Time scale invariance in Inhibition: The other side of the coin

Peter Balsam, C.R. Gallistel, cast of thousands

Conditioned inhibition of behavior is generally thought to occur when a cue signals that an otherwise expected unconditioned stimulus will not occur. Consider the procedure used by Rescorla (1969) in his classic experiments on contingency (Figure 1). The three top rows depict positive, zero and negative contingencies between the conditioned stimulus (CS) and unconditioned stimulus (US). In all three protocols, the CS state (the presence of a tone) is superimposed on the background state or “context” (the presence of the chamber in which the conditioning is conducted). Although the probability of a US in the presence of the CS is identical in all three protocols, the positive contingency results in excitatory conditioned responses; the zero contingency results in no systematic conditioning ; and the negative contingency results in inhibition of conditioned responses. These data were a foundation of contingency theory as well as subsequent theories in which the associative value of a CS was determined both by the USs delivered in the presence of the CS and the background and by the USs delivered in the presence of only the background e.g. (Rescorla & Wagner, 1972).



**Figure 1.** *CS-US contingency: The presence of the CS may increase the expected rate of reinforcement (top) have no effect on it (middle) or decrease it (bottom two rows).*

More recently we have suggested that understanding blocking, background conditioning, and overshadowing phenomena must be understood in the light of the extensive evidence that subjects learn temporal structure (P. D. Balsam, Drew, & Gallistel, 2010; P. D. Balsam, Fairhurst, & Gallistel, 2006; P.D. Balsam & Gallistel, 2009; Ward, Gallistel, & Balsam, 2013; Ward et al., 2012). Informativeness was defined as the factor by which the presence of the CS *increases* the expected *rate* of reinforcement which is also the factor by which its presence *decreases* the *expected wait* for the next reinforcement. This factor determines the subject’s information gain from the CS, because it describes the reinforcement entropy in the presence of the CS relative to the reinforcement entropy in its absence. The reinforcement entropy is , where is the currently expected rate of reinforcement. Since is the expected wait till the next reinforcer, the reinforcement entropy measures the subject’s uncertainty about how long it should expect to wait for the next reinforcement; the lower the entropy the less the subject’s uncertainty. Put another way, the subject’s uncertainty about when to expect the next reinforcement grows in proportion to the logarithm of the average interval between reinforcements. We suggested (see also Fantino, Prestin & Dunn, 1993) that the learning rate, operationally defined as the reciprocal of trials to acquisition, was proportional to informativeness {Balsam, 2010 #8621;Balsam, 2009 #8102;Kalmbach, 2019 #415}.

A related formulation (Gallistel & Wilkes, 2016) is that the learning rate is proportional to the *information gain* from the CS, as measured by the Kullback-Leibler divergence *of* the CS state *from* the background state, denoted . The Kullback-Leibler divergence is also known as the relative entropy of the two entropy states. We italicize ‘of’ and ‘from’ because the divergence is asymmetric. Given two unequal rates of reinforcement, and , such that , the information gain from a CS that signals the transition from to , (from the lower entropy state to the higher entropy state) is greater than the gain from a CS that signals the opposite transition, from the higher entropy state to the lower entropy state. From an information-theoretic perspective, this asymmetric divergence is the most intuitive objective correlate of a learning rate, because it measures the rate at which information about the divergence of one distribution from another accumulates as the number of observations increases (Cover & Thomas, 1991). The asymmetry in the divergence means that an increase in entropy by a given factor is objectively easier to detect than a decrease. Consider partial reinforcement as an example. It will take a single instance of non-reinforcement for a subject to detect a transition from 100% to say 90% reward. Whereas it will take many more reinforced trials before a subject has good evidence that there has been a transition from 90% reward to 100%. The Kullback-Leibler divergence objectively describes this asymmetry.

Consider the bottom row of Figure 1 from a temporal learning point of view. A subject will encode the times between USs and compute the average rate of USs in the context. The subject should also compute the average rate of USs signaled by the onset of the CS and then the informativeness. This would lead to a negative value for the informativeness of the CS and perhaps this is what regulates inhibitory control and the rate of learning. In a formal sense this represents an increase in the uncertainty about when a US will occur relative to uncertainty in the context alone. Perhaps a more intuitive way to understand the temporal parsing of the protocol is to consider the inverse of the rates, the average delays to reward. When the CS comes on it signals an increase in the average delay to reward relative to the context alone. Thus from a temporal point of view the degree of inhibition will depend on the average delay to the next US signaled by the onset of the CS. In contrast,the Wilkes & Gallistel point of view suggests that it is the information gain from the CS that matters. The gain is positive regardless of whether the expected wait decreases or increases. It depends only on the ratio of the expected rates in the presence and absence of the CS. The gain varies depending on whether the CS increases the rate by a given factor or decreases it by that same factor; in other words, it depends on both the factor by which the rate changes and the sign of the change.

Another question is whether the factor(s) that determine the rate of learning are the same as those that determine asymptotic performance. On our first hypothesis, we expect them both to be driven by the same factor namely the change in the expected wait until the next reinforcement. On the information-gain hypothesis, there is no reason to expect that the factor that determines the learning rate will be the same as the factor(s) that determine asymptotic performance, because the latter may be expected to depend on what the expected rate is when the CS is present and on how long that state is expected to last, whereas the rate of learning will depend only on the factor by which the CS changes the expected rate and the sign of the change.

