periods, F (2, 24) = 7.21 $p < .05$ and a significant groups by counting periods interaction F (2, 24) = 4.62. $p < .05$. The interaction was the result of more movement occurring to the onset of the CS- in the CS-alone group than in the truly-random group.

In the bottom half of Figure 9 are shown the mean HR responses of the groups to CS+ on the six paired excitatory conditioning trials plotted as a function of 2-sec counting periods after CS+ onset. Focusing first on the data of the explicitly-unpaired groups depicted in the three left-most panels, it is clear that none of the groups displayed HR decelerations comparable to those occurring to CS+ on the original excitatory conditioning trials on day 1 (see Figure 2). In fact, most of the HR changes of the groups appeared to be slightly accelerative in direction. A 3 by 3 by 2 by 3 (day 2 dose by day 3 dose by CS frequency by counting periods) analysis of variance performed on the data of the explicitly-unpaired groups provided a significant

counting periods effect, F (2, 54) = 3.30, $p < .05$, a significant CS frequency by counting periods interaction, F (2, 54) = 6.51, $p < .01$, and a significant day 2 dose by CS frequency by counting periods interaction, F (4,54 = 3.66, $p < .01$. The CS frequency by counting periods interaction resulted from the fact that the change in HR tended to be larger to the onset of the 8-kHz CS than to the 4-kHz CS. The day 2 dose by CS frequency by counting periods interaction was produced mainly by the fact that the difference in the onset reactions to the two CSs was not as pronounced in the group given .8 g/kg of ethanol on day 2 as it was in the other day 2 groups. In spite of the reduction in the magnitude of the cardiodecelerative CRs to CS+, which Figure 9 reveals, a four-way analysis of variance (day 2 dose by day 3 dose by CS+ vs "unpaired" CS by counting periods) established that the overall magnitudes of the responses to CS+ were reliably different from those exhibited to CS-, F (1, 63) = 22.08, $p < .001$. This analysis also provided a significant counting periods effect, F (2, 126) = 16.45, $p < .001$, and significant interactions between counting periods and day 2 dose, F (4, 126) = 3.64 $p < .01$ and day 3 dose, F (4, 126) = 2.63, $p < .05$. In addition, the CS+ vs CS- by counting periods interaction was significant, F (2, 126) = 19.04, $p < .001$, revealing that the topographies of the responses to the two CSs were reliably different.

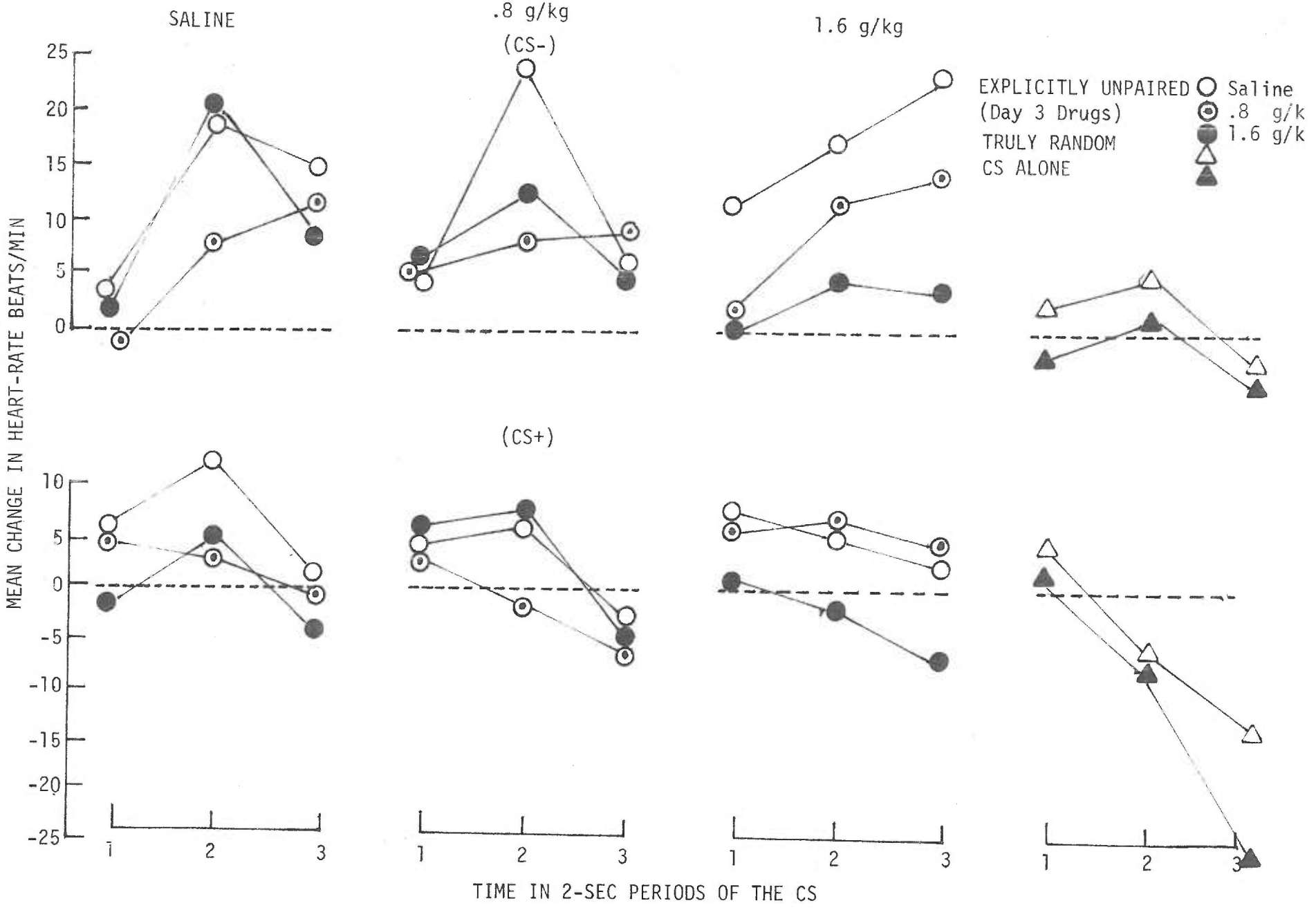
The HR responses of the truly-random and CS-alone groups to CS+ are plotted in the bottom far right panel of Figure 9. Here it is clear that in contrast to the explicitly-unpaired groups, the reconditioning performance of these groups showed little evidence of interference from the preceding "unpaired" trials. Thus, the truly-random and CS-alone groups exhibited HR responses whose decelerative direction and topography matched those that

Figure 9. Top. Mean heart-rate responses of all explicitly-unpaired groups, and the truly-random and CS-alone groups to the unpaired CS (CS-) in successive 2-sec periods and averaged over the six trials of the unpaired phase of Day 3.

Bottom. Mean heart-rate responses of all explicitly-unpaired groups and the truly-random and CS-alone groups to the paired CS (CS+) in successive 2-sec periods and averaged over the six trials of the paired phase of Day 3.

FIGURE 9

EXPLICITLY-UNPAIRED GROUPS



occurred to CS+ during original excitatory conditioning on day 1 (see Fig. 2). A 2 by 2 by 3 (groups by CS frequency by counting periods) analysis of variance provided a significant effect of counting periods, F (2, 24) = 27.00, $p < .001$, establishing that the change in HR over CS+ was reliable. In keeping with what was found for the explicitly-unpaired groups, the overall magnitudes of the responses of the truly-random and CS-alone groups to CS+ and to CS- were significantly different, F (1 12) = 4.49, $p < .05$. The topographies of the responses to the two CSs were also significantly different from each other, F (2, 24) = 5.62, $p < .05$.

Although not shown, movement activity of all of the groups to CS+ during reconditioning was similar to that shown during original excitatory conditioning on day 1 (see right side of Fig. 2). Basically, the responses consisted of a relatively large startle-type burst of activity in the first 2-sec period of the CS followed by progressively less activity during the second and third 2-sec periods of the CS. In general, most groups showed below-baseline decreases in movement during the third counting period. A 3 by 3 by 2 by 3 analysis of variance (day 2 dose by day 3 dose by CS frequency by counting periods) carried out on the movement data of the explicitly-unpaired groups supported only an effect of counting periods, F (2, 126) = 3.48, $p < .001$. A 2 by 2 by 3 (groups by CS frequency by counting periods) analysis performed on the data of the truly-random and CS-alone groups also provided a reliable counting periods effect, F (2, 24) = 10.74, $p < .001$.

HR and movement during the induction phase of Day 3.

Each induction trial consisted of presenting the CS-, waiting 6 sec and

then presenting the CS+. Recall that the intent of these induction trials was to determine what effect the close proximity of CS- would have on the HR responses to CS+. Figure 10 illustrates the mean HR responses of each group to CS- and to CS+ averaged over the 12 induction trials. The top half of the figure depicts the responses produced by CS- while the bottom half displays the responses elicited by CS+. Heart-rate difference scores for the two different CSs were computed on the basis of the respective 6-sec pre-CS periods preceding the onset of each CS. Focusing first on the three left-most panels at the top of Figure 10, it is readily apparent that the responses of the explicitly-unpaired groups to the CS- were characteristically accelerative just as during the preceding "unpaired" phases of the study. Moreover, for most of the groups, the magnitudes of the cardioaccelerations were larger during the second and third periods of CS- than during the first period. A visual comparison of the overall magnitudes of the HR responses among the explicitly-unpaired groups on the basis of day 2 drug dose (i.e., between panel comparisons), indicates that the groups within the .8-g/kg and 1.6-g/kg treatment conditions tended to show slightly smaller accelerative responses to CS- than did the groups within the day 2 saline condition. However, the figure provides no consistent evidence that the presence of ethanol on day 3 (i.e., within panel comparisons) either enhanced or reduced the magnitudes of the responses to CS-.

Next, shifting attention to the three left-most panels at the bottom of Figure 10, several prominent features appear characteristic of the responses of the explicitly-unpaired groups to CS+. First, as was true of the reactions produced by CS+ during excitatory conditioning, the directions of the HR responses of all of the groups were generally decelerative. Second, the topographies of the responses matched those that occurred to CS+ on

previous excitatory conditioning trials in that maximum cardiodecelerations occurred toward the end of the CS. As was true of the responses to CS-, the figure provides no evidence that the cardiodecelerations to CS+ were affected by the day 3 ethanol treatments. Also in keeping with the responses to CS-, the figure shows that the HR decelerations to CS+ were slightly smaller in those groups given ethanol on day 2 than in the day 2 saline group. A four-way analysis of variance (day 2 dose by day 3 dose by CS- vs CS+ by counting periods) provided a significant effect of type of CS, F (1, 63) = 123.93, $p < .001$, establishing that the overall responses to the two CSs were reliably different from each other. A significant effect of counting periods, F (2, 126) = 33.54, $p < .001$, and a significant courting periods by type of CS interaction, F (2, 126) = 75.18, $p < .001$, revealed that the change in HR across the CSs was reliable and that this change was different for the two CSs. There was also a significant day 2 dose by type of CS interaction, F (2, 63) = 3.88, $p < .05$, which can be attributed to the fact that both the accelerative and decelerative responses of the day 2-ethanol groups tended to be slightly smaller than those of the day-2 saline group.

The upper and lower right-hand portions of Figure 10 show the mean HR response of the truly-random and CS-alone groups to CS- and to CS+, respectively, averaged over the 12 induction trials. It is clear from the upper part of the figure that the truly-random group displayed a slight accelerative response to CS-, whereas the CS-alone group showed almost no HR change. The bottom portion of the figure shows that both groups displayed decelerative HR responses to CS+ that were not dissimilar in magnitude and topography to those exhibited by the explicitly-unpaired groups. Thus, Figure 10 provides no evidence that the magnitude of the HR change elicited by CS+ was

facilitated or reduced in any group by presenting CS- shortly before CS+. At the same time, however, in spite of the presence of substantial cardio-accelerations to CS-, the explicity-unpaired groups displayed cardiode-celerations to CS+ that matched those shown by the CS-alone and truly-random groups. A four-way analysis of variance (groups by frequency of CS by type of CS by counting periods) on the data of the truly-random and CS-alone groups shown in Figure 10 provided a significant type of CS effect, F (1, 12) = 14.62, $p < .001$, establishing that the overall responses to CS-and to CS+ were reliably different. A significant frequency of CS by type of CS interaction, F (1 12) = 5.08, $p < .05$, was the result of the 8-kHz CS- producing HR responses that were less decelerative, and in some cases more accelerative than those produced by the 4-kHz CS-. In the case of CS+, the HR decelerations to both frequencies were equivalent. The analysis also provided a significant effect of counting periods, F (2, 24) = 5.19, $p < .001$, and a significant counting periods by type of CS interaction, F (2, 24) = 6.65, $p < .001$, confirming that HR changed differently across the 2-sec periods of CS- and CS+.

A detailed examination of the HR responses of the explicitly-unpaired groups to CS- and to CS+ showed that the magnitude of the responses to the respective CSs remained nearly constant across the induction trials. Thus, the responses of the combined explicitly-unpaired groups to CS- and to CS+ averaged over successive blocks of four trials each were +8.0, +8.6, +9.8, and -9.6, -11.1, -8.6, respectively. An analysis of variance carried out on the trial data produced a significant overall difference between the two CSs, F (1, 63) = 125.93, $p < .001$. There were no significant outcomes involving trials as a factor.