In the experiments described below we explore the these ideas by studying protocols like the one shown in the bottom row of Figure 1. However, in the current experiments there are never any USs presented during the cue so we refer to it as a CS-. First, if as contingency theory suggests, the degree of inhibition is determined by the difference in the rate of reward in the presence and absence of a cue then duration of a CS- should have no impact on inhibitory control. In all the procedures (see figure 2) of the current experiment the rate of reward in the CS- is 0 regardless of its duration. However, if the delay to reward signaled by a CS- controls inhibition then the durations will matter. The average delay to the next reward is equal to the duration of the CS- plus the average delay to reward once the CS is terminated. If this average delay controls inhibition then the longer the CS- the greater should be the inhibitory control of that cue. On the other hand, if it is the magnitude and direction of the rate change that drives learning, then the presence of the CS lowers the expected rate of reinforcement by an amount equal to the rate attributed to the background alone, as in Rate Estimation Theory (Gallistel, 1990; Gallistel & Gibbon, 2000), according to which the matrix-algebra computation attributes negative rates to inhibitory state cues. In the course of testing various protocols, we separate the effect of CS duration on the expected wait till the next reinforcement from its effect on the expected change in reinforcement rate, enabling us to decide between these different hypotheses about the real-time variables that determine the rate of learning and asymptotic level of performance.

There is considerable evidence that subjects do in fact learn about time during Pavlovian conditioning. Since the time of Pavlov it has been known that if a US is presented a fixed delay after CS onset that the early parts of the CS may become inhibitory See Balsam, Drew & Gallistel, 2010 for a review) . Additionally, if subjects undergo inhibitory conditioning after learning to expect a US at a specific time, the transfer of inhibition to new exciters is greatest if the transfer excitors bear the same temporal relationship to the US as the original training exciter The inhibitor is best at inhibiting the expectation of a US that is expected at the exact time that the added cue had previously signaled the omission of the US {Barnet, 1996 #48;Burger, 2001 #49;Denniston, 2004 #50}. Here we investigate whether temporal knowledge affects the speed and degree of inhibitory learning.

**Experiment 1**

The purpose of experiment 1 was to investigate whether the duration of a CS- affected inhibitory learning. In this experiment, pellet US’s were presented at unpredictable times during the intertrial interval (ITI) with an average of 20s between them. When an auditory CS- was presented no US’s occurred. The durations of the CS- cues ranged from 10 to 80 seconds in different groups of subjects. These protocols highlight a fundamental difference between trial-based contingency theories of associative learning (e.g. Rescorla, 1969) and real-time theories. The probability of reinforcement in the presence of the CS- is 0 in all of our protocols no matter what the CS duration. Therefore, the difference between the probability of reinforcement on CS- trials and the probability of reinforcement on Background-alone trials is independent of CS duration. In the Rescorla-Wagner model, US presentations in the background create an excitatory context and the CS- plus Background compound signals extinction. This causes the CS- to become inhibitory. Because it is a trial based model, each CS- presentation represents a single trial regardless of its duration. Even if one were to divide the ITI and CS- periods into arbitrary trial units then longer CS durations would consist of more non-reinforced trials and one might predict more rapid acquisition of inhibition with longer cue durations. However, no matter how one construes trials in the Rescorla-Wagner model all groups should eventually obtain the same degree of inhibition. In contrast, the time-based theories outlined above, predict that the longer the CS- the faster and deeper the inhibition.

We have previously tested this idea in an operant discrimination paradigm{Kalmbach, 2019 #415}. Note that an operant discrimination is identical to the contingency protocol in that reinforcers are presented in the presence of one stimulus but not in the absence of that cue. We varied the duration of the cue that signaled the absence of reward and found that the speed of learning and the degree of discrimination were related to the informativeness of the positive discriminative stimulus. Here we explore how the duration of a CS- affects learning in Pavlovian conditioning.

**Method**

Subjects. The Institution Animal Care and Use Committees at Columbia University and the New York State Psychiatric Institute approved all protocols used in the present studies. Forty male Sprague-Dawley rats were housed in groups of two in a colony room on a 12:12 hour light:dark cycle. Water was available ad lib in the home cages. The rats were fed in their home cages for one hour after experimental sessions, which occurred 5 days per week. On weekends. the rats had ad lib access to food until approximately 22 hours prior to the first weekday session of each week. Rats were approximately 9 weeks old at the start of the first training session and had been handled for one week prior to testing.

Apparatus. Eight identical experimental chambers (30.5 cm x 24.1 cm x 21.0 cm) located in ventilated and soundproof boxes were used during experimental procedures. Each chamber was equipped with a speaker, a house light, and a magazine food pellet dispenser (Model ENV-203, Med Associates), which delivered pellets into a head-entry-detecting trough (Models ENV-200R7 and ENV-254-CB, Med Associates). A computer running the Med-PC software controlled experimental events and recorded the time during which the events occurred.

Procedure. Subjects were randomly assigned to 5 groups of 8 rats. All groups received 2 sessions of magazine training, during which 40 pellets were delivered at random times during a 20 minute session (random time 30s schedule), followed by 35 sessions of experimental testing. One session was administered to each rat per day. The experimental groups are depicted in figure 2. In the CS-10 experimental group, rats experienced 32 trials of 10-second tones (1000 hz, 80 db) followed by inter-trial-intervals (ITI) in each session. Pellet reinforcers were delivered only during the ITI on a schedule defined by an exponential distribution with a mean of 20s. The duration of individual ITI periods was determined by an additional exponential distribution also with a mean of 20s. The CS-20, CS-40 and CS-80 groups were treated identically to the CS-10 group except for the duration of each group’s respective CS-, with CS-20 rats receiving 20s tones, CS-40 rats receiving 40s tones, and CS-80 subjects receiving an 80s tone during which no reinforcers were presented. The fifth group of rats in the Random Control group experienced all 4 durations (8 of each) in a single experimental session and received an equal rate of reinforcements in the presence and absence of the CS. In order to achieve this, the 32 reinforcers that were earned during the ITI in the CS- groups were randomly distributed over whole test session. Consequently, the average time between reinforcers was about 57.5s in both the presence and absence of the CS-. ITI durations for the Random group were generated by the same schedule as the other 4 groups. In all groups each session lasted for a total of 8 tone presentations.

Data Collection and measures. The time of occurrence of each head entry and the time of onset and termination of all stimulus events were recorded with 10ms resolution throughout all sessions. Head entry rates into the feeder area were computed separately for the CS- period and the ITI period. All head entries within 2 sec following a pellet delivery were excluded from the analyses so the measures reflected anticipatory responding and not US evoked responding.

**Results**

Figure 2a shows that the duration of a CS- had a large impact on inhibitory learning. The figure shows the average difference between responding during the ITI and CS- for all groups. In order to evaluate the speed of learning as well as the depth of inhibition we examined individual subject’s performance to obtain measures of acquisition speed and asymptotic levels of inhibition. Acquisition speed was obtained by estimating the point at which responding during the CS- dropped below the ITI response rate. We used an algorithm that examines the data for each subject trial by trial and identifies the point at which the cumulative difference score reaches a maximum prior to becoming negative. We took this point to be the trial on which the differences scores begin to become consistently negative (less responding in the CS- than during the ITI). This criterion agreed fairly well with our own visual assessment of the change points from the cumulative records (See supplemental figures) As expected, we did not obtain any change points for subjects in the random group, indicating that they did not slow responding during the CS. Figure 2B shows the cumulative distribution of change points for each group. The speed of acquisition was generally faster the longer the duration of the CS-. Group differences were tested with the Kolmogorov–Smirnov (K-S) test. Group CS-80 acquired the inhibition faster than….

We characterized asymptotic performance by computing a post-acquisition slope for every subject that represents the degree of inhibition evoked by the CS-. In the random group and for subjects that never met the acquisition criterion a line was fit to the entire data set and that slope was used in the analysis. Figure2C shows the mean slope for each group with individuals represented as dots. A between groups ANOVA on slopes showed that there was a significant difference between groups [F(4,xx)= YY.YY, p<.zz]. Post hoc pairwise comparisons showed that the Random group differed significantly from all groups except …. …. The CS-xx and CS-yy groups also differed.

We also examined the within CS- pattern of responding. The average of the last X days is shown in figure 7 for each of the experimental groups. In the CS-10 and CS-20 groups responding slowly declined across the trial while in the CS-40 and CS-80 groups responding reached a minimum between 40% and 60% of the trial and then began increasing in anticipation of the resumption of US presentations after the termination of the CS-. An ANOVA …..

The difference scores can change because of changes in the ITI as well as changes during the CS-. Consequently, we separately analyzed responding during each of these stimulus conditions over days. We found that there was a

**Discussion**

The duration of a CS- affected both the speed of inhibitory learning as well as the asymptotic level of inhibition. In all cases, in which there was a CS- there was a perfect negative contingency between the CS- and the US. Contrary to the predictions of contingency theory the duration of the CS- had a big influence on inhibitory learning.

The results of the current experiment are consistent with the time based formulations mentioned above. As the duration of the CS- increases the factor by which the US is delayed increases. Additionally, in the current procedure as the duration of the CS- increases so does the duration of session. Because the number of US’s was fixed the overall session rate of US presentation is decreased. Thus the the rate of US’s during the ITI is more divergent than from the overall rate the longer the CS-. We deal directly with this issue in experiment 5.

At an empirical level, one might wonder if the current procedure is a form of extinction. Though it has been suggested otherwise{Gallistel, 2000 #30}. ( previous research has shown that when the duration of a cue is varied during extinction, the speed of extinction depends on the number of trials and not on the duration of the cue being extinguished (drew bouton). One might anticipate then that the duration of the extinction cue would have little impact on the speed and depth of response loss. Clearly that was not the case in the current experiment.

Experiment 2

In experiment 1, all subjects were exposed to the same number of CS- presentations. Consequently, the longer the CS- the greater the cumulative non-reinforced exposure to the cue. For example, in experiment 1 the 40s CS- group received 4 times the non-reinforced exposure to the CS- than did the CS-10 group. We examined the contribution of cumulative exposure to the development of inhibition in three groups of subjects. Two of the groups were treated identically to the counterpart groups of experiment 1. Group CS-10 and CS-40 received the same number of cue presentations. The third group (CS-10X4) was exposed to the 10s CS- but had 4 times as many trials as the other two groups. This group had the same cumulative non-reinforced exposure to the CS- as subjects in the CS-40 group. If cumulative non-reinforced exposure is important then the CS-10X4 group should show greater inhibition than the CS-10 group and perhaps as much as the CS-40 group. Trial-based Rescorla-Wagner type models predicts faster inhibition in the CS-40 group than in the CS-10 group under the assumption that the 40s CS- is composed of more hypothetical trials than the 10s CS-. In this view, the CS-10X4 group should show inhibition that was at least as strong as the inhibition in the CS-40 group. In contrast, the time based models predict that the duration of the CS- should be the important aspect of the protocol and that both CS-10 groups should show less inhibition than the CS-40 group.

**Method**

**Subjects**. Thirty-two male Sprague Dawley rats were housed, fed and handled under identical conditions as the rats from the previous experiment.

**Apparatus**. In Experiment 3, eight experimental chambers identical to those used in Experiment 1 were used.

**Procedure**. Rats were tested in three different groups of 8rats each. All rats received 2 sessions of magazine training, identical to the training in the previous experiment, followed by 35 sessions of experimental testing. Rats were assigned randomly into one of the following groups: CS-10, CS-40, , CS-10X4. As in the previous experiment, during experimental testing, all subjects received pellets on an exponential distribution with a mean of 20 seconds during the ITI and no pellets during the CS- presentations, which were always of fixed duration. In groups CS-10 and CS-40, rats were exposed to 32 tones during each session. . Group CS-10X4 received 128, 10s CS- presentations per session. ITI reinforcers could resume immediately following termination of the tone CS-

**Results**

Figure 8 shows again that the duration of a CS- had a large impact on inhibitory learning but cumulative exposure to the CS- did not. The figure shows the average difference between responding during the ITI and CS- for all groups. As in the previous experiment we analyzed the data in more detail to obtain measures of acquisition speed and asymptotic levels of inhibition. Figure 8 suggests that the speed of acquisition was faster for subjects in CS-40 than for those in CS-10. It also shows that greater number of exposures to the 10s CS- in group CS-10X4 did not alter acquisition speed or the final level of inhibition.