Figure 10. Top. Mean heart-rate responses of all explicitly-unpaired groups, and the truly-random and CS-alone groups to CS- plotted as a function of 2-sec periods and averaged over the 12 induction trials.

Bottom. Mean heart-rate responses of the above groups to CS+ in successive 2-second periods and averaged over the 12 induction trials.

FIGURE 10

EXPLICITLY-UNPAIRED GROUPS

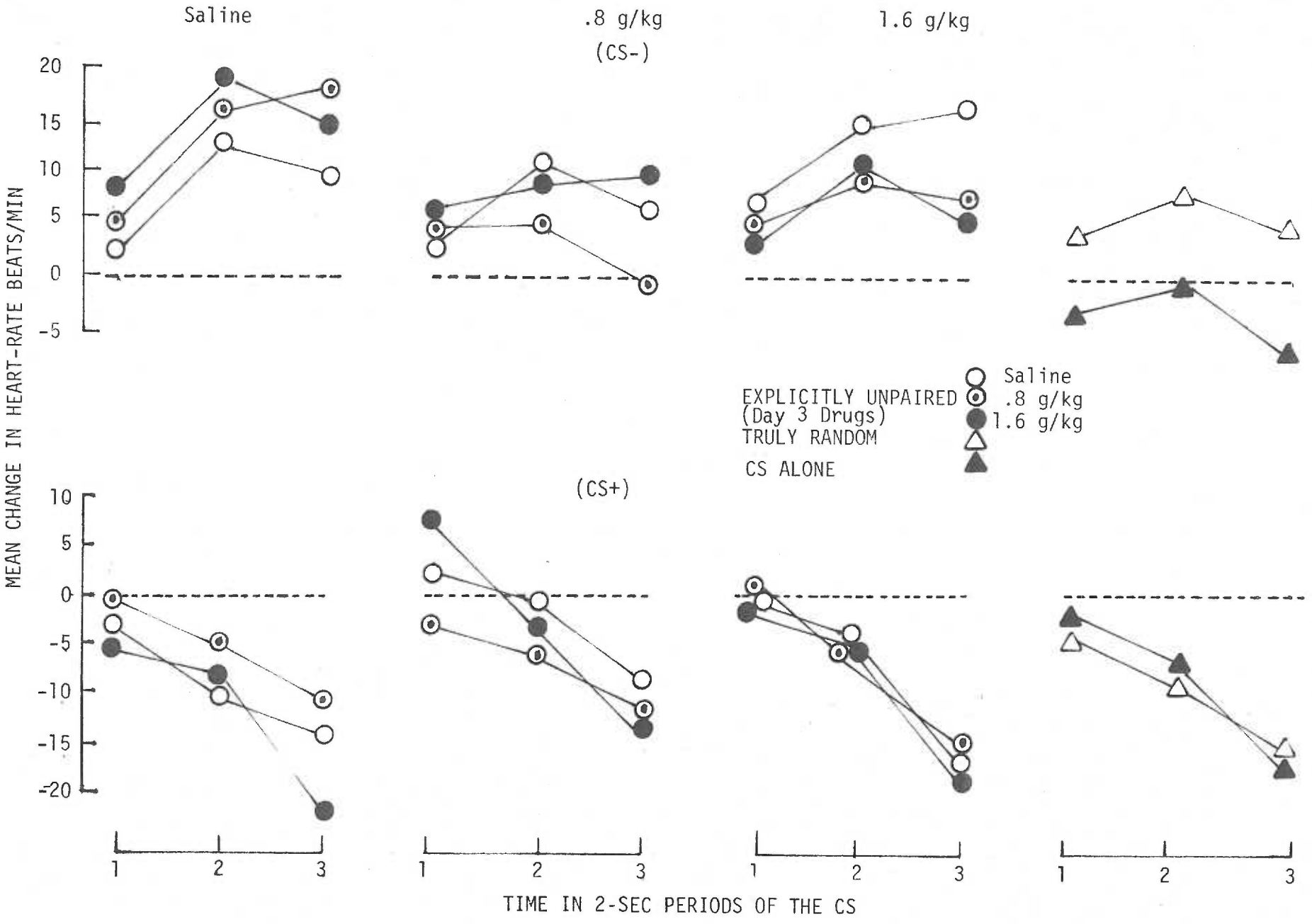


Figure 11 presents the mean movement responses of the groups in 2-sec periods of CS- and CS+ averaged over the 12 induction trials. As in the previous figure, the top half of the figure depicts the responses to CS- while the bottom half displays the responses to CS+. The responses to both CSs were computed by subtracting the appropriate pre-CS movement activity from activity during the CSs. A brief overview of the three left-most panels at the top of the figure shows that the movement responses of all of the explicitly-unpaired groups to CS- were highly similar in magnitude and topography regardless of drug treatment, thus all of these groups exhibited relatively large increases in movement during the first 2-sec period of CS- followed by progressively less movement during the second and third periods. However, it may be noted that in all groups, considerable movement existed during the second counting period and that only during the third counting period was movement near baseline levels.

Inspection of the three left-most panels at the bottom of Figure 11, indicates that in general, all of the explicitly-unpaired groups, regardless of their drug treatment, showed comparable movement responses to CS+. In comparing the responses to the two types of CSs, it is apparent that the onset reaction produced by CS+ was somewhat smaller than that elicited by CS-. Moreover, the responses to CS+ during the second and third counting periods were almost uniformly below-baseline decreases, whereas for CS- they were, at least for the first and second counting periods, above-baseline increases. Although the opposing directions of these movement responses correspond in a general way with the opposing directions of the HR responses elicited by the two CSs (see Fig. 10) on the induction trials, it is important to note that the topographies of the movement and HR response to

CS- did not correspond with each other. Thus, the amount of movement to CS- became smaller during the course of the CS (see Fig. 11), while the magnitude of the HR increase became larger (see Fig. 10).

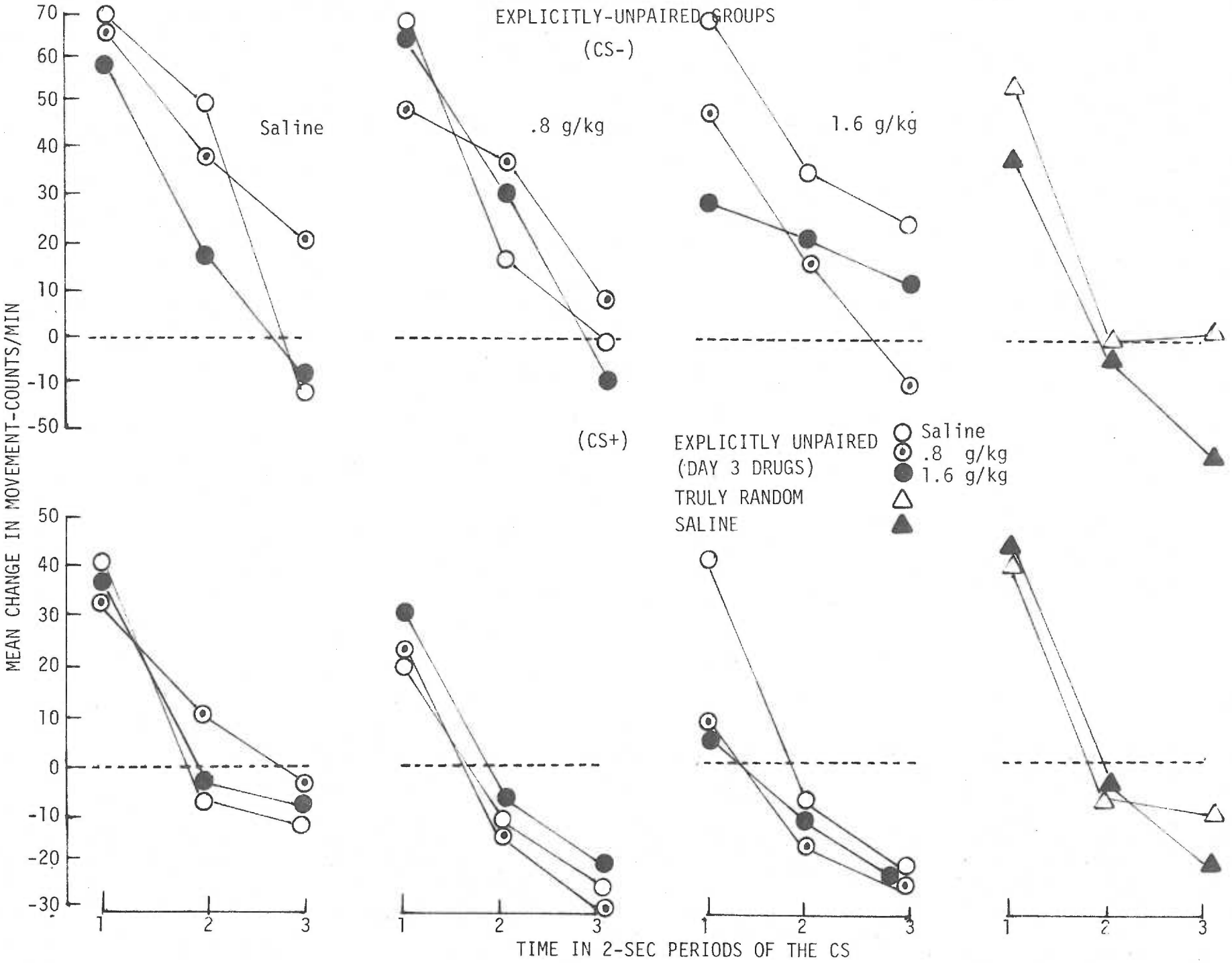
A 3 x 3 x 2 x 3 (day 2 dose by day 3 dose by type of CS by counting periods) analysis of variance on the movement data of the explicitly-unpaired groups shown in Figure 11 provided a significant type of CS effect, F (1, 63) = 36.24, $p < .001$, and a significant counting periods effect, F (2, 126) = 51.92, $p < .001$. These outcomes support the reliability of the previously noted tendency for CS- to be associated with more movement than CS+ and the tendency for movement to both CSs to be maximal during the first counting period and to fall off during the latter two counting periods.

Next, focusing on the upper right hand panel of Figure 11, it is clear that the movement responses of the truly-random and CS-alone groups to CS- were similar with both groups showing a burst of activity to CS onset comparable to that displayed by the explicitly-unpaired groups. However, in the case of the truly-random and CS-alone groups, movement activity dropped to baseline or below baseline during the second and third counting periods. Observation of the bottom right corner of Figure 11 shows that the movement responses of the truly-random and CS-alone groups to CS+ were similar and in this case also much like those shown by the explicitly-unpaired groups. A 2 by 2 by 2 by 3 (groups by CS frequency by type of CS by counting periods) analysis of variance indicated that the movement responses of the truly-random and CS-alone groups to CS- and to CS+ were not reliably different. The test did result in a significant frequency of CS by type of CS interaction, F, (1, 12) = 6.97, $p < .05$, which was due to the fact that the 8-kHz CS- tended to produce more activity than did the 4-kHz CS-. A significant frequency of CS

Figure 11. Top. Mean movement responses of the explicitly-unpaired groups and the truly-random and CS-alone groups in 2-sec periods of the CS- and averaged over the 12 induction trials.

Bottom. Mean movement responses of the above groups in 2-sec periods of the CS+ and averaged over the 12 induction trials.

FIGURE 11


EXPLICITLY-UNPAIRED GROUPS
(CS-)
Saline
.8 g/kg
1.6 g/kg
(CS+)
EXPLICITLY UNPAIRED
(DAY 3 DRUGS)
TRULY RANDOM
SALINE
Saline
.8 g/kg
1.6 g/kg
MEAN CHANGE IN MOVEMENT-COUNTS/MIN
70
60
50
40
30
20
10
0
-10
-50
50
40
30
20
10
0
-10
-20
-30
1
2
3
TIME IN 2-SEC PERIODS OF THE CS

by type of CS by counting periods interaction, F (2, 24) = 6.59, $p < .05$, indicated that this difference in movement activity was more pronounced in the first counting periods of the CSs than in the second and third counting periods. The final significant outcome of the test was that of counting periods, F (2, 24) = 29.64, $p < .001$.

Individual t tests were made comparing the movement responses of each explicitly-unpaired group (collapsed across the day 2 drug treatment) to the CSs on the induction trials with those shown by the truly-random and CS-alone groups. The movement responses of the explicitly-unpaired groups to CS- were reliably greater than that of the CS-alone group, (df = 30, $p <$ .005, in all cases) but not different from that of the truly-random group. No significant differences among the movement responses of the groups to CS+ were obtained.