As in the previous experiment we found an acquisition point for each subject. Figure 9 shows the cumulative distribution of change points for each group. The K-S test shows. .. . There was a significant effect of CS- duration for these three groups and groups CSxx and CSyy differed significantly from one another

We characterized asymptotic performance by computing a post-acquisition slope for every subject. Figure 10 shows the mean slope for each group with individuals represented as dots. A between groups ANOVA on slopes showed that there was a significant difference between groups [F(2,xx)= YY.YY, p<.zz]. Post hoc pairwise comparisons showed that the CS-10 group did/did not differ ….

**Discussion**

Experiment 2 shows that cumulative exposure to the CS- is not the variable determining the speed of emergence or depth of inhibition. Rather the important variable is related to the delay until the resumption of US’s signaled by a CS- . In the next experiment we ask whether or not it was important that this delay be of a fixed duration.

Experiment 3

In studies of excitatory conditioning the average rate of US’s signaled by a CS seems to be the important determinant of acquisition speed (Ward et al., 2012) and excitatory value (Harris papers). The first two experiments showed that the speed and degree of inhibition depended on the duration of the CS- cues. In all cases the duration of the cues was fixed. This raises the possibility that the ability to anticipate the resumption of US presentations played a role in determining the effect of CS- durations. It is possible that being certain that US’s won’t occur for a known duration might be important for determining the speed of learning and/or the degree of inhibition. Alternatively, inhibition might be regulated by the average time until reward resumes after the onset of the CS-, as may be the case in excitatory learning. We investigated the importance of fixing cue duration on inhibition in experiment 3 by comparing CS-‘s that were always of fixed duration to CS-‘s that were variable in duration but which had the same mean duration as the fixed cues.

Subjects. Thirty-two male Sprague Dawley rats were housed, fed and handled under identical conditions as the rats from the previous experiment.

Apparatus. In the first phase of Experiment 3, eight experimental chambers identical to those used in Experiment 1 were used. However, in the second phase of the experiment, one fixed response lever (Model ENV-110M, Med Associates) was installed to the left of the pellet dispenser.

ProcedureRats were assigned randomly into one of the following groups: CS-30Fix, CS-30Var, CS-50Fix, CS-50Var. All rats received 2 sessions of magazine training, identical to the training in the previous experiment, followed by 35 sessions of experimental testing. In groups CS-30Fix and CS-50Fix, rats were exposed to tones of fixed durations and in groups CS-30Var and CS-50Var tones were of variable durations. CS durations were fixed at either 30 or 50 seconds, or variable at either 30 or 50 seconds. In the variable groups the duration of the tone was determined by an approximately exponential distribution with the appropriate average. Consequently, the likelihood of the tone ending at any point in time was constant. As in the previous experiment all subjects received pellets on an exponential distribution with a mean of 20 seconds during the ITI and no pellets curing the CS- presentations. After 35 sessions of inhibitory tone exposure, the fixed levers were placed into the experimental chambers, and rats were trained to bar press for food on a VI-30 schedule of reinforcement, followed by 7 sessions of a CS- training identical to the sessions of the first experimental phase. Subsequently, a Pavlovian to Instrumental Transfer (PIT) test was conducted, consisting of two sets of 8 tone presentations while rats were given the opportunity to bar press during an extinction test session.

**Results**

Figure 11 shows again that the average duration of a CS- had an impact on inhibitory learning but whether the CS- was of fixed or variable duration did not have a consistent effect. The figure shows the average difference between responding during the ITI and CS- for all groups. Figure 11 shows stronger inhibition in the CS-50 groups than in the CS-30 groups. However, the figure gives the impression that there was no difference between the fixed and variable CS-50 groups butthere might have been a difference in the CS-30 groups.

As in the previous experiment we found an acquisition point for each subject. Figure 12 shows the cumulative distribution of change points for each group. The K-S test shows. .. . There was a significant effect of CS- duration for these three groups and groups CSxx and CSyy differed significantly from one another

We characterized asymptotic performance by computing a post-acquisition slope for every subject. Figure 13 shows the mean slope for each group with individuals represented as dots. A between groups ANOVA on slopes showed that there was a significant difference between groups [F(2,xx)= YY.YY, p<.zz]. Post hoc pairwise comparisons showed that the CS-10 group did/did not differ ….

**Discussion**

As in the previous experiments, the longer the duration of the CS- the faster inhibition develops and the deeper it becomes over training. The purpose of the experiment was to evaluate whether subjects were sensitive to the mean delay signaled by a CS- or if fixing the duration of the CS- contributed to the development of inhibition. The data of the current experiment suggest that the mean duration may be what is important but our data were mixed. There was no effect of CS- variability in the 50s groups but the CS-30Var group was facilitated relative to the CS-30Fix group.

Experiment 4

The prior experiments suggest that the variable that determines inhibition is the average delay to the resumption of reward signaled by the CS-, The speed of excitatory conditioning is regulated by the average delay to reward signaled by a CS+ relative to the average overall rate of reward (Balsam & Gallistel, 2009; Balsam, Drew & Gallistel, 2010; Ward et al., 2012). The purpose of the fourth experiment therefore was to examine whether inhibitory conditioning depended on the absolute duration of CS- or the durationrelative to the rate of US’s in the absence of the CS-. In this experiment, different groups of subjects were presented with food pellets with different average delays during the ITI as well as different CS- durations. These durations were chosen to assess whether inhibition was determined by the absolute duration of a CS – or by the relative increase in delay to reward signaled by the CS- relative to the expected inter-reward interval (IRI) during the ITI.