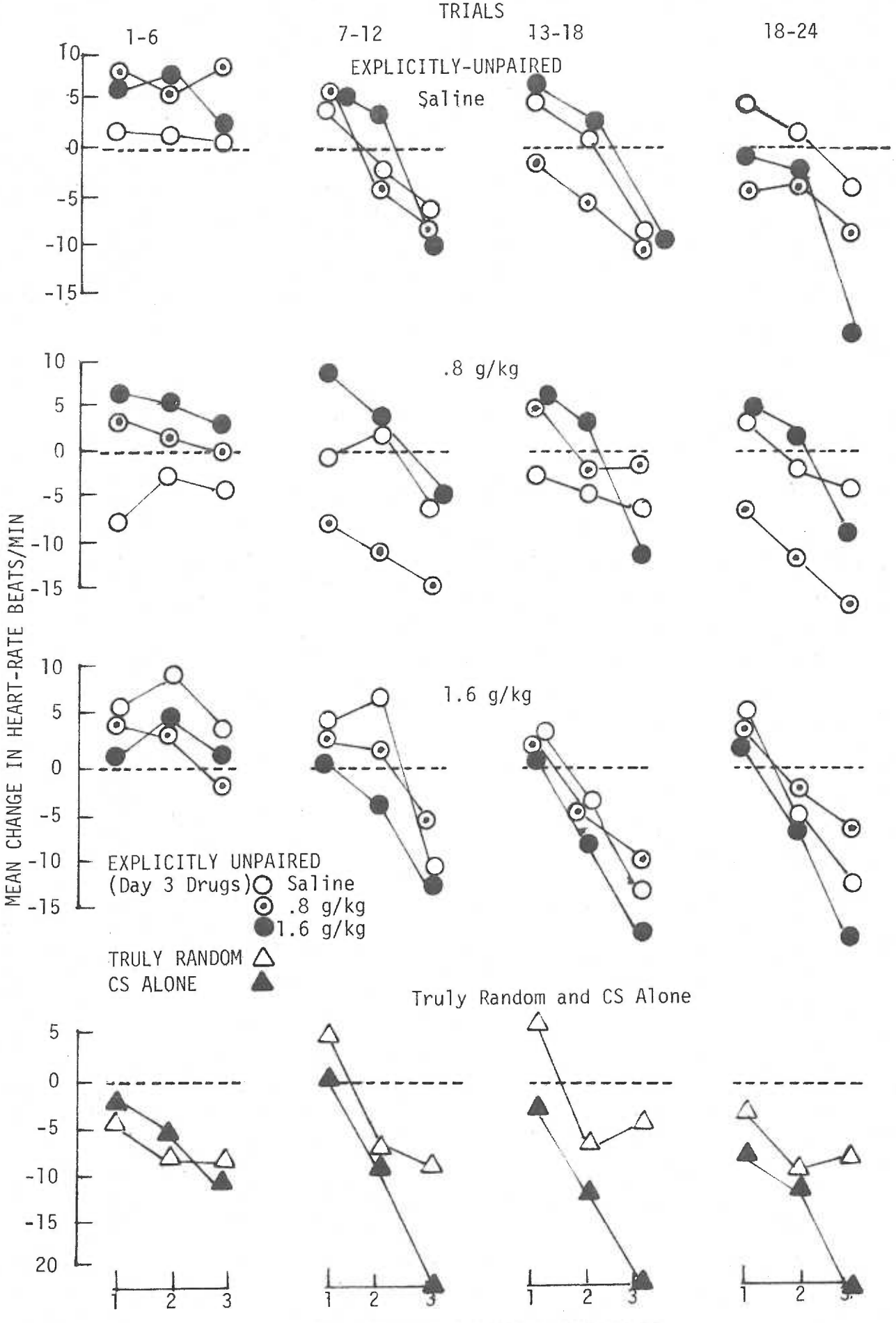
HR and movement during reversal conditioning on Day 3

Reversal conditioning consisted of selecting what had previously been the "unpaired" CS (CS-) and now pairing it with the US. The first reversal conditioning trial was given 2-3 min following the last induction trial. Figure 12 depicts the HR responses of all groups during reversal conditioning in 2-sec periods of the CS averaged over successive blocks of six trials each. The three top sections of the figures illustrate the data of the explicitly-unpaired groups, while the bottom section presents the data of the truly-random and CS-alone groups. Focusing first on the left sides of each section, it is clear that in general, the cardioaccelerations of the explicitly-unpaired groups observed earlier to CS- during the "unpaired" and induction phases were still present during the first six trials of reversal conditioning. However, for the truly-random and CS-alone group, small

magnitude HR decelerations occurred to CS- on these early reversal conditioning trials. In the case of the CS-alone group, these relatively small cardiodecelerations rapidly developed into larger responses having the same topography as that of the responses observed during regular excitatory conditioning on day 1 (see Fig 2). On the other hand, the responses of the explicitly-unpaired groups as well as those of the truly-random group appeared to be transformed into cardiodecelerations at a slower rate. Moreover, in general the magnitudes of the reactions of these groups did not reach the same levels as those achieved by the CS-alone group. A four-way analysis of variance (day 2 dose by day 3 dose by trial blocks by counting periods) on the data of the explicitly-unpaired groups provided significant effects of trial blocks, F (3, 189) = 14.72, $p < .001$, of counting periods, F (2, 126)= 64.00, $p \leq .001$, and of the trial blocks by counting periods interaction, F (6,378)=7.43, $p \leq .001$ indicating that the change in the topography of the HR responses across trials was reliable. The test also demonstrated that the following interactions were significant: day 2 dose by counting periods, F (4,126)= 2.55, $p \leq .05$, day 3 dose by counting periods, F (4, 126) = 4.11, $p < .01$, and day 2 dose by day 3 dose by trial blocks, F (12, 89) = 2.17, $p < .05$. Although difficult to see in Figure 12, the two interactions involving counting periods were both due to the fact that the groups given the .8-g/kg dose of ethanol either on day 2 or on day 3, tended to show smaller accelerative responses in the first counting period of the CS than did the saline or the 1.6 g/kg ethanol groups. The decelerative responses of the various groups were similar in the third counting period of the CS. The three-way interaction reflected the tendency for the HR cardiodecelerations to develop more rapidly in those groups receiving the same dose of ethanol on day 2 and day 3

Figure 12. Mean heart-rate responses of all explicitly-unpaired groups and the truly-random and CS-alone groups plotted as a function of 2-second periods of the CS and averaged over successive blocks of six trials during the reversal phase.

FIGURE 12


TRIALS
1-6
7-12
13-18
18-24
EXPLICITLY-UNPAIRED
Saline
.8 g/kg
1.6 g/kg
10
5
0
-5
-10
-15
MEAN CHANGE IN HEART-RATE BEATS/MIN
EXPLICITLY UNPAIRED
(Day 3 Drugs) Saline
.8 g/kg
1.6 g/kg
TRULY RANDOM
CS ALONE
Truly Random and CS Alone
5
0
-5
-10
-15
20
1
2
3
TIME IN 2-SEC PERIODS OF THE CS

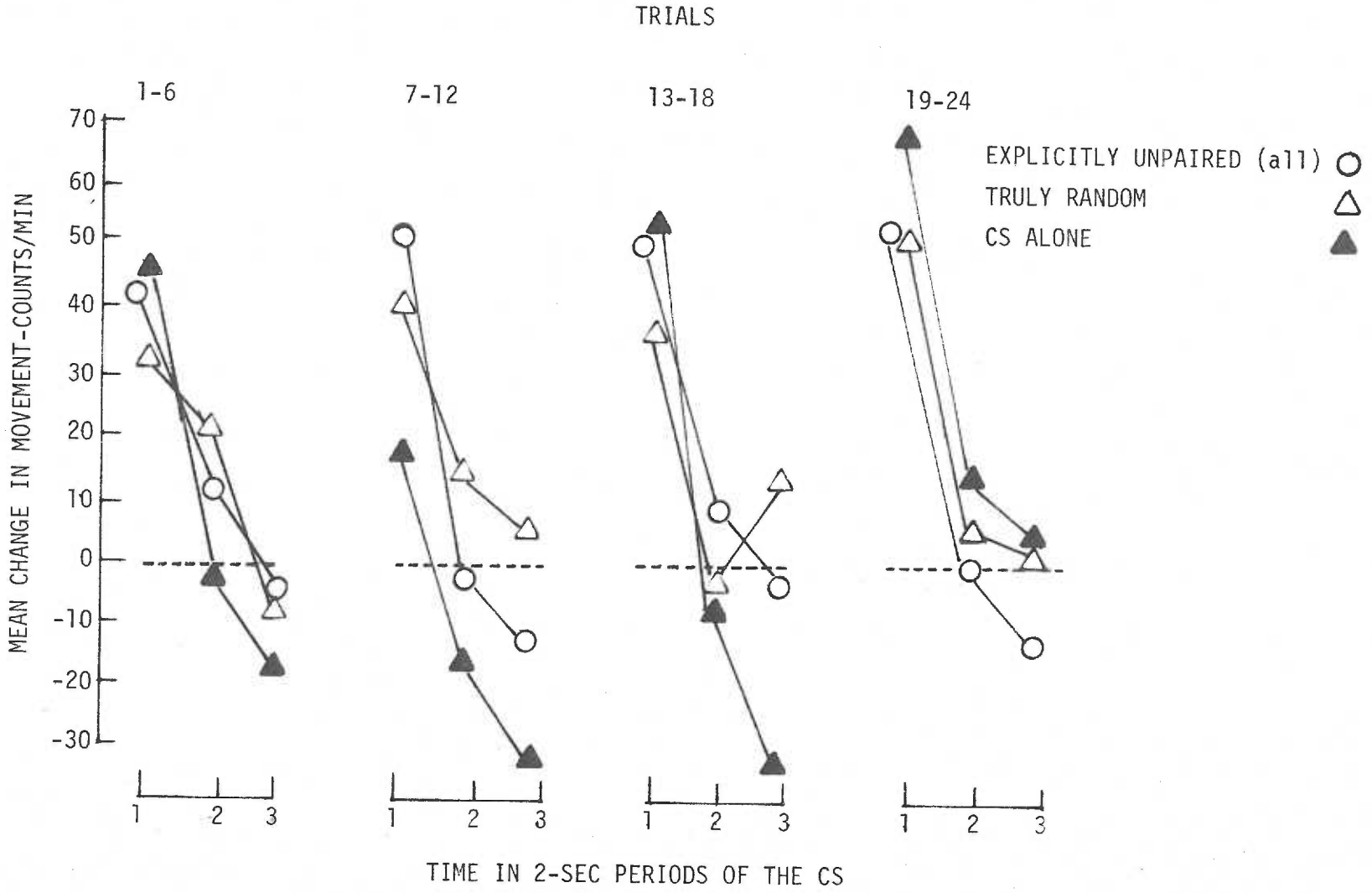
than in those groups that were shifted on day 3 to either saline or to the other ethanol dose.

A four way analysis of variance (groups by CS frequency by trial blocks by counting periods) carried out on the data of the truly-random and CS-alone groups displayed in Figure 12 provided a significant effect of counting periods, F (2,24) = 25.64, $p < .001$, and a significant groups by counting periods interaction, F (2,24) = 4.76, $p < .05$, confirming that reliable differences existed between the HR responses of the truly-random and CS-alone groups. The test also produced a significant trial blocks by counting periods interaction, F (6, 72) = 3.51, $p < .001$, showing that the responses of the two groups changed reliably across trials.

The CS minus pre-CS movement responses of the truly-random, CS-alone and combined explicitly-unpaired group in 2-sec periods of the CS averaged over successive six-trial blocks of reversal conditioning are illustrated in Figure 13. A single explicitly-unpaired group was formed after it was determined that neither the day 2 nor day 3 drug treatments had a significant effect on the movement responses of the separate groups. From an inspection of this figure, it is clear that the three groups showed essentially the same pattern of movement activity to the CR during reversal conditioning. This pattern matched closely the movement responses that occurred during original excitatory conditioning (see right side of figure 2) and consisted of a burst of activity at the onset of the CS followed by

Figure 13. Mean movement responses of all explicitly-unpaired groups and the truly-random and CS-alone groups plotted as a function of 2-second periods of the CS and averaged over blocks of six trials during the reversal phase.

FIGURE 13


TRIALS
1-6
7-12
13-18
19-24
EXPLICITLY UNPAIRED (all)
TRULY RANDOM
CS ALONE
MEAN CHANGE IN MOVEMENT-COUNTS/MIN
70
60
50
40
30
20
10
0
-10
-20
-30
1
2
3
TIME IN 2-SEC PERIODS OF THE CS

progressively less activity during the rest of the CS. Although there was some tendency, especially in the CS-alone group, for movement during the second and third counting periods to be below baseline, this was not consistent and was not visible on the last block of trials. In general the movement responses of the groups shown in Figure 13 did not appear to change directions across trials in the same way that HR did (see figure 12). A two-way (trial blocks by counting periods) analysis of variance carried out on the collapsed explicitly-unpaired groups provided only a significant effect of counting periods, F (2,781)= 113.11, $p<.001$. A four-way (groups by frequency of CS by trial blocks by counting periods) analysis of variance performed on the results of the truly-random and CS-alone groups demonstrated that the counting periods effect, F (2,24)= 24.90. $p<.001$, and the counting periods by frequency of CS interaction, F (2,24)= 4.13, $p<.05$,were significant. The significant interaction reflected the fact that movement during the first 2-sec counting period was more vigorous to the 8-kHz CS than to the 4-kHz CS.

Outcomes of t tests comparing the mean-movement responses of all groups at each of the trial blocks in Figure 13 were uniformly nonsignificant.

HR during the inhibition of delay phase of Day 3

During the inhibition of delay phase, all of the groups were first given six regular excitatory conditioning trials using a CS-US interval of 10 sec instead of the previously employed 6-sec interval. Following these trials the CS-US interval was extended to 20 sec and six additional excitatory conditioning trials were administered. The CS on all of these trials was the same as the one that had been used during the reversal

conditioning and during the "unpaired" phase of the study (i.e., CS-).

Figure 14 presents the mean HR responses of the groups in 2-sec periods of the CS averaged over the six trials in which the CS-US interval was 10 sec. It is clear from this figure that the main effect of increasing the length of the CS-US interval was that of permitting further decreases in HR to occur prior to the delivery of the US. With the possible exception of the truly-random group, none of the groups provided evidence that maximum HR deceleration had been achieved by the end of the 10-sec interval. There was some indication that the .8 g/kg dose of ethanol of day 2 reduced the magnitude of the responses. A three way analysis of variance (day 2 dose by day 3 dose by counting periods) conducted on the data of the explicitly-unpaired groups provided a significant counting periods effect, F (4,252)= 84.3, $p<.001$, and a significant day 2 dose by counting periods interaction, F (8,252)= 2.16, $p<.05$. A separate analysis performed on the truly-random and CS-alone groups provided a significant counting periods effect, F (4,56)=16.12, $p<.05$, and a significant counting periods interaction, F (4,56)= 4.28, $p<.05$.

The mean HR responses of the groups in each 2-sec period of the CS averaged over the six trials in which the CS-US interval was 20 sec are shown in Figure 15. This figure reveals that all of the groups showed consistent HR deceleration throughout the 20 sec CS-US interval with the magnitudes of the reactions reaching asymptotic levels around the fifth counting period. Although HR decelerations continued to occur in succeeding counting periods, the magnitudes of the reactions were fairly constant. In general the reactions of the explicitly-unpaired groups given

Figure 14. Mean heart-rate responses of all explicitly-unpaired groups and the truly-random and CS-alone groups plotted as a function of 2-second periods of the CS and averaged over the six trials in which the CS-US interval was 10 seconds.

FIGURE 14

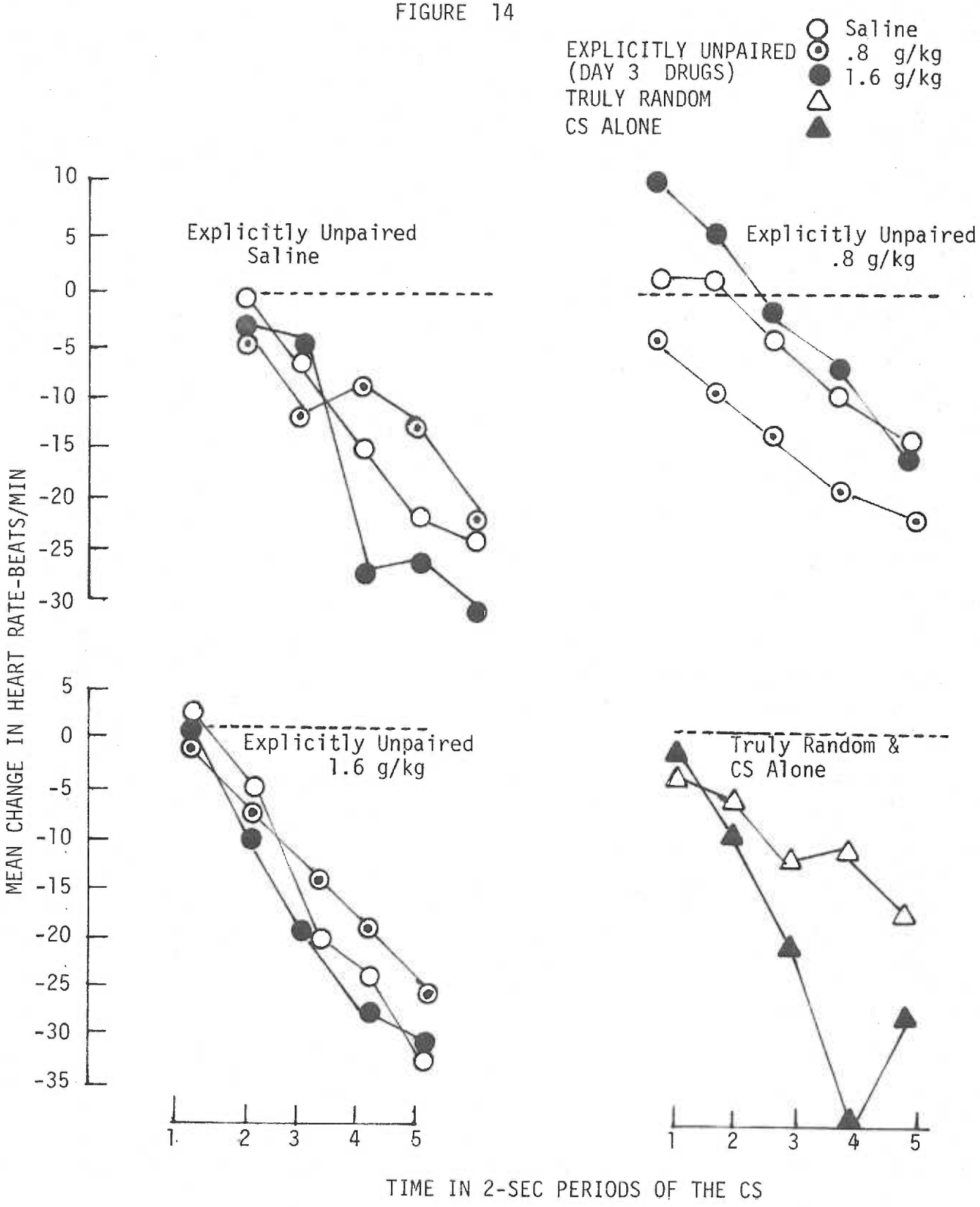
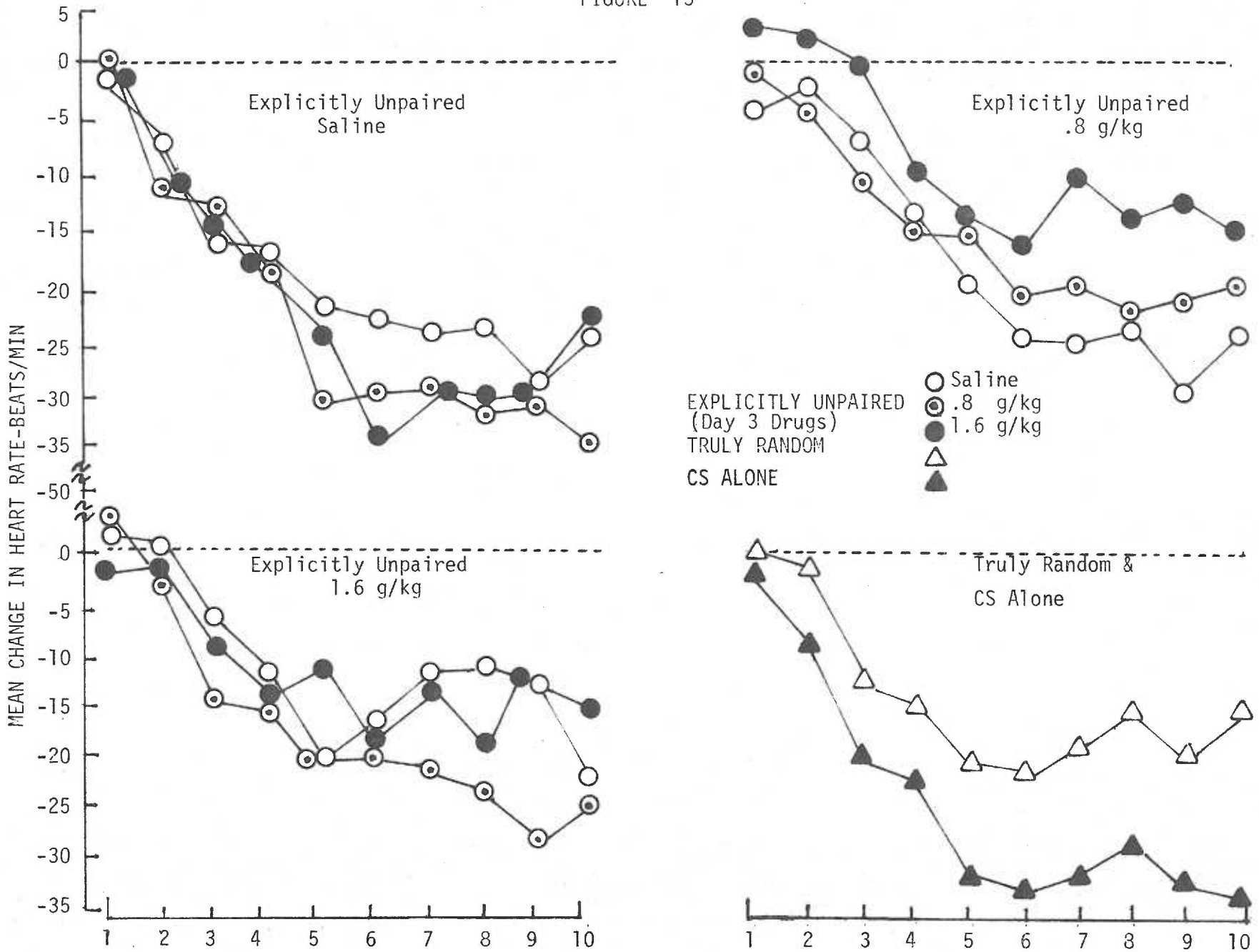

EXPLICITLY UNPAIRED
(DAY 3 DRUGS)
TRULY RANDOM
CS ALONE
Saline
.8 g/kg
1.6 g/kg
Explicitly Unpaired
Saline
Explicitly Unpaired
.8 g/kg
Explicitly Unpaired
1.6 g/kg
Truly Random &
CS Alone
MEAN CHANGE IN HEART RATE-BEATS/MIN
10
5
0
-5
-10
-15
-20
-25
-30
-35
1
2
3
4
5
TIME IN 2-SEC PERIODS OF THE CS

Figure 15. Mean heart-rate responses of all explicitly-unpaired groups and the truly-random and CS-alone groups plotted as a function of 2-second periods of the CS and averaged over the six trials in which the CS-US interval was 20 seconds.

FIGURE 15


Explicitly Unpaired
Saline
Explicitly Unpaired
.8 g/kg
Explicitly Unpaired
1.6 g/kg
Truly Random &
CS Alone
EXPLICITLY UNPAIRED
(Day 3 Drugs)
TRULY RANDOM
CS ALONE
Saline
.8 g/kg
1.6 g/kg
MEAN CHANGE IN HEART RATE-BEATS/MIN
5
0
-5
-10
-15
-20
-25
-30
-35
-50
1 2 3 4 5 6 7 8 9 10
TIME IN 2-SEC PERIODS OF THE CS

saline on day 2 (i.e., upper left-hand panel) were larger than those given ethanol on day 2. Also, the overall response level of the CS-alone group was consistently greater than that of the truly-random group. A three-way analysis of variance (day 2 dose by day 3 dose by counting periods) provided a significant effect of day 2 dose, F (2,63) = 4.05, $p<.05$ and a significant effect of counting periods, F (9,567) = 70.38, $p<.001$. A similar analysis on the results of the CS-alone and truly-random groups gave a significant counting periods effect, F (9,126) = 20.68, $p<.001$.

Baseline HR and movement during the seven phases of Day 3

Table 1 presents the mean baselevel HR and movement of the explicitly-unpaired, truly-random, and CS-alone groups during all six phases of day 3. In the case of the explicitly-unpaired groups, the data were collapsed across the drug treatment dimension of day 2. Focusing first on the upper half of the table, it is clear that the baselevel HRs of the two explicitly-unpaired groups given ethanol were consistently higher than those of the explicitly-unpaired saline group in each phase of day 3. It should be recalled that a similar relationship existed between the explicitly-unpaired ethanol and saline groups on day 2. The table also reveals that all three of the explicitly-unpaired groups showed a progressive decline in baselevel HR over the successive phases of day 3. Appropriate analyses of variance established that the differences among the explicitly-unpaired groups were reliable in each of the six phases of day 3, F (2,69), $p<.05$ in all cases). Subsequent comparisons of the group means using Newman-Keuls tests indicated that the ethanol groups were not reliably different from each other, but that both were significantly different from the saline group in all

phases ($p<.05$ in each case).

It may also be seen from an inspection of Table 1 that the baselevel HR of the truly-random group was considerably lower than that of the CS-alone group throughout day 3. This finding is consistent with what was found on both day 1 and day 2 of the study. The reliability of the differences between the baselevel HRs of the truly-random and CS-alone groups during each of the seven phases of day 3 was supported by individual one way analyses of variance (F (1,14), $p<.01$ in all cases). Individual t tests indicated that the baselevel HRs of all of the explicitly-unpaired groups were sigficantly higher than those of the truly-random group in all phases (df= 30, $p<.005$ in all cases). There were no significant differences between any of the explicitly-unpaired groups and the CS-alone group.

An inspection of the lower half of Table 1 indicates that the baseline levels of movement in the explicitly-unpaired groups were similar to each other in each of the phases of day 3. Thus, in contrast to HR, background levels of movement were not elevated by either dose of ethanol during the various test phases of day 3. Examination of the table also reveals that the amount of baseline movement of the truly-random group was generally lower than that of the CS-alone group throughout the phases of day 3. In addition, the CS-alone group showed marked increases in motor activity during the "unpaired", the paired, and the induction phases of day 3. Separate one way analyses of variance indicated that these elevations were significantly different from the movement levels of the truly-random group in the paired phase, F (1,14) = 8.56, $p<.05$, and in the induction phase, F (1,14)= 7.48, $p<.05$. On the basis of t tests, all of the explicitly-unpaired groups

were found to differ significantly from the truly-random group during the paired and induction phases, (df = 30, $p<.05$ in all cases).