**Method**

*Behavioral Apparatus*

Twenty matching operant experimental chambers identical to those used in experiment 1 were used in this experiment.

*Subjects*

The subjects were 40 male rats that weighed no less than 350 grams and no younger than 100 days old at the start of the experiment were housed two per cage. For both phases, to motivate rats to earn rewards in the operant tasks they were maintained on a restricted feeding schedule consisting of 30 grams per day per cage. This schedule allowed for normal growth throughout the experiment, but ensured adequate motivation for the food rewards presented during training. Rats were trained 5 days a week. Water was available ad libitum except for during the experimental sessions.

*Behavioral Method*

As in the previous studies the each trial consisted of 1kHz tone (80 db), during which no pellet was delivered. Five groups of rats (n=8) were trained on IRI:CS- duration ratio of 1:2, 1:1, and 2:1 with IRI durations of 20 or 40s and CS- duration of 20, 40, or 80s. The groups were designated as 20:20, 20:40, 40:20, 40:40, and 40:80; the first number representing the average IRI and the second representing the CS- duration Each session was 32 trials long and there were 44 sessions.

**Results**

**Figure 14 shows again the average difference between responding during the ITI and CS- for all groups. It is evident that the relative increase in the delay to reward controlled inhibition**. Independent of the absolute duration of a CS- both the speed with which inhibition developed and the final level of inhibition were controlled by the relative increase in the delay to reward signaled by the CS-. The absolute duration of the cue was not a determinant of the behavior.

**As in the previous experiment we found an acquisition point for each subject. Figure 15 shows the cumulative distribution of change points for each group. The K-S test shows. .. . There was a significant effect of CS- duration for the three groups trained with the 40 s IRI and for the 2 groups trained with the 20 s IRI. However, there was no significant difference between the two groups trained at the 1:1 nor was there a difference between the two groups trained at the 2:1 ratio.**

**Again, we characterized asymptotic performance by computing a post-acquisition slope for every subject. Figure 16 shows the mean slope for each group with individuals represented as dots. A between groups ANOVA on slopes showed that there was a significant difference between groups [F(2,xx)= YY.YY, p<.zz]. Post hoc pairwise comparisons showed that ….**

**Discussion**

The speed with which inhibiton emerges as well as the depth of that inhibition is determined by the relative temporal relationship between the average duration of a CS- and the average interval between US presentations during the ITI. Extant theoretical approaches to inhibition do not have an easy way of dealing with this finding. Contingency theory predicts that the degree of inhibition will depend on the rate of US presentation in the absence of the CS- and in the cases where the US rate is constant the asymptotic inhibition should be the same in all CSs regardless of their duration. Both of these predictions are contradicted by the dependence of inhibition on the relative temporal relationship. The Rescorla-Wagner theory also does not have an intrinsic`way of accommodating these findings. In that view, asymptotic inhibition should depend on the rate of reward in the ITI but not on the duration of the CS-.

The dependence of inhibition on relative time is similar to the dependence that excitation has on relative time (Jenkins, Gibbon & Balsam, Gallistel & Gibbon, Balsam & Gallistel). However, there are multiple possibilities about what is being compared in the emergence of inhibition. We consider the alternatives in the next experiment.