Comparison of the Explicitly-unpaired, Truly-random, and CS-alone Groups During all of the Phases of Day 3

"Unpaired" Phase

The overall mean HR responses of the explicitly-unpaired groups collapsed across the drug treatments of day 2 were compared with the responses of the truly-random and CS-alone groups. Outcomes of t tests supported the presence of reliable differences between the explicitly-unpaired saline group and the truly-random group, $t(30)=2.36$, $p<.05$, and between all of the explicitly-unpaired groups and the CS-alone group ($p<.05$, df=30, in each case).

Paired Phase

The results of t tests comparing the mean HR responses of the explicitly-unpaired groups collapsed across day 2 treatments with the truly-random and CS-alone groups supported reliable differences among only the explicitly-unpaired groups and the CS-alone group ($p<.05$, df=30, in each case).

Induction Phase

The overall mean HR responses of the explicitly-unpaired groups to CS- and CS+ collapsed across the day 2 drug treatment were compared with the responses of the truly-random and CS-alone groups using t tests. Reliable differences in responses existed between all explicitly-unpaired groups and the CS-alone group ($p<.05$, df=30, in all cases). No reliable differences were found between the explicitly-unpaired groups and the truly-random group. There were no significant differences among the responses of the groups to CS+.

Reversal Phase

The HR responses of the explicitly-unpaired groups to CS- during reversal conditioning were compared with those of the truly-random and CS-alone groups with individual t tests. These tests indicated that the overall mean responses of the explicitly-unpaired groups collapsed across the day 2 drug treatment differed significantly from those of the CS-alone group ($p<.05$, df=30, in all cases). The differences between the explicitly-unpaired and truly-random group were not significant. Comparisons of the mean responses of the groups during the first block of six reversal trials showed that there were significant differences between the explicitly-unpaired groups and both the truly-random and CS-alone groups ($p<.05$, df=78, in each case). During later trial blocks the groups did not differ.

Inhibition of Delay Phase, 10 sec and 20 sec CS-US intervals.

A comparison of the overall mean HR responses of the explicitly-unpaired groups collapsed across the day 2 drug treatment with the truly-random and CS-alone groups failed to show the presence of significant differences among the groups during either the 10 sec or 20 sec CS-US intervals.

Table 1

Baseline Heart Rate and Movement During the Six Phases of Day 3

Heart Rate (beats-per-minute)

	30-min Adapt.	Unpaired	Paired	Induction	Reversal	Iniibition of Delay 10 sec	20 sec
Explictly Unpaired							
Saline	451	452	449	441	443	427	422
.8 g/kg	484	483	477	482	477	468	465
1.6g/kg	481	478	476	481	474	464	460
Truly Random	416	416	398	392	397	371	389
CS-alone	470	468	480	475	450	442	444

Movement (counts-per-minute)

Explicitly Unpaired							
Saline	37	56	62	48	27	51	22
.8 g/kg	35	44	32	49	43	37	20
1.6g/kg	33	29	51	42	32	38	35
Truly Random	33	39	10	12	14	18	10
CS-alone	17	107	105	82	30	14	29

DISCUSSION

The main findings of the study were that: (1) The directions of the HR CRs of all groups to CS+ during excitatory conditioning were decelerative and were of equivalent magnitude and topography; (2) during the "unpaired" phase of the study, the directions of the HR responses of the three groups to CS- were not the same. For the explicitly-unpaired group, HR deceleration was gradually replaced by HR acceleration. For the truly-random group, the HR reactions tended to be variable, consisting mostly of small decelerative changes with occassional small HR accelerations. The CS-alone group displayed HR decelerations to CS- throughout the "unpaired" phase with these responses being similar to those occurring to CS+ during excitatory conditioning; (3) during induction, the responses of the three groups to CS+ were similar, even though their reactions to CS- presented 6 sec earlier were not. Thus, responding to CS- did not appear to modify the reactions to CS+ as would be expected if positive induction had been operating. The only effect of the induction procedure appeared to be that of attenuating extinction of the responses to CS- and to CS+; (4) performance of the explicitly-unpaired group during reversal conditioning was retarded relative to that of both the truly-random and CS-alone groups. Reversal learning in the truly-random group was impaired slightly compared to that of the CS-alone group. The explicitly-unpaired groups that were maintained on the same drug regime during the "unpaired" and reversal phases displayed more rapid reversal conditioning than did the groups switched from either saline to ethanol or ethanol to

saline; (5) the extension of the CS-US interval from 6 to 10 sec on the inhibition of delay trials permitted the observation of larger magnitude HR CRs. Increasing the interval from 10 to 20 sec did not further increase peak HR CRs. However, even with this rather long CS-US interval the HR decreases that were reached within 10 sec were maintained at full strength for the remaining 10 sec of the interval; (6) HR and movement were not closely correlated during most phases of the study. However, during the "unpaired" phase HR and movement increases in the explicitly-unpaired group tended to go together; (7) while ethanol uniformly increased base-level HR, these increases were not systematically related to the magnitude of either decelerative or accelerative HR changes.

"Unpaired" Phase

The different directions of the HR responses exhibited by the explictly- unpaired, truly-random, and CS-alone groups during the "unpaired" phase were consistent with one of the basic assumptions of contemporary theories of conditioned inhibition. Both Hearst (1972) and Rescorla (1969, 1975a) have proposed that one of the requirements for a conditioned inhibitor is that it produce a response opposite to that produced by a conditioned excitor. Consistent with this suggestion, during the "unpaired" phase, the explicitly-unpaired group displayed accelerative HR responses that were directionally opposite the decelerative HR responses shown to CS+ during excitatory conditioning. The failure of the truly-random and CS-alone groups to show HR accelerations to CS- suggests that such accelerations may only occur when there is a negative relationship between CS-

and the US, i.e., when the CS predicts the absence of the US.

The HR responses of all groups at the beginning of the "unpaired" phase were decelerations whose topography or form were similar to the decelerative CRs to CS+. In both cases, response magnitude was greater at the end than at the beginning of the CS. Over the course of the "unpaired" phase, the responses of the explicitly-unpaired groups changed from a deceleration to a biphasic deceleration/acceleration and then to uniform acceleration. This transformation in the direction of the HR change was particularly rapid in the explicitly-unpaired saline group in that it occurred after only 12 trials. However, within 18 trials, the responses of all three explicitly-unpaired groups were accelerations. Once established, the magnitude, direction, and topography of the responses of all explicitly-unpaired groups were highly stable. At the end of the "unpaired" phase, the topography of the accelerative responses was similar to that of the decelerative CRs to CS+. Thus, the accelerative responses were smallest during the first 2-sec of the CS- becoming increasingly more accelerative during the remainder of the CS.

In contrast to the present findings, Cunningham et al. (1977) observed very little accelerative HR responding in an explicitly-unpaired group until 20 or more unpaired trials had been given. One difference between the two investigations that may help account for the slightly slower development of the accelerative response in the Cunningham et al. study has to do with when the "unpaired" phase was given. Cunningham et al. initiated the "unpaired" trials on the same day immediately after excitatory conditioning, while in the present study, the "unpaired" phase

was not begun until approximately 24 hours after excitatory conditioning. It may be that giving inhibitory training with a CS- shortly after excitatory training with a CS+ may make it more difficult for accelerations to become established to CS- than if a long delay is introduced between the two phases. In this regard, Cunningham et al. observed that the initial responses to CS- were cardiodecelerations that were similar in magnitude and topography to the excitatory CRs to CS+. A comparable outcome was observed in the present study except that the magnitude of the decelerative responses to CS- tended to be slightly smaller. It may be, therefore, that the relatively long interval between excitatory conditioning and the "unpaired" phase that was used here allowed the CS+ to lose some of its excitatory potential which in turn permitted HR accelerations to develop more rapidly.

Additional evidence bearing on the relative difficulty of establishing inhibitory response tendencies (i.e., HR accelerations) in close temporal proximity to excitatory responding was provided by Martin and Fitzgerald (1978). They found using a differential conditioning paradigm that while it was possible to establish conditioned decelerative HR CRs to CS+ it was not possible to develop HR accelerations to CS-.

The outcomes of the "unpaired" phase also bear on the assumption that has traditionally been made concerning the establishment of inhibitory response tendencies (Pavlov, 1927; Gray, 1975; Rescorla, 1975a). It was assumed by Pavlov that internal inhibition developed to a CS only if the CS had been previously associated with some excitation. In fact, Pavlov maintained that the amount of inhibition that accrued to a CS was directly

proportional to the prior excitatory potential of the CS. Apparently CS+ had to initially elicit some level of responding before inhibition could be measured. To a certain extent, this assumption has persisted to the present time (Gray, 1975; Rescorla, 1975a; Zimmer-Hart & Rescorla, 1974).

While the necessity of having a base of excitatory responding is obvious in studies of inhibition involving response decrements, the role of excitatory conditioning per se in the acquisition of inhibition is still open to question. In the present investigation, the initial decelerative HR responding to CS- that was noted at the beginning of the "unpaired" trials, suggests that some excitatory potential may have transferred from CS+ to CS-. However, whether this was required for subsequent HR accelerations to develop cannot be answered on the basis of the present results. Some preliminary work conducted during the pilot phase of this study suggested that prior excitatory training might in fact be a prerequisite for HR acceleration but a definite answer to this question will require further work.

The HR reactions of the truly-random group to CS- during the "unpaired" phase were consistent with a second premise of the conditioned inhibition theory proposed by Rescorla (1969, 1975a). According to Rescorla, truly-random procedures should provide a CS with neutral or balanced excitatory and inhibitory properties. Therefore, responding to such a CS might deviate very little from pre-CS levels of activity. Compared to the marked accelerative HR responses of the explicitly-unpaired group and the decelerative responses of the CS-alone group, the truly-random group

did in fact display small HR responses to CS-. The only exception to this was at the beginning of the "unpaired" phase when consistent HR decelerations occurred. As noted previously, these responses can be attributed to stimulus generalization between the previous CS+ and the new CS-.

An ideal outcome in selecting a control condition in studies of classical conditioning is that it gererate a zero level of responding. In this study, truly-random CS and US exposures led to relatively small HR changes in the presence of the CS. While these results suggest that a truly-random control may be preferable to explicitly-unpaired and CS-alone paradigms in the context of HR conditioning experiments, its exclusive use appears problematic. Thus, the fact that the truly-random group showed some accelerative HR responses toward the end of the unpaired-phase, temporary though they were, suggests that HR changes may occur in all control procedures given a sufficient number of trials.

In several studies where the truly-random procedure has been used the CS elicited responses that appeared to be excitatory in nature (Kremer & Kamin, 1969; Kremer, 1971; Ayres et al., 1975). Cunningham et al (1977) measured decelerative HR reactions in a truly-random group that were somewhat larger than those obtained in the current investigation. In their study the decelerations tended to be restricted to the onset of CS- and overall the responses were not unlike the orienting responses elicited by the CS prior to training. In the present study, those HR changes that were found in the truly-random groups were not associated in any systematic way with a particular segment of CS-.

The performance of the CS-alone group during the "unpaired" phase

was not inconsistent with the outcomes of prior habituation stiudes involving repeated presentations of a nonreinforced stimulus (Graham & Clifton, 1966; Horn & Hinde, 1970; Stein, 1966). It has generally been reported that CS-alone presentations produce a reduction in the magnitude and frequency of responses to the CS over trials. However, in this study even though the initial magnitude of the decelerative HR responses of the the CS-alone group to CS- declined during the "unpaired" phase, substantial decelerative changes in HR were still present at the end of the 54 "unpaired" trials. This could mean that the prior excitatory conditioning trials somehow maintained the HR reaction on the CS-alone trials.

The difference in the HR responses of the explicitly-unpaired, truly-random, and CS-alone groups during the "unpaired" phase of the present study may also be applied to theoretical and empirical considerations regarding extinction. The traditional procedure that has been used to extinguish excitatory CSs consists of presenting the CS repeatedly by itself in the absence of the US following a period of conditioning (Woodworth & Schlosberg, 1954; Kimble, 1961). This procedure typically leads to a decrease in the frequency and/or magnitude of excitatory CRs as a function of trials. While there is considerable evidence that this technique is effective in bringing about a reduction in the CR, few attempts have been made to compare it against other possible paradigms.

It may be recalled that Konorski (1948) questioned Pavlov's assumptions about inhibition and his choice of extinction procedures. Konorski suggested that the most effective way to extinguish a CR was to modify the reinforcing properties of the US. While he felt that this could be done

by reducing the intensity of the US or presenting the US in the complete absence of the CS, Konorski considered backward conditioning to be the optimal procedure for exinguishing a CR and establishing stable inhibitory potential to a CS. The backward procedure was felt to be most effective because it not only reduced the reinforcing value of the US but it also effectively weakened the positive associative relationship between the US and the CS.

Frey and Butler (1977) have advanced an argument that is similar to that proposed by Konorski (1948). They provided evidence that an explicitly unpaired procedure was more effective than a conventional CS-alone extinction procedure in eliminating excitatory responding. Frey and Butler found that while the CS-alone procedure resulted in slightly more rapid CR extinction than an explicitly-unpaired procedure, extinction in the unpaired group appeared to generate more inhibition because of the fact that reversal conditioning was impeded in the unpaired group. Frey and Butler suggested that the apparent presence of more inhibition in the explicitly-unpaired may have occurred because the explicitly-unpaired affected both associative and non-associative processes while regular extinction (i.e., CS-alone) had only non-associative effects.

Rescorla (1975a,b) and Rescorla and Holland (1976) have also discussed the issue of extinction and have basically agreed with Konorski's views about the necessity of reducing the salience of the US in order to produce permanent extinction. Rescorla and Holland (1976) cited a number of studies in which reductions of CR strength were achieved through independent manipulations of the US.

In the present study, evidence bearing on the comparative effectiveness of different extinction procedures is somewhat indirect. Presumably because of stimulus generalization between CS+ and CS-, all groups initially displayed HR responses to CS- similar to those performed to CS+. It might therefore be assumed that the responses at the start of the "unpaired" phase were excitatory in nature and that the subsequent treatments in the "unpaired" phase represented different extinction methods. If these assumptions can be tentatively accepted, then the outcomes of the "unpaired" phase suggest that the explicitly-unpaired procedure is more effective in bringing about excitatory response loss (i.e., elimination of HR deceleration) and establishing inhibitory potential to a CS than either the traditional CS-alone procedure or the truly-random paradigm. Such an outcome is consistent with Konorski's assumptions about extinction, but contrasts with most empirical findings on extinction (Frey & Butler, 1977; Rescorla 1975a; Rescorla & Holland, 1976).

It is clear that the explicitly-unpaired procedure, despite the presence of the US, resulted in much more rapid loss of excitatory CR responding than did the CS-alone procedure. Additionally, when the reversal-test results are considered it is apparent that the extinction of the decelerative HR responses in the explicitly-unpaired group were more permanent than in the CS-alone group. Apparently, the influence of the explicit nonpairing of the CS and US on associative strength in the explicitly-unpaired

group outweighed any potentially reinforcing effects that the US may have had on the excitatory responses.

It should be cautioned, however, that the present findings are only suggestive of some important issues that should perhaps be examined in much greater detail. It seems likely that in some cases traditional CS-alone extinction procedures may not be optimal for eliminating CRs. Considering the important position that extinction has in theories of conditioning and the widespread use of extinction procedures in behavioral therapy, more systematic research should be conducted to determine optimum parameters for extinguishing different types of responses.

Induction

In spite of substantial differences in the HR responses elicited by CS- prior to the beginning of the induction trials, evidence of positive induction was not found in the current experiment. Thus, while the explicitly unpaired, truly-random, and CS-alone groups displayed different responses to CS- in the induction phase, the responses to CS+ were not reliably different. Several factors can be mentioned that may have contributed to this outcome. Pavlov (1927) specified a number of variables that appeared to be important in the occurrence of induction. These included, (1) the physical similarity of CS- and CS+; (2) the extent to which discriminated responding between CS- and CS+ had been learned; and (3) the temporal interval between the presentation of CS- and CS+. According to Pavlov, the optimum conditions for positive induction existed if CS- and CS+ were physically very similar, the responses to CS- and CS+ were not well differentiated, and the interstimulus interval was less than 2 min. More recently, Ischlondsky (1949)

has stressed the importance of using short intervals between CS- and CS+, preferably not more than a few seconds in order to produce an induction effect.

The interval separating CS- and CS+ in this study was 6 sec which was well within the 2 min maximum specified by Pavlov (1927) and near the optimum time suggested by Ischlondsky (1949). Also the two stimuli were physically very similar, a fact demonstrated by the large amount of stimulus gereralization that occurred between CS+ and CS- at the beginning of the "unpaired" phase. On the other hand, the fact that the responses to CS- and CS+ were well established prior to the test for induction could have contributed to the absence of induction. This may have been due either to a ceiling effect (i.e., HR decreases to CS+ were at their maximum levels) or to some other process having to do with overtraining. A second major difference between the present study and prior experiments demonstrating an induction effect relates to the specific training procedures that were used . In most studies showing induction, the animals received discrimination training involving contemporaneous presentations of CS+ and CS- with induction trials consisting of delivery of CS- shortly before CS+. In the current investigation training trials with CS+ and CS- were given in separate blocks widely spaced from each other. Even though this technique resulted in obvious differential responding to the two CSs it apparently lacked a necessary ingredient for induction.

In this regard, it is also worth noting that in the discrimination procedure producing induction, CS- has a negative relationship with the US in that it is always delivered in the absence of the US. This same relationship was present in the explicitly-unpaired paradigm employed in the current

experiment and yet induction was not produced. However, it is possible that induction would have been found if test trials with the explicitly-unpaired CS- and CS+ had been given within the same session prior to the time that the reactions to the two stimuli were fully developed.

Reversal Conditioning

In the reversal test of inhibition it was found that it was more difficult to establish decelerative HR CRs to CS- in the explicitly-unpaired groups than in the truly-random and CS-alone groups. This finding adds additional support to the proposition that the explicitly-unpaired paradigm generated a CS with properties that were different from those established with the truly-random and CS-alone procedures. Taken together, the results of the "unpaired" phase and the observed decrement in reversal conditioning suggest that the explicitly-unpaired CS and US paradigm provided CS- with inhibitory tendencies.

During the initial part of the reversal conditioning phase, the explicitly-unpaired groups displayed HR accelerations that generally matched their terminal responses to CS- during the "unpaired" phase. It should be noted that the occurrence of these accelerative responses followed an elapsed time of nearly 2 hours, six reconditioning trials to CS+ and 12 induction trials with CS+ and CS-. The persistence of these responses is consistent with the view that inhibitory responses may be very resistant to extinction (Frey & Butler, 1977; Zimmer-Hart & Rescorla, 1974).

To some extent, the observed differences in the performance of the groups during reversal conditioning may have been due to the fact that the CS-alone group showed rather rapid acquisition of the CR. This might

have been expected since the CS-alone group exhibited decelerative HR responses to CS- throughout the "unpaired" phase. Moreover, studies have shown that CS-alone trials of the type given the CS-alone group can facilitate subsequent HR conditioning (Fitzgerald & Hoffman, 1976; Ray & Brener, 1973). Together, these findings suggest that in the absence of a special relationship with a US, CS-alone trials do not generate inhibitory response characteristics in heart rate.

Two alternative explanations to that of conditioned inhbition have been proposed to account for the slowdown in conditioning that has been observed following experience with explicitly-unpaired training paradigms (Cunningham et al, 1977; Hearst, 1972; Gray, 1975). One view that has been suggested is that subjects receiving unpaired CSs and USs are not attentive to CS- during subsequent reversal conditioning (Hearst, 1972; Mackintosh, 1975; Sutherland & Mackintosh, 1971). This explanation does not fit the present findings since the explicitly-unpaired groups demonstrated their attentiveness to CS- by responding with HR accelerations upon it presentation.

A second explanation accountsfor a decrement in reversal conditioning on the basis of peripheral responses that are assumed to interfere or compete with the target responses (Osgood, 1953; Kimble, 1961). Guthrie (1935) was one of the earliest proponents of a competing response interpretation of response decrements. On this view, retarded reversal performance would be attributed to the prior acquisition of a response to CS- which directly interferred with the development of the excitatory CR. Impeded reversal learning in the explicitly-unpaired groups of the present study

would therefore be due to the fact that their accelerative HR responses to CS- were opposite in direction to their decelerative responses to CS+. Since the truly-random and CS-alone groups did not display accelerative HR responses to CS-, retardation of re-conditioning would not be expected in these groups according to this hypothesis.

In evaluating the competing response hypothesis, Cunningham et al. (1977) noted that the presence of accelerative HR responses to a CS had not been shown to retard conditioning in a prior study (Fitzgerald & Hoffman, 1976). In fact, conditioning in that experiment was facilitated to such a CS. In the absence of further results, however, Cunningham et al. concluded that a final decision on this point could not be made.

Cunningham et al. (1977) suggested that the cardioaccelerations observed in their study to the explicitly-unpaired CS might have reflected activity in a central state that had the capacity to impede conditioning of cardiodeceleration. They proposed thatthis state may have involved increased sympathetic output which would be antagonistic to increased vagal firing that was previously demonstrated to be largely responsible for the decelerative HR CSs (Fitzgerald, Martin, & O'Brien, 1973).

The problem of selecting between a central inhibition and a peripheral competing-response interpretation of the outcomes of tests of conditioned inhibition has been addressed by a number of authors with no satisfactory resolution of the issue (Black, 1971; Gormezano & Kehoe, 1975; Rachlin 1973; Trapold & Overmier, 1972). Rachlin (1973) reflected the general sentiments on this question by noting that is was problematic whether a distinction between the presence of a central inhibitory state without

peripheral concommitants was empirically testable.

Inhibition of Delay

The major outcome of the 10-sec inhibition of delay phase was that the magnitude of the decelerative CRs of each group increased progressively during the full length of the 10-sec interval. Thus, while the HR CRs during the first 6 sec of the 10-sec interval were equivalent to those obtained during excitatory conditioning, the additional 4 sec allowed subjects to achieve greater maximum responses. This result is consistent with those of earlier studies in which a positive relationship was observed between the length of the CS-US interval and CR magnitude. The duration of CS-US intervals has been found to be positively related to the magnitude of both accelerative HR CRs (Black & Black, 1967; Church & Black, 1958) and decelerative HR CRs (Fitzgerald & Teyler, 1970; Fitzgerald & Martin, 1971).

Since changes in the HR responses were shown within the first few trials using the 10-sec CS-US interval, the increases in the magnitudes of the HR CRs were probably not based on associative processes. Rather, extending the CS-US interval from 6 to 10 sec seemed to provide an opportunity for the animals to exhibit more completely what had already been learned on previous trials with the shorter CS-US interval. These results suggest that CS-US intervals of 6 sec or less that have typically been used in other studies of HR conditioning in rats (Holdstock & Schwartzbaum, 1965; Fitzgerald & Martin, 1971; Fitzgerald & Stainbrook, 1977), may not have provided an accurate estimate of the full excitatory strength of the

CR. Maximum HR changes in prior experiments have generally averaged 20 to 25 bpm, whereas in the current experiment they reached 30 to 35 bpm with the extended CS-US interval.

In this study, response suppression or inhibition of HR changes were not observed during the early part of either the 6 sec or 10 sec CS-US interval. Thus, HR decreases were apparent in each group within the first 2-sec periods of the CS using both intervals. In most investigations providing information on inhibition of delay, the response systems have involved such reactions as salivation and leg flexion (Pavlov, 1927; Konorski, 1948). In contrast to HR, these responses typically show relatively low levels of background activity. Evidence of the presence of inhibition of delay with these discrete reactions has been reflected by the latency of the first sign of activity after the presentation of the CS. The longer the latency, the greater the amount of inhibition of delay. In studies of conditioned HR, the term inhibition of delay has been used descriptively to characterize observations of positively accelerated response gradients (Church & Black, 1958; Fitzgerald & Martin, 1971; Lynch, 1973). These gradients reflected the fact tht the magnitude of the HR change increased as the time for the presentation of the US approached. Empirically, this is what occurred in the current experiment using both the 6-sec and the 10-sec CS-US interval.

Extension of the CS-US interval to 20 sec in the second inhibition-of-delay phase did not produce an increase in the magnitude of the HR CRs beyond what was found with the 10-sec interval. Also, there was no evidence of suppression of the HR CR during the early part of the CS-US

interval, with each group showing small HR decreases shortly after CS onset. The failure to observe a further increase in the magnitude of the HR CR when the CS-US interval was extended from 10 sec to 20 sec could indicate that the CR had reached a ceiling with the 10-sec interval. At the same time, however, it is important to note that while peak HR decelerations were reached within the first 10 sec of the 20-sec interval, the decelerations were maintained at full strength for the remainder of the interval. In some animals, this meant that HR decelerations measuring 50 bpm or more were maintained for over 10 sec. The magnitude and duration of these HR changes suggest that it may be worthwhile to explore the use of long CS-US intervals in studies of the involvement of chronic fear or anxiety on cardiovascular abnormalities.

Ethanol Findings

Both the .8 and 1.6-g/kg doses of ethanol retarded the development of HR accelerations of the explicitly-unpaired groups to CS- during the early part of the "unpaired" phase. This interference occurred within 12 trials or during a period from about 30 to 90 min after the administration of ethanol. On subsequent trials, there were no differences between the saline and ethanol explicitly-unpaired groups. As a consequence, the accelerative HR responses of all the explicitly-unpaired groups were equivalent during nearly two thirds of the "unpaired" phase.

One explanation that may account for the temporary retardation of the accelerative HR responses in the ethanol groups concerns the process of discrimination. It will be recalled that all of the groups exhibited decelerative responses to CS- at the beginning of the "unpaired" phase. However, the responses of the explicitly-unpaired ethanol groups were slightly

larger in magnitude than those of the saline group. Earlier, it was suggested that the presence of these initial HR decelerations to CS- were probably due to stimulus generalization between CS+ and CS-. If this assumption is granted, then it might be argued that stimulus generalization was simply augmented by ethanol. The plausibility of this suggestion is strengthened by other observations showing that ethanol can disrupt or make difficult discriminative responding to dissimilar stimulus events (Overton, 1967, 1974; Thompson & Pickens, 1971; Barry, 1974).