Experiment 5

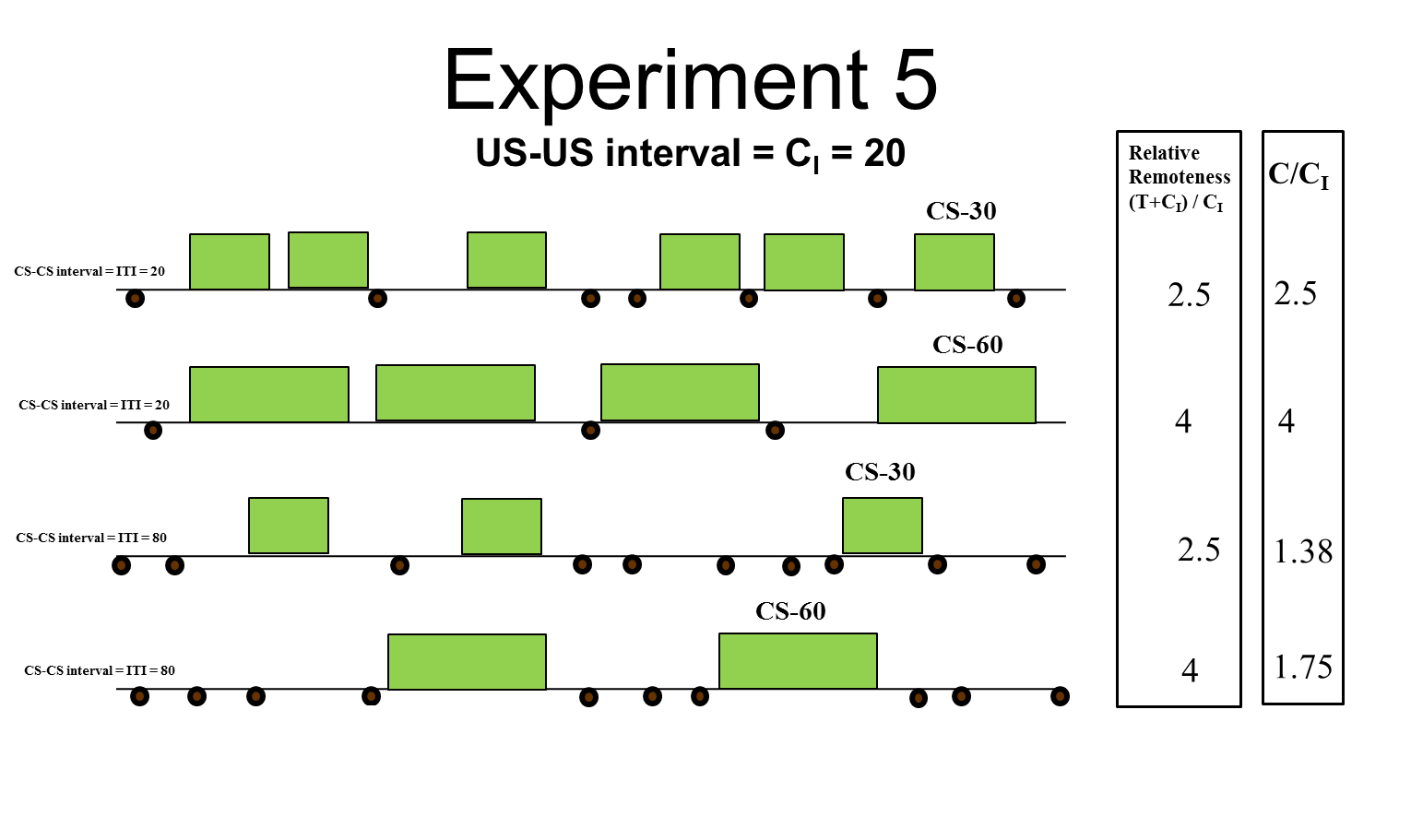
Experiment 4 demonstrated that it is the duration of a CS- relative to the average IRI in the ITI that determines the speed and degree of inhibition to a CS-. When changing the duration of a CS- several intervals are altered. The duration of the CS- is altered but so is the interval that the CS- signals about when the next US might be expected. For example when the average IRI is 20s, the expected time at which USs will resume is equal to the duration of the CS- plus 20s. Similarly if the IRI is 40s then this time must be added to the CS- duration to compute an expected time at which USs resume. On this view, the expected delay to reward signaled by the CS- in groups (IRI:CS- duration) 20:20, 20:40, 40:20, 40:40, and 40:80 increases the delay by a factor of 2,3,1.5,2, and 3, respectively. Thus the temporal relativity might be based on these intervals.

Additionally, as a consequence of the procedure we used in the first four experiments, when CS- duration increased the duration of a session increased. Consequently, the longer the CS-, the lower was the overall rate of US presentation in the context. In fact, the average IRI in the context increases by a factor proportional to the duration of the CS- . Because the prior experiments decreased the overall rate of reward in a session in proportion to the duration of a CS-, it was not possible to identify specifically the mechanisms by which variation in temporal factors alters behavior. One possibility is that inhibition depends on a comparison between average delay between US’s during the ITI (in the absence of the CS- ) to the average delay signaled by the CS-. A second possibility is that inhibition depends on a comparison of the average overall delay between US’s across the whole session and the delay to the US signaled by a CS-. Though there is no theoretical view of inhibition that would anticipate this, it is possible in the earlier experiments, that short CS- durations were less potent than long ones because of the higher overall rate of US presentations in the context. To test these hypotheses, in the current experiment, we kept the average delay between US’s in the ITI constant as well as the average delay to a US signaled by a CS- while varying the overall average delay to the US in a session. If inhibition depends on the comparison between the delay signaled by the CS- and the average delay in the ITI all groups with the same CS- duration should be equivalent. Alternatively, if the comparison is between CS- and the overall session delay between US’s those subjects with a higher overall density of US’s relative to CS- duration should show less inhibition.

**Method**

During the experiment the subjects were 32 male rats that weighed no less than 350 grams and no younger than 100 days old at the start of the experiment were housed two per cage.

*Behavioral Method*

**

In these experimental chambers, the rats were trained as in the previous experiments. Pellets were delivered on the inter-reinforcement interval during the inter-trial interval on a VT-20 schedule. Each trial consisted of 1 kHz tone where no pellet was delivered. For half the subjects the CS- duration was 30s and for the remainder of the subjects it was 60s. For half the subjects the ITI averaged 20s and for the remainder of the subjects the ITI was 80s. For the subjects with the 20s ITI there were 32 CS- presentations in each session. For the subjects with the 80s ITI there were 8 CS- presentations in each session. Thus there were four experimental groups: Group32\_30\_20; Group8\_30\_80; Group32\_60\_20; Group8\_60\_80; The group designations refer to the number of CS- presentations in each session, the duration of the CS- and the average duration of the ITI. In all groups with the 30s CS-, the average time from CS- onset to the next US was 50s and in all groups with the 60s CS- the average time from CS- onset to the next US was 80s. If the delay from CS- onset to the next US controls inhibition then the two CS- 60s groups should be equal and show more inhibition than the two equivalent CS- 30s groups. However, if the overall rate of reward in the background influences the development of inhibitory control then the groups with 8 CS- presentations will have higher background rates than the groups with the 32 CS- presentations. All groups receive on average 32 USs/session. In the group with the 32, 30s trials the and 3*2,* 20s ITIs, the total session time is 1600s. Thus the average time between USs is 50s. In contrast, the duration of a session with 8, 30s trials and 8, 80s ITIs is 880s. Thus the average time between US’s is reduced to 27.5s in this group. Similarly, the average time between USs in the group 32\_60\_20 is 80s while the average time between USs in the group 8\_60\_80 is 35s.

**Results**

**Figure 17 shows again the average difference between responding during the ITI and CS- for all groups. It is evident that the change in cv the background rate of reward was inversely related to the degree of inhibition**. The figure shows that the top 3 groups 80s tones (32\_CS-80\_ITI20; 64\_CS-80\_ITI10 ; 8\_CS-80\_ITI80 ) were not equivalent. The most inhibition ….