In a prior study of the effects of ethanol on HR conditioning (Fitzgerald & Stainbrook, 1977), it was found that a large dose of the drug measuring 2.4 g/kg eliminated the decelerative HR CR and modified the HR UR. A lower dose of .8 g/kg had little or no effect on the responding. Fitzgerald and Stainbrook (1977) observed that with the 2.4 g/kg dose accelerative HR changes to shock were reduced while decelerative changes were augmented. The induction phase in the current experiment provided an opportunity to assess the effects of ethanol on both accelerative and decelerative HR changes. In keeping with what has been observed previously (Fitzgerald & Stainbrook, 1977) for learned HR responses, the HR reactions to CS- and CS+ on the induction trials were not modified by the presence of ethanol.

Two factors can be mentioned that may have contributed to this outcome. First, there was a relatively long interval between the administration of ethanol and the beginning of the induction phase (approximately 60 min). It may be recalled that the interferring effects of ethanol that were found in the "unpaired" phase occurred within 30 to 60 min after the ethanol was

given. Another factor that may be relevant is the amount of training that was used to instill the HR reaction to CS- and CS+ prior to the induction test. Thus, the responses to CS- and CS+ had been well differentiated, with consistent accelerative and decelerative HR changes occurring to each CS, respectively. There is some evidence that well established responses are less easily disrupted by ethanol than are newly or partially learned responses (Overton, 1967).

The main effect of ethanol during reversal conditioning was that subjects given saline or ethanol on both day 2 and day 3 showed more rapid reversal than those subjects switched from saline to ethanol or from ethanol to saline. This suggests that the potential interfering effects of the accelerative response tendencies developed during the "unpaired" phase were partially decremented when subjects were switched from one drug state to the other. This outcome is consistent with the findings of a considerable number of other experiments (Overton, 1967, 1974) showing that learning is more rapid when the drug state is kept constant than when it is changed. This effect has been labeled state-dependent learning and represents a major focus of contemporary research efforts.

While both the .8-and 1.6-g/kg ethanol doses elevated baseline HR during all phases of day 2 and day 3, corresponding increases in baseline movement were not observed. This outcome reflects an independent relationship between HR and movement. The elevation of HR by ethanol is consistent with the results of a number of prior investigations (Doctor et al., 1966; Riff et al., 1969; Fitzgerald & Stainbrook, 1977; Webb & Degerli, 1965). Fitzgerald and Stainbrook (1977) found that a low dose of ethanol

(.8 g/kg) elevated HR, while a high dose (2.4 g/kg) depressed HR. The results of the current study and those of Fitzgerald and Stainbrook (1977) suggest that low to moderate doses of ethanol (0.5 - 2.0 g/kg) are associated with HR increases, while high doses (greater than 2.0 g/kg) depress cardiac rate (Juchems & Klobe, 1969; Fitzgerald & Stainbrook,1977; Webb & Degerli, 1965).

The observation that ethanol elevated HR bears importantly on the choice of an explanation of the accelerative HR responses shown by the explicitly-unpaired group to CS- during the "unpaired" phase. According to the Law of Initial Values (Wilder, 1967), the direction and magnitude of autonomically mediated responses are often determined by the baselevel activity prior to the delivery of the eliciting stimulus. The higher the baselevel, the more difficult it is to obtain increases in activity. On this basis, the development of accelerative HR responses should have been more difficult to obtain in the explicitly-unpaired-ethanol groups than in the explicitly-unpaired saline group. The absence of an apparent effect of baselevel HR on the direction or magnitude of HR responses in rats agrees with what has been found in several other investigations (e.g., Fitzgerald & Teyler, 1970; Fitzgerald & Stainbrook, 1977).

Finally, although ethanol markedly influenced HR, it had very little effect on movement. The only reliable effect of ethanol on movement occurred during the early part of the "unpaired" phase or approximately 30 min after the ethanol was administered. At this time, the .8 g/kg dose of ethanol was associated with a considerable increase in baselevel movement. Other experiments have also shown that low doses of ethanol can produce

increases in motor activity (Buckalew & Cartwright, 1968; Eriksson & Walgren, 1967). While outcomes of this type have been used as evidence of the disinhibiting effects of ethanol, they can also be accounted for by assuming that certain doses of ethanol have an apparent energizing or excitatory effect on behavior.

SUMMARY AND CONCLUSIONS

An examination was made of the inhibitory response eliciting properties of CSs employed in explicitly-unpaired, CS-alone, and truly-random procedures. Measurement of heart-rate responses and skeletal-motor activity was made during both training and testing phases. The subjects were 88 rats each of which was trained and tested in successive phases over a period of three consecutive days. All animals were first given 30 excitatory conditioning trials with CS (CS+) consistently being paired with the US. Subjects were then randomly assigned to one of three principal treatment groups, explicitly-unpaired, CS-alone, or truly-random. During the "unpaired" phase, the explicitly-unpaired group was given 54 negatively correlated CS and US presentations, the truly-random group received an equivalent number of CSs and USs which were programmed randomly and independently. Finally, the CS-alone group was given the same number of CS exposures as the two other groups but did not receive any US presentations. Uniformly, the CS (CS-) employed in this phase was different from the (CS+) used during excitatory conditioning. In addition, an evaluation of the influence of two doses of ethanol (.8 g/kg and 1.6 g/kg) on inhibitory responding in subgroups of the explicitly-unpaired group was made both during the "unpaired" phase and in subsequent test phases. Following the "unpaired" phase an assessment of the comparative inhibitory characteristics of the CSs of the three principal groups was made. Subjects were tested in reversal conditioning, Pavlovian positive induction, and inhibition of delay procedures.

The principal findings were that during excitatory conditioning the HR responses of all groups were characteristically decelerative. However, in the "unpaired" phase the directions of the HR responses of the three basic groups were distinctly different. In the explicitly-unpaired group, HR deceleration was progressively replaced by HR acceleration. The direction and magnitude of this response was opposite the excitatory HR CR. On the other hand, the response of the truly-random group was quite small and variable, while that of the CS-alone group was uniformly decelerative. Excitatory conditioning of the explicitly-unpaired group during the reversal test was retarded relative to that to the CS-alone group. Differential outcomes among the groups were not obtained in the positive induction and inhibition of delay procedures. While ethanol reliably elevated heart-rate levels, the high rates were not systematically related to the magnitude of either decelerative or accelerative HR changes to the CSs.

The finding that the explicitly-unpaired groups developed marked accelerative HR responses during the "unpaired" phase which were directionally opposite their excitatory HR CRs suggested that the CS- might have been inhibitory. This assumption was strengthened by the fact that the development of excitatory conditioning to the CS- in the explicitly-unpaired groups during reversal was retarded. Taken together, these outcomes suggest that explicit-unpairing of CSs and US may be a necessary and sufficient condition for establishing an inhibitory CS. It was however noted that the outcomes might also be attributed to the presence of competing or antagonsitic peripheral responses. The difficulty of clearly distinguishing between a conditioned inhibition and peripheral competing response hypothesis was discussed.

REFERENCES

Andreyev, L.A. The effect of single and repeated doses of alcohol on conditioned reflexes in the dog. Archives Internationales de Pharmacodynamie et de Therapie, 1934, 48, 117-128.

Anokhin, P.K. Biology and neurophysiology of the conditioned reflex and its role in adaptive behavior. New York: Pergamon Press, 1974.

Ayres, J.J.B., Benedict, J.O., & Witcher, E.S. Systematic manipulation of individual events in a truly-random control in rats. Journal of Comparative and Physiological Psychology, 1975, 88, 97-103.

Barry, H. III. Classification of drugs according to their discriminable effects in rats. Federation Proceedings, 1974, 33, 1814-1824.

Beritoff, I.S. Neural mechanisms of higher vertebrate behavior. Boston: Little Brown & Company, 1965.

Bindra, D. & Reichert, H. The nature of dissociation: Effects of transitions between normal and barbiturate-induced states on reversal learning and habituation. Psychopharmacologica (Berlin), 1967, 10 330-344.

Black, A.H. Autonomic aversive conditioning in infrahuman subjects, In F.R. Brush (Ed.) Aversive conditioning and learning. New York; Academic Press, 1971.

Black, R.W. & Black, P.E. Heart-rate conditioning as a function of interstimulus interval in rats. Psychonomic Science, 1967, 8, 219-220.

Boakes, R.A., & Halliday, M.S. Inhibition and learning. London: Academic Press, 1972.

Buckalew, L.W. & Cartwright, G.M. General and differential effects of five ethanol doses on the albino rat. Psychological Reports, 1968, 23, 1151-1154.

Bull, J.A., & Overmier, J.B. Additive and subtractive properties of excitation and inhibition. Journal of Comparative and Physiological Psychology, 1968, 66, 511-514.

Caul, W.F. Effects of amobarbital on discrimination acquisition and reversal. Psychopharmacologica (Berlin), 1967, 11, 414-421.

Chacto, C., & Lubow, R.E. Classical conditioning and latent inhibition in the white rat. Psychonomic Science, 1967, 9, 135-136.

Church, R.M., & Black, A.H. Latency of the conditioned heart rate as a function of CS-US interval. Journal of Comparative and Physiological Psychology, 1958, 51, 478-482.

Cunningham, C.L., Fitzgerald, R.D., & Francisco, D.L. Excitatory and inhibitory consequences of explicitly-unpaired and truly-random conditioning procedures on heart rate in rats. Animal Learning & Behavior, 1977, 5, 135-142.

Doctor, R.G., Naitoh, P., & Smith, J.C. Electroencephalographic changes and vigilance behavior during experimentally induced intoxication with alcoholic subjects. Psychosomatic Medicine, 1966, 28, 605-615.

Dworkin, S., Bourne, W., & Raginsky, B.B. Changes in conditioned responses brought about by anesthetics and sedatives. Canadian Medical Association Journal, 1937, 37, 136-139.

Eriksson, K., & Wallgren, H. Behavior of rats under the influence of ethyl alcohol in an open-field situation. Scandanavian Journal of Psychology, 1967, 8, 257-267.

Fearing, F. Reflex action; A study in the history of physiological psychology. New York: Williams and Wilkins, 1930.

Fitzgerald, R.D., & Hoffman, J.W. Classically conditioned heart rate in rats following preconditioning exposure to the CS. Animal Learning & Behavior, 1976, 4, 58-60.

Fitzgerald, R.D., & Martin, G.K. Heart-rate conditioning in rats as a function of inter-stimulus interval. Psychological Reports, 1971, 29, 1103-1110.

Fitzgerald, R.D., Martin, G.K., & Hoffman, J.W. Classical conditioning of heart rate in rats using direct vagal stimulation as a US. Physiology and Behavior, 1975, 14, 449-456.

Fitzgerald, R.D., Martin, G.K., & O'Brien, J.H. Influence of vagal activity on classically conditioned heart rate in rats. Journal of Comparative and Physiological Psychology, 1973, 83, 485-491.

Fitzgerald, R.D., & Stainbrook, G.L. Effects of ethanol on classically conditioned heart rate in restrained rats.(Submitted for publication, 1977).

Fitzgerald, R.D., & Teyler, T.J. Trace and delayed heart-rate conditioning in rats as a function of US intensity. Journal of Comparative and Physiological Psychology, 1970, 70, 242-253.

Fitzgerald, R.D., Vardaris, R.M., & Brown, J.S. Classical conditioning of heart-rate deceleration in the rat with continuous and partial reinforcement. Psychonomic Science, 1966, 6, 437-438.

Fitzgerald, R.D., Vardaris, R.M., & Teyler, T.J. An on-line method for measuring heart rate in conditioning experiments. Psychophysiology, 1968, 4, 352-353.

Frey, P.W., & Butler, C.S. Extinction after aversive conditioning: An associative or nonassociative process? Learning & Motivation, 1977, 8, 1-17.

Frey, P.W. & Ross, L.E. Differential conditioning of the rabbits eyelid response with an examination of Pavlov's induction hypothesis. Journal of Comparative and Physiological Psychology, 1967, 64, 277-283.

Gantt, W.H. Effect of alcohol on cortical and subcortical activity measured by the conditioned-reflex method. Bulletin of the Johns Hopkins Hospital, 1935, 56, 61-83.

Gantt, W.H. Acute effect of alcohol on autonomic (sexual, secretory, cardiac) and somatic responses, in H.Himwich (Ed) Alcoholism: basic aspects and treatment. American Association for the Advancement of Science, Washington, D.C., 1957.

Gantt, W.H. Cardiovascular component of the conditioned reflex to pain, food, and other stimuli, Physiological Reviews, supplement #4, 1960, 266-291.

Goldman, P.S., & Doctor, R.F. Facilitation of bar pressing and suppression of conditioned suppression in cats as a function of alcohol. Psychopharmacologica, 1966, 9, 64-72.

Gormezano, I., & Kehoe, E. Classical conditioning: Some methodological-conceptual issues. In W.K. Estes (Ed.) Handbook of learning and cognitive Processes. vol 2, New Jersey: Lawrence Earlbaum, 1975.

Graham, F.K., & Clifton, R.K. Heart-rate change as a component of orienting response. Psychological Bulletin, 1966, 65, 305-320.

Gray, J.A. Elements of a two process theory of learning. London: Academic Press, 1975.

Guthrie, E.R. The psychology of learning. New York: Harper & Row, 1935.