**As in the previous experiment we found an acquisition point for each subject. Figure 18 shows the cumulative distribution of change points for each group. The K-S test shows. .. . There was a significant effect of**

**Again, we characterized asymptotic performance by computing a post-acquisition slope for every subject. Figure 19 shows the mean slope for each group with individuals represented as dots. A between groups ANOVA on slopes showed that there was a significant difference between groups [F(2,xx)= YY.YY, p<.zz]. Post hoc pairwise comparisons showed that ….**

Experiment 6

The result of experiment 5 suggest that to a large extent the degree of inhibition is mediated by the changes in the background reward rate produced by changing the duration of the CS-., not directly controlled by the increased delay of reward signaled by the CS-. Because this was such an unexpected result we thought it important to replicate the effect of this manipulation. Additionally, we wondered if the basis for the effect of changing the background rate of reward was to alter the excitatory value of the ITI. Though we approached the current experiments as studying negative contingencies, consideration of the protocols used in all contingency experiments can be viewed as simultaneously arranging both negative and positive contingencies. In the case of a negative contingency, there is a positive contingency in the absence of the CS-. Symmetrically, in a positive contingency there is a negative contingency in the absence of a CS+. In the current experiments, if one considers the ITI period a CS+ then the symmetry is clear. By increasing the CS- durations the time between positive trials is increased and excitatory conditioning enhanced (Gibbon & Balsam, 1981; Gallistel & Gibbon, 2002; Balsam & Gallistel, 2009; Ward et al., 2012). Thus the effect of increasing CS- duration is to enhance excitatory conditioning of the ITI and thus the CS- cue must inhibit the stronger excitatory response. We examined this possibility in the current experiment. We kept the average delay between US’s in the ITI constant as well as the average delay to a US signaled by a CS- while varying the overall average delay to the US in a session. If inhibition depends on the comparison between the delay signaled by the CS- and the average delay in the ITI all groups with the same CS- duration should be equivalent. Alternatively, if the strength of inhibitory control is determined indirectly by the excitatory value of the ITI then a higher overall density of US’s in a session will reduce excitation in the ITI and reduce the inhibitory control of the CS-.

**Method**

During the experiment the subjects were 32 male rats that weighed no less than 350 grams and no younger than 100 days old at the start of the experiment were housed two per cage.

*Behavioral Method*

In these experimental chambers, the rats were trained as in the earlier experiements. Pellets were delivered on the inter-reinforcement interval during the inter-trial interval on a VT-20 schedule. Each trial consisted of 1 kHz tone where no pellet was delivered, separated from an IRI where pellets were delivered randomly (mean 20s). Table 1 shows the parameter values for all of the experimental conditions. One group, 32\_CS-80\_ITI20, was identical to the CS-80 group of the earlier experiment and was exposed to 32, CS- presentations with an IRI of 20s between US’s during the 20s ITI. Group 64\_CS-80\_ITI10 received 64 presentations of the 80s CS- with an average IRI of 20s between US’s during the 10s ITI. In this group a US was delivered on average once for every two ITI periods. The subjects in group 8\_CS-80\_ITI80 received only 8, 80s CS- presentations but the ITI in this group lasted for 80s during which the average time between USs was 20s. Group 32\_CS-160\_ITI20 was exposed to 32, 160 sec CS- presentations. The ITI for this group lasted for an average of 20s and IRI between USs was 20s. Table 1 also shows how the relative relationship between intervals changes in the different experimental groups. In all of the first three groups with 80s tones and RI20s schedules in effect during the ITIs (32\_CS-80\_ITI20; 64\_CS-80\_ITI10 ; 8\_CS-80\_ITI80 ) the CS- signals that the wait till the next reward is 5 times longer than the wait during the ITI. For the fourth group the wait signaled by the CS- is 9 times longer than the ITI wait. If the factor by which the CS- increases the delay to the next US is the controlling variable the fourth group should show the greatest inhibition and the other three groups should show less but equivalent inhibition. Alternatively, inhibition maybe driven the level of ITI excitation. This level of excitation should depend on the ratio of the average delay between USs in the background to the average delay during the ITI. This ratio is 5 for group 32\_CS-80\_ITI20 , 9 for 64\_CS-80\_ITI10, 2 for 8\_CS-80\_ITI80 and 9 for 32\_CS-160\_ITI20. Thus the pattern of results will allow us to distinguish between these possible explanations.

**Results**

**Figure 17 shows again the average difference between responding during the ITI and CS- for all groups. It is evident that the change in the background rate of reward was inversely related to the degree of inhibition**. The figure shows that the top 3 groups 80s tones (32\_CS-80\_ITI20; 64\_CS-80\_ITI10 ; 8\_CS-80\_ITI80 ) were not equivalent. The most inhibition ….

**As in the previous experiment we found an acquisition point for each subject. Figure 18 shows the cumulative distribution of change points for each group. The K-S test shows. .. . There was a significant effect of**

**Again, we characterized asymptotic performance by computing a post-acquisition slope for every subject. Figure 19 shows the mean slope for each group with individuals represented as dots. A between groups ANOVA on slopes showed that there was a significant difference between groups [F(2,xx)= YY.YY, p<.zz]. Post hoc pairwise comparisons showed that ….**

One group, 32\_CS-80\_ITI20, was identical to the CS-80 group of the earlier experiment and was exposed to 32, CS- presentations with an IRI of 20s between US’s during the 20s ITI. Group 64\_CS-80\_ITI10 received 64 presentations of the 80s CS- with an average IRI of 20s between US’s during the 10s ITI. In this group a US was delivered on average once for every two ITI periods. The subjects in group 8\_CS-80\_ITI80 received only 8, 80s CS- presentations but the ITI in this group lasted for 80s during which the average time between USs was 20s. Group 32\_CS-160\_ITI20 was exposed to 32, 160 sec CS- presentations. The ITI for this group lasted for an average of 20s and IRI between USs was 20s. Table 1 also shows how the relative relationship between intervals changes in the different experimental groups. In all of the first three groups with 80s tones (32\_CS-80\_ITI20; 64\_CS-80\_ITI10 ; 8\_CS-80\_ITI80 ) the CS- signals that the wait till the next reward is 5 times longer than the wait during the ITI. For the fourth group the wait signaled by the CS- is 9 times longer than the ITI wait. If the factor by which the CS- increases the delay to the next US is the controlling variable the fourth group should show the greatest inhibition and the other three groups should show less but equivalent inhibition. Alternatively, inhibition be driven the level of ITI excitation. This level of excitation should depend on the ratio of the average delay between USs in the background to the average delay during the ITI. This ratio is 5 for group 32\_CS-80\_ITI20 , 9 for 64\_CS-80\_ITI10, 2 for 8\_CS-80\_ITI80 and 9 for 32\_CS-160\_ITI20. Thus the pattern of results will allow us to distinguish between these possible explanations of the earlier results.

**Discussion**

**Experiment 5 provided a startling result, the degree of inhibition was inversely related to the overall rate of US presentation in the context.**



|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Group (MPC Program) Name | ITI= Time between CSs (sec) | Tone CS dur (sed) | Total rewards (2 Pellets each) | Total NUM CS in session | I=US-US interval in the ITI | Total sess dur (secs) | C= average US-US interval in whole session | lambda i/ lamda c (C/I) | T= Cson to US | lambda T/lambda I (T/I) |
| 32\_CS80\_ITI20 | 20 | 80 | 32 | 32 | 20 | 3200 | 100 | 5 | 100 | 5 |
| 64\_CS80\_ITI10 | 10 | 80 | 32 | 64 | 20 | 5760 | 180 | 9 | 100 | 5 |
| 8\_CS80\_ITI80 | 80 | 80 | 32 | 8 | 20 | 1280 | 40 | 2 | 100 | 5 |
| 32\_CS160\_ITI20 | 20 | 160 | 32 | 32 | 20 | 5760 | 180 | 9 | 180 | 9 |

Experiment 1 demonstrated that the longer the duration of a CS- the faster and stronger was the inhibition generated by that cue. This was inconsistent with contingency theory but consistent with the Rescorla-Wagner theory if one assumes that longer times provide for a greater number of learning trials. In the latter framework inhibition developed more rapidly with longer CS-‘s because longer cues provide a greater number of non-reinforced trials than shorter ones. If this is the case than increasing the number of non-reinforced short duration CS- presentations should ultimately result in the same level of inhibition as a longer CS-. In experiment 2 , we compared the development of inhibition to a 40 sec CS- (CS-40) to two groups that received a 10s CS- (CS-10). One of the groups exposed to the 10s cue had the same cumulative exposure to tehCS- as the 40s CS- group, yet only the 40s CS- produced significant inhibitory control. The first twonexperiments show that the duration of a CS- doesnaffect inhibition. The third experiment showed that the average duration of a CS- was the controlling factorin these experments as there was little difference between cues of fixed or variable duration in the development of inhibitory control. The fourth experiment showed that it was not the absolute duration of a cue that determined the level of inhibitory control, rather it was this curation relative to the time between US’s in the absence of the cue. It appeared that the factor by which a CS- increases the expected delay to the US was the determining factor. In the first four experiments changing this factor was confounded with changes in the overall rate of us’s in a session. In experiment 5 and 6 we held the factor by which a CS- signals an increase in the delay to a US constant but unconfouded this with changes in the overall rate of reward. We found that the overall rate of reward had a large impact on inhibition. Taken together the results suggest that in a negative contingency experiment the comparison of the rate of US’s in the abence of the CS- relative to the overall session rate of US’s determince the *excitartory* value of the ITI. In turn this means that the negative cue must exert stronger ontrol when there is greater excitation in the ITI.

This view of inhibition suggests that excitation and inhibition are both determined by the informativeness of exciatory cues. Previously we suggested that informativeness determined the speed of acquisition in excitatory conditioning (ref). We now extend this formulation to suggest that inhibition is similarly determined albeit as an affect of modulating excitation. This is similar to other suggestions that inhibition requires an excitatory context for both learning and expression of the inhibition (refs)

Figure xx show the data of all 6 experiments replotted as a function of the informativeness. It shows that both acquisition speed and final levels of inhibition are largely determined by temporal informativeness. Temporal factors thus appear to be a major determinant of both excitation and inhibition.

Balsam, P. D., Drew, M. R., & Gallistel, C. R. (2010). Time and Associative Learning. *Comparative Cognition & Behavior Reviews, 5*, 1-22.

Balsam, P. D., Fairhurst, S., & Gallistel, C.R. . (2006). Pavlovian contingencies and temporal information. *Journal of Experimental Psychology: Animal Behavior Processes, 32*, 284-294.

Balsam, P.D., & Gallistel, C.R. (2009). Temporal maps and informativeness in associative learning. *Trends in Neurosciences, 32*(2), 73-78. doi:<http://dx.doi.org/10.1016/j.tins.2008.10.004>

Ward, R. D., Gallistel, C. R., & Balsam, P. D. (2013). It's the information! *Behav Processes, 95*, 3-7.

Ward, R. D., Gallistel, C. R., Jensen, G., Richards, V.L., Fairhurst, S., & Balsam, P.D. (2012). Conditional stimulus informativeness governs conditioned stimulus-unconditioned stimulus associability. *Journal of Experimental Psychology: Animal Behavior Processes, 38*(1), 217-232. doi:10.1037/a0027621