Hearst, E. Some persistent problems in the analysis of conditioned inhibition. In R.A. Boakes & M.S. Halliday (Eds), Inhibition and learning. London: Academic press, 1972.

Hearst, E. Besley, S., & Farthing, G. Inhibition and the stimulus control of operant behavior. Journal of the Experimental Analysis of Behavior, 1970, 14, 373-409.

Hammond, L.J. Increased responding to CS- in differential CER. Psychonomic Science, 1966, 5, 337-338.

Hammond, L.J. Retardation of fear acquisition by a previously inhibitory CS. Journal of Comparative and Physiological Psychology, 1968, 66, 756-759.

Hilgard, E.R. & Marquis, D.G. Conditioning and Learning. New York: Appleton-Century-Crofts, 1949.

Holdstock, T.L., & Schwartzbaum, J.S. Classical conditioning of heart rate and galvanic skin response in the rat. Psychophysiology, 1965, 2, 25-38.

Holloway, F.A., and Wansley, R.A. Factors governing the vulnerability of DRL operant performance to the effects of ethanol. Psychopharmacologica, 1973, 28, 351-362.

Holloway, F.A. and Vardiman D.R. Dose response effects of ethanol on appetitive behaviors Psychonomic Science, 1971, 24, 218-220.

Horn, G., & Hinde, R.A. (Eds.) Short-term changes in neural activity and behavior. London: Cambridge University Press, 1970.

Ischlondsky, N.E. Brain and behavior: Induction as a fundamental mechanism of neuro-phychic activity. St. Louis: C.V. Mosby company, 1949.

Jensen, D.D. Operationism and the question "is this behavior learned or innate?" Behavior, 1961, 7, 1-8.

Juchems, R., & Klobe, R. Hemodynamic effects of ethyl alcohol in man. American Heart Journal, 1969, 78, 133-134.

Kimble, G.A. (Ed.) Hilgard & Marquis' Conditioning and Learning (rev. ed.) New York: Appleton-Century, 1961.

Konorski, J. Conditioned reflexes and neuron organization. Cambridge, England: Cambridge University Press, 1948.

Konorski, J. Integrative activity of the brain: An interdisciplinary approach. Chicago: University of Chicago Press, 1967.

Kremer, E.F. Truly-random and traditional control procedures in CER conditioning in the rat. Journal of Comparative and Physiological Psychology, 1971, 76, 441-448.

Kremer, E.F., & Kamin, L.J. Truly-random control procedure: associative or nonassociative effects in rats? Journal of Comparative and Physiological Psychology, 1971, 74, 203-210.

Laties, V.G., & Weiss, B. Effects of alcohol on timing behavior. Journal of Comparative and Physiological Psychology, 1962, 55, 85-91.

Leonard, D.W., Weimer, J., & Albin, R. An examination of Pavlovian induction phenomena in differential instrumental conditioning. Psychonomic Science, 1968, 12, 89-90.

Lubow, R.E. Latent inhibition. Psychological Bulletin, 1973, 79, 398-407.

Lubow, R.E., & Moore, A.U. Latent inhibition: the effect of non-reinforced preexposures to the conditioned stimulus. Journal of Comparative and Physiological Psychology, 1959, 52, 416-419.

Lynch, J.L. Pavlovian inhibition of delay in cardiac and somatic responses in dogs. Psychological Reports, 1973, 32, 1339-1346.

Mackintosh, N.J. The psychology of animal learning. New York: Academic Press, 1974.

Maier, S.F., Rapaport, P., & Wheatley, K.L. Conditioned inhibition and the UCS-CS interval. Animal Learning and Behavior, 1976, 4, 217-220.

Martin, G.K., & Fitzgerald, R.D. Factors affecting the duration of classically conditioned heart-rate responses of rats: influence of reinforcement contingencies, degree of restraint, and skeletal-motor activity (Submitted for publication, 1978).

Moscovitch, A., & LoLordo, V.M. Role of safety in the pavlovian backward conditioning procedure. Journal of Comparative and Physiological Psychology, 1968, 66, 673-678.

Naitoh, P. The effect of alcohol on the autonomic nervous system of humans In B. Kissin and H. Begleiter (Eds.) The biology of alcoholism, vol 2: Physiology and Behavior. New York; Plenum Press, 1972, 367-425.

Nikiforovsky, P.M. (Ethanol effects on classically conditioned salivary responses) Thesis, St Petersburg, 1910. Archives Internationales de Pharmacodynamie et de Therapie, 1934, 48, 118.

O'Gorman, J.G. Habituation of the orienting reaction as a function of stimulus information. Psychonomic Science, 1971, 22, 331-332.

O'Gorman, J.G. Change in stimulus conditions and the orienting response. Psychophysiology, 1973, 10, 465-470.

Osgood, C.E. Method and theory in experimental psychology. New York: Oxford University Press, 1953.

Overton, D.A. Dissociated learning in drug states (state-dependent learning) In D.H. Efron (Ed.) Psychopharmacology: A Review of Progress 1957-1967, Public Health Service Publication no. 1836, Washington, D.C. 918-930.

Overton, D.A. Experimental methods for the study of state-dependent learning. Federation Proceedings, 1974, 33, 1800-1813.

Pavlov, I.P. Conditioned reflexes. (Translated and edited by G.V. Anrep). New York: Dover, 1927.

Plotkin, H.C. & Oakley, D.A. Backward conditioning in the rabbit (Oryctolargus Cuniculus). Journal of Comparative and Physiological Psychology, 1975, 88, 586-590.

Prokasy, W.F. Classical eyelid conditioning: Experimenter operations, task demands, and response shaping. In W.F. Prokasy (Ed.) Classical conditioning: A symposium. New York: Appleton-Century-Crofts, 1965.

Rachlin, H. Contrast and Matching. Psychological Review, 1973, 80, 217-234.

Ray, R.D., & Brener, J. Classical heart rate conditioning in the rat: the influence of curare and various setting operations. Conditional reflex, 1973, 8, 224-235.

Reiss, S., & Wagner, A.R. CS habituation produces a "latent inhibition effect" but no active conditioned inhibition. Learning and Motivation, 1972, 3, 237-245.

Rescorla, R.A., & LoLordo, V.M. Inhibition of avoidance behavior. Journal of Comparative and Physiological Psychology, 1965, 59, 406-412.

Rescorla, R.A. Predictability and number of pairings in pavlovian fear conditioning. Psychonomic Science, 1966, 4, 383-384.

Rescorla, R.A. Pavlovian conditioning and its proper control procedures. Psychological Review, 1967, 74, 71-80.

Rescorla, R.A. Inhibition of delay in Pavlovian fear conditioning. Journal of Comparative and physiological Psychology,1967(a)64, 114-120.

Rescorla, R.A. Pavlovian conditioned fear in Sidman avoidance learning. Journal of Comparative and Physiological Psychology, 1968, 65, 55-60.

Rescorla, R.A. Pavlovian conditioned inhibition. Psychological Bulletin, 1969, 72, 77-94.

Rescorla, R.A. Conditioned inhibition of fear resulting from negative CS-US contingencies. Journal of Comparative and Physiological Psychology, 1969 (a), 67, 504-509.

Rescorla, R.A. Summation and retardation tests of latent inhibition. Journal Of Comparative and Physiological Psychology, 1971, 75, 77-81.

Rescorla, R.A. Pavlovian excitatory and inhibitory conditioning. In W.K. Estes (Ed.) Handbook of learning and cognitive processes, vol 2, New Jersey: Lawrence Earlbaum, 1975 (a).

Rescorla, R.A. A model of pavlovian conditioning. In V.S. Rusinov (Ed.) Mechanisms of formation and inhibition of conditional reflexes. Moscow: "Nauka" Academy of Sciences of the U.S.S.R., 1975 (b).

Rescorla, R.A., & Wagner, A.R. A theory of pavlovian conditioning: variations in the effectiveness of reinforcement and nonreinforcement. In A.H. Black & W.F. Prokasy (Eds.), Classical conditioning II: Current theory and research. New York: Appleton-Century-Crofts, 1972.

Rescorla, R.A., & Holland, P.C. Some behavioral approaches to the study of learning. In E. Bennett & M. Rosenzweig (Eds.), Neural mechanisms of learning and memory. Cambridge, Mass: MIT Press, 1976.

Riff, D.R., Jain, A.C., & Doyle, J.T. Acute hemodynamic effects of ethanol on normal human volunteers. American Heart Journal, 1969, 78, 592-597.

Sanders, S.H., & Pilley, J. Effects of alcohol on timing behavior in rats. Quarterly Journal of Studies on Alcohol, 1973, 34, 367-372.

Sechenov, I. Reflexes of the brain. Cambridge, Mass.:MIT Press, 1965.

Senf, G.M., & Miller, N.E. Evidence for positive induction in discrimination learning. Journal of Comparative and Physiological Psychology, 1967, 64, 121-1277.

Sidman, M. Technique for the assessment of drug effects on timing behavior. Science, 1955, 122, 925.

Siegel, S. Effects of CS habituation on eyelid conditioning. Journal of comparative and Physiological Psychology, 1969, 68, 245-248.

Siegel, S., & Domjan, M. Backward conditioning as an inhibitory procedure. Learning and Motivation, 1971, 2, 1-11.

Siegel, S., & Domjan, M. The inhibitory effect of backward conditioning as a function of the number of backward pairings. Bulletin of the Psychonomic Society, 1974. 4, 122-124.

Sokolov, E.N. Neuronal models and the orienting reflex. In M.A. Brazier (Ed.), The central nervous system and behavior. New York: Josiah Macy Jr. Foundation, 1960.

Sokolov, E.N. Higher nervous functions: the orienting reflex. Annual Review of Physiology, 1963, 25, 545-580.

Stein, L. Habituation and stimulus novelty: A model based on classical conditioning. Psychological Review, 1966, 73, 352-356.

Stevens, S.S. Handbook of experimental psychology, New York: Wiley, 1951.

Sutherland, N.S., & Mackintosh, N.J. Mechanisms of animal discrimination learning. New York: Academic Press, 1971.

Thompson, G. & Pickens, R. (Eds) Stimulus properties of drugs, New York: Appleton-Century-Crofts, 1971.

Trapold, M.A., & Overmier, J.B. The second learning process in instrumental training. In A.H. Black and W.F. Prokasy (Eds.), Classical Conditioning II. New York: Academic Press, 1972.

Wagner, A.R., & Rescorla, R.A. Inhibition in pavlovian conditioning: Application of a theory. In R.A. Boakes & M.S. Halliday (Eds), Inhibition and learning. London: Academic Press, 1972.

Webb, W.R. & Degerli, I.U. Ethyl alcohol and the cardiovascular system. Journal of the American Medical Association, 1965, 191, 77-80.

Weber, W. & Weber, E. Early work on inhibition published in 1845. Cited in F. Fearing, Reflex action: A study in the history of physiological psychology, Cambridge, Mass. MIT Press, 1970.

Wilder, J. Stimulus and response: the law of initial value. Bristol: John Wright & Sons, 1967.

Woodworth, R.S., & Schlosberg, H. Experimental psychology (Rev ed.). New York: Holt, Reinhart, and winston, 1954.

Zavadski, I.V. (The effect of ethanol on classical conditioning),Transactions of the Society of Russian Physicians, 1908. Archives internationales de Pharmacodynamie et de Therapie, 1934, 48, 117-118.

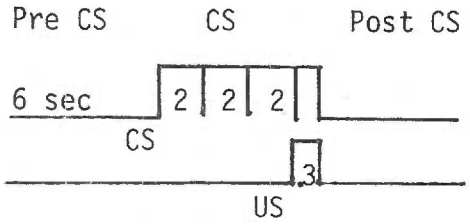
Zimmer-Hart, C.L., & Rescorla, R.A. Extinction of pavlovian conditioned inhibition . Journal of Comparative and Physiological Psychology, 1974, 86, 837-845.

EXPERIMENTAL DESIGN

Day 1 — Three Phases

Adaptation	CS-alone	Excitatory Conditioning (CS+)
	12 4KHz & 12 8KHz tone CSs	30 paired CSs and USs 4 or 8 KHz CSs
	ITI 60, 90, 120 sec (M=90)	ITI 120, 150, 180 sec (M=150) 6.3 sec CS, .3 sec US
30 min	30 min	75 min

Delayed Procedure



Day 2 — Two Phases

Adaptation — "Unpaired" phase (CS-)

Basic Groups	Drug Treatment	Stimulus Exposure
CS-alone	Saline	54 CS only,
Truly-random	Saline	54 CS and 54 US (random)
Explicilty-unpaired	Saline	
	.8 g/kg ethanol	54 CS and 54 US (negatively correlated)
	1.6 g/kg ethanol	

ITI 240, 300, 360 sec (M=300)
270 min (4½) hr

30 min

Day 3 — Six Phases

Adaptation	"Unpaired"	Paired	Induction	Reversal	Inhibition of Delay
	6 CS-	6 CS+	12 CS-/12 CS+	24 (CS-)-US	12 (CS-)-US
Basic Groups					
CS-alone	ISI 6 sec	ISI 6 sec	ISI 6 sec	ISI 6 sec	ISI 10 & 20 sec
Truly-random					
Explicitly-un Saline					
Saline .8 g/kg	ITI 120, 150, 180 sec (M=150) all phases				
1.6 g/kg					
30 min	30 min	15 min	30 min	60 min	30 